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P1

Cyclic stretch induces apoptosis in alveolar type II cells A549

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Critical Care 2006, **10(Suppl 1):**P1 (doi:10.1186/cc4348)

Objective To examine the effects of short-term cyclic stretch on apoptosis in alveolar type II cells (A549). To study *in vitro* the direct influence of alveolar type II cells on mechanical stretch.
Methods A549 were treated with different doses of lipopolysaccharide (LPS), 0 ng/ml, 1 ng/ml, 10 ng/ml, 100 ng/ml, 1000 ng/ml, and then A549 were lengthened 5%, 15%, 30% using a FLEXCELL tension unit 4000, a vacuum-driven device that applies strain to cells, which were cultured in six-well plates coated with collagen-I, and 12 cycles/min for 4 hours. Apoptosis was measured using the flow cytometry method that measures annexin V and propidium iodide (PI) staining. The morphological changes of apoptotic cells were observed by transmission electron microscope.
Results Apoptosis could be induced in alveolar type II cells (A549) by mechanical stretch. The percentage of annexin V + PI cells increased after being treated with cyclic stretch for 4 hours by 5%, 15%, 30% in all groups. The morphological features of apoptotic cells demonstrated by transmission electron microscope were as follows: shrinkage of the cell, chromatin condensation and aggregation under the nuclear membrane as a crescent or lump, membrane-encapsulated nuclear fragment or cell organ formed by invagination of the cell membrane, and apoptotic body formation followed by vacuolization.
Conclusion Apoptosis induced by mechanical stretch and LPS is dose dependent. Mechanical stretch aggravates apoptosis especially in cells treated with LPS. Annexin V and PI double staining is a specific, sensitive, and quantitative method for analyzing apoptotic cells. It is also helpful to clarify the protective mechanism of low-volume ventilation in ARDS.
Acknowledgement The study was funded by the 'One Hundred People' project of Shanghai Sanitary Bureau (03-77-20).

P2

Fecal peritonitis in pigs as a model of extrapulmonary ALI/ARDS

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Critical Care 2006, **10(Suppl 1):**P2 (doi:10.1186/cc4349)

Introduction Although extrapulmonary ALI/ARDS is a common clinical entity, most animal models used to study this disease are induced by direct lung injuries. Our intention was therefore to investigate whether a condition resembling ALI/ARDS develops during the course of a fecal peritonitis in pigs; in that case experimental peritonitis would also prove as a clinically relevant ARDS model.
Methods In 10 anesthetized, mechanically ventilated, and instrumented pigs fecal peritonitis was induced by inoculating autologue feces pellets suspended in saline. Mechanical ventilation was set with VT = 8 ml/kg, FiO_2 to reach a SaO_2 target of >90%, PEEP = 10 cmH_2O if PaO_2/FiO_2 > 300 and 12 cmH_2O if PaO_2/FiO_2 < 300, and respiratory rate to obtain a $PaCO_2$ of 35–45 mmHg. Before as well as 12 and 24 hours after peritonitis induction we measured the PaO_2/FiO_2 ratio, the total compliance of the respiratory system (C), calculated as VT/($P_{plateau}$ – PEEP) and inspiratory airway resistance (R_i) calculated as (P_{max} – $P_{plateau}$) / mean inspiratory flow. Data are mean [range].
Results For data see Table 1. During the course of the 24-hour study period, six of 10 animals developed gas exchange deteriorations consistent with the ARDS definition; two further animals fulfilled the gas exchange referred to as ALI. Impairment in lung mechanics over time is reflected by the decreasing C values.

Table 1 (abstract P2)

	Control	12-hour peritonitis	24-hour peritonitis
PaO_2/FiO_2	430 [421; 440]#	380 [349; 397]	165 [68; 289]#
C (ml/cmH_2O)	28 [24; 32]*	18 [16; 21]*	12 [8; 17]*
R_i (cmH_2O/l/s)	4.1 [3.9; 4.5]	4.5 [4.3; 5.1]	5.1 [3.7; 7.9]

#$P < 0.05$ control vs 24-hour peritonitis, *$P < 0.05$ control vs 12-hour and 24-hour peritonitis.

Conclusions We conclude that an ALI/ARDS-like state is developed by most pigs during fecal peritonitis and that this peritonitis model may therefore serve as an extrapulmonary ARDS model. However, this condition develops after a prolonged period of approximately 12–18 hours, and the severity of the condition in single animals may be less predictable when compared with ARDS models induced by direct lung injury. Furthermore, it should be emphasized that pulmonary function in pigs is markedly different from humans in as much as no collateral ventilation exists in this species [1], and that pulmonary blood flow regulation is far more susceptible to hypoxia in pigs when compared with other species including humans [2]. Lung function data derived from pig models should therefore always be interpreted cautiously if clinically relevant conclusions have to be drawn.
Acknowledgement M Matejovic was supported by a grant from the Alexander von Humboldt Stiftung.
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P3

Computer-advised insulin infusion in postoperative cardiac surgery patients: a randomized prospective controlled multicenter trial

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Introduction Tight blood glucose (BG) control has been shown to decrease morbidity and mortality in critically ill patients [1] but is difficult to achieve using standard insulin infusion protocols. We evaluated glucose control, using a software model predictive control (MPC) insulin administration algorithm, in a prospective randomized controlled multicenter comparison with standard care in three European hospitals (Royal Brompton Hospital [RBH], Medical University Graz [MUG], Charles University Hospital [CUP]).
Methods Sixty ventilated patients (20 in each center) admitted to intensive care following elective cardiac surgery, with an arterial BG > 6.7 mmol/l within 4 hours of admission, were randomized to BG control by the standard insulin protocol of the participating ICU or MPC advised insulin infusion. All patients had BG measured hourly. Standard care (n = 30) involved insulin infusion in two centers (RBH, CUP) and insulin boluses in the third (MUG). The MPC algorithm was derived from software developed for closed loop glucose control in ambulatory diabetic patients [2]. MPC, installed on a bedside computer, requires input of patient chronic insulin requirements, weight, carbohydrate intake and BG concentration. Insulin infusion rate advice for the next hour is displayed, targeted to maintain BG at 4.4–6.1 mmol/l. The study was continued for at least 24 hours with a maximum duration of 48 hours.
Results The percentage of glucose measurements in the target range were significantly greater in the MPC group over the first 24 hours compared with standard care: 52% (17–92) vs 19% (0–71), (median [min–max]), $P < 0.01$. Two hypoglycemic events (BG < 3 mmol/l) occurred in patients receiving standard care.
Conclusion The MPC algorithm was safe and effective in controlling postoperative hyperglycaemia in this patient group.
Acknowledgements This study is part of CLINICIP project funded by the EC (6th Framework). Addenbrooke's Hospital also received support from EPSRC (GR/S14344/01).
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P4

Intravital endoscopy of alveoli: a new method to visualize the mechanical alveolar dynamics

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Critical Care 2006, **10(Suppl 1):**P4 (doi:10.1186/cc4351)

Introduction In the frame of protective lung ventilation, alveolar biomechanics become more and more the focus of scientific interest. New microscopic techniques and experimental setups enabled a view of the alveoli dynamically changing their geometry under mechanical ventilation [1]. Although of fascinating image quality the alveoli are observed at an open chest wall under a glass plate representing an artificial situation. To circumvent this restriction we developed a method of intravital endoscopy and tested it on an animal rat model.
Methods In cooperation with Schoelly GmbH (Denzlingen, Germany) we developed an endoscope with an outer tube diameter of 2.7 mm (including the optical fiber). To prevent the alveoli under observation from mechanical deformation due to the tip of the endoscope we developed a flushing catheter that continuously produces a thin fluid film between the endoscope tip and the alveoli being in the optical focus. The endoscope tube can be introduced by minimally invasive thoracotomy, thus enabling microscopic videos of the alveolar dynamics. The thorax remains intact.
Results Figure 1 shows a tissue area after lavage of 0.8 mm diameter. This region is displayed at different time points during a breath. Four snapshots were taken in inspiration (upper row) and four in expiration (lower row). In the middle of the figure the corresponding P–V loop (left) and the intratidal dynamic compliance (right) are shown.
Conclusion This new minimal invasive method of intravital endoscopy enables microscopic observations of the mechanical alveolar dynamics *in situ*. The concurrent observation of respiratory mechanics and alveolar dynamics provides a promising tool to correlate global measurements with local alveolar properties.
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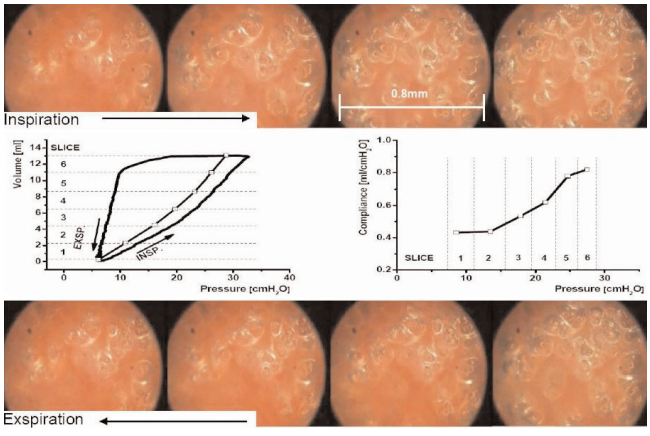
Figure 1 (abstract P4)



P5

Influence of the blood on the time course of pancreatitis-induced lung injury evaluated in isolated blood-perfused rat lungs

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We evaluated the time course of pancreatitis-induced lung injury using an isolated blood-perfused rat lung preparation with lungs harvested 2, 6 or 18 hours after pancreatitis induced by injecting taurocholic acid into the pancreatic duct. This allowed us to separate and to determine the specific role of pancreatic blood vs normal blood on the expression of injury evidenced during isolated lung reperfusion. After 6 hours of pancreatitis (but not after 2 or 18 hours despite similar elevated serum amylase concentrations and persisting evidence of systemic inflammation) lung reperfusion

with autologous blood or with homologous blood collected from normal rats revealed lung endothelial cell injury manifested by the formation of progressive lung oedema (~1 g/hour) accompanied by alterations in dynamic and static lung mechanics resulting in a final increased wet-to-dry lung weight ratio (7.5 ± 0.6; $P < 0.01$ vs control or time-matched sham-operated animals). In contrast, reperfusing normal lungs with pancreatic blood collected from rats 6 hours after taurocholate injection did not produce any alterations in lung weight and dynamic or static lung mechanics compared with normal control lungs. However, pancreatic blood collected 2 hours after taurocholate injection produced a moderate alteration in lung function but without significant increase in the wet-to-dry lung weight ratio (5.4 ± 0.5). Our results indicate that in this acute rat pancreatitis model lung injury occurred early, between 2 and 6 hours, and was completely reversible despite persistent elevated amylase concentration and systemic inflammation. Isolated lung reperfusion with normal homologous blood did not modify the expression of the pancreatic *in-vivo*-induced lung injury. Furthermore, pancreatic blood collected early (after 2 hours, but not after 6 hours) and used as perfusate for normal isolated lungs produced mild lung oedema and a moderate increase in dynamic lung compliance, suggesting that its potential toxic effects on the lungs were completely neutralized after 6 hours of pancreatitis.

P6

Rats surviving after high tidal volume ventilation show marked and reversible pulmonary and systemic changes

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Rationale High tidal volume (VT) ventilation (HTVV) induces pulmonary inflammation. The time course of pulmonary and systemic HTVV-induced vascular dysfunction is unknown. We tested whether rats receiving HTVV survive the insult, and we describe the time-course of the HTVV-induced vascular changes.
Methods Normal anesthetized Sprague–Dawley rats were tracheostomized and ventilated for 1 hour with either VT = 9 ml/kg + PEEP 5 cmH_2O, or VT = 35 ml/kg + ZEEP. After the HTVV period, the tracheostomy was closed, and rats were sent back to their cages breathing room air. Other rats were sacrificed at this point in time (t = 1 hour). Rats surviving the acute period of HTVV were again intubated, monitored and then sacrificed at different points in time (24 hours, 72 hours, 168 hours). We measured the mean arterial pressure, aortic blood flow (QAo), arterial blood gases, and total protein, AST, ALT, IL-6, and VEGF serum and BAL fluid concentrations. Aortic segments and pulmonary micro vessels were mounted in myographs, and responses to acetylcholine in norepinehrine-precontracted rings were tested. Histological lung changes were studied.
Results All lungs showed diffuse alveolar damage after HTVV at 1 and 24 hours, but histology was completely normal at t = 72 hours. HTVV induced hypotension, decreased QAo, hypoxemia, increased protein, AST, ALT, IL-6, and VEGF BAL fluid/serum concentration ratio. Acetylcholine and norephineprine-induced responses were impaired after HTVV in aortic rings. Moreover acetylcholine-induced responses in pulmonary microvessels were impaired. All these biochemical and vascular function changes normalized at t = 168 hours.
Conclusions About half the rats receiving for a short period of time ventilation using very high VT survive. HTVV induces in a reversible fashion pulmonary and systemic inflammation and vascular dysfunction.
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P7

Automatic recruitment maneuvers in porcine acute lung injury based on online PaO_2 measurements

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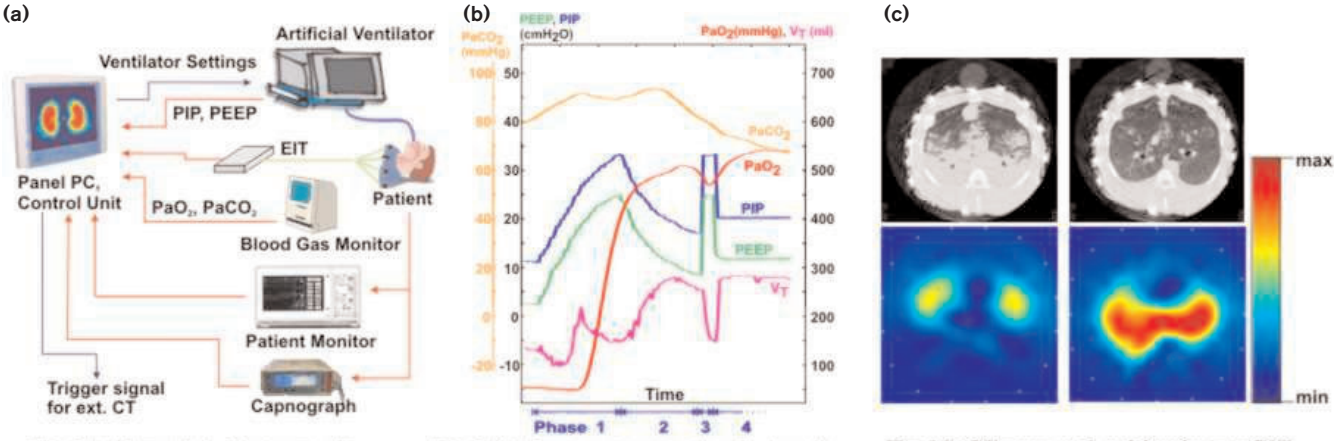
Introduction The individualization of lung protective ventilation strategies (e.g. recruitment maneuvers [RM] and PEEP titration to keep the lungs open) requires careful bedside observations. Many parameters must be monitored, which calls for computer aid. A fuzzy-logic ventilation expert system has been tested regarding its

Figure 1 (abstract P7)



(a) Setup featuring sensor fusion and automatic ventilation control. **(b)** Pulmonary parameters during all phases of an automatic RM ($FiO_2 = 1.0$). **(c)** CT scans and end-inspiratory EIT images before and after automatic RM.

ability to automatically conduct RMs based on the open lung concept (OLC).

Methods Three pigs received lavages to induce ARDS and baseline ventilation of 8 ml/kg Vt, RR = 25, I:E = 1:1 and FiO_2 = 1.0. The block diagram of the ventilation setup is depicted in Fig. 1a. It is capable of conducting automatic RMs while continuously recording pulmonary parameters. Fuzzy controllers handle the four phases of OLC-RM. They were fed with medical knowledge from experienced physicians. An electrical impedance tomograph (EIT) provided images of the ventilation distribution and CT scans were made. During phase 1 of RM, the controller increased the PEEP level (PCV, Pdelta = 8 cmH_2O) until the lung was supposed to be open according to online PaO_2 measurements (Paratrend 7). In the closing phase 2, PEEP was automatically titrated until PaO_2 started to decrease. After re-opening, steady-state ventilation (phase 4) was established at a PEEP = 2 cmH_2O above the closing pressure.

Results The pulmonary parameters of one pig during an RM cycle can be seen in Fig. 1b. After 20 min, PaO_2, Vt and compliance Crs (= Pdelta/Vt) were significantly increased in all animals and $PaCO_2$ reduced to normal values. Phases 1–3 of the RM process lasted approximately 5 min, partially due to the dynamic latency (15 s) of the PaO_2 measurement system. An optimization of the fuzzy controller and additional sensors will shorten the execution time and reduce the heart's pressure load. Figure 1c shows the CT and EIT images before and after RM. Atelectases are removed and ventilation is increased, more evenly distributed and shifted from ventral to dorsal regions.

Conclusion Automatic RM with a sustained improvement of PaO_2 and Crs could be achieved. The EIT showed a high potential to visualize and assess RM with a high temporal resolution.

P8

Comparison of regional lung recruitment in electrical impedance tomograms and CT scans in experimental acute lung injury

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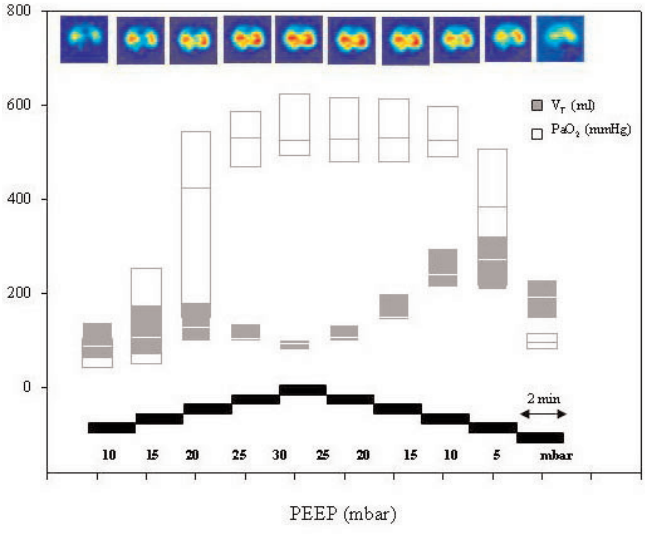
Introduction Assessment of regional alveolar recruitment and derecruitment during protective respiratory therapy in lung failure is necessary to predict the process of ventilatory therapy and to avoid pulmonary complications. Different studies showed that clinical management of ARDS can successfully be controlled by CT scan analysis [1]. Information about regional distribution of ventilation can also be assessed by the bedside method of electrical impedance tomography (EIT) [2]. To correlate the assessment of pulmonary recruitment with EIT and CT scans as a reference technique during a PEEP trial, we designed an experimental study with porcine saline-lavage-induced lung injury.

Methods In six pigs (25–34 kg), acute lung injury was induced by repetitive lung-lavage. After stabilisation of the lung injury model (> 1 hour) a stepwise PEEP trial with 2 min at each pressure ramp was performed (10 up to 30 mbar and 30 down to 5 mbar) with an electrically controllable ventilator (Servo 300; Siemens-Elema). During the PEEP trial, the animals were ventilated with pressure-controlled ventilation (delta 8 mbar), respiratory rate (RR) 25, I:E 1:1 and FiO_2 1.0. Ventilatory, hemodynamic and gas exchange parameters were continuously recorded during the stepwise PEEP trial. EIT measurements were realized at a juxtadiaphragmatic thoracic level. Simultaneously, a CT scanner was triggered to obtain reference images of the same slice for each PEEP level at the end of each pressure ramp. Three ROI in nondependent, middle and dependent lung areas were defined to compare the EIT data with the reference data of the CT slices. The correlation between the changes in air content between both methods was determined. To compare the amount of pulmonary recruitment/derecruitment at each PEEP level expressed by CT (Hounsfield units) measurement and relative impedance changes, the effect size (ES) [3] was calculated. ES levels were defined: small: <0.2, medium: 0.2–0.5, high: >0.8.

Results The measured tidal volumes and PaO_2 clearly showed a nonlinear lung hysteresis and recruitment of nonaerated lung areas at the descending part of the pressure ramp (Fig. 1). The highest but not significant correlation between EIT measurements and X-ray attenuation (HU) was found in the dependent lung areas. The effect of PEEP on pulmonary recruitment/derecruitment was very high at lower pressure levels. The display of pulmonary recruitment in the EIT in comparison with CT scans at the ascending part of the pressure ramp showed a higher ES. ES values were reduced in EIT, if the tidal volume was reduced (Table 1).

Figure 1 (abstract P8)



Development of tidal volume and PaO_2 during a stepwise PEEP trial (n = 6).

Table 1 (abstract P8)

Effect size values of alveolar recruitment/derecruitment in end-expiratory CT and EIT tomograms

PEEP trial	10–5 mbar	10–15 mbar	15–20 mbar	20–25 mbar	25–30 mbar	30–25 mbar	25–20 mbar	20–15 mbar	15–10 mbar
CT (ES)	3.42	1.7	1.12	0.73	0.58	0.21	0.33	0.7	2.03
EIT (ES)	2.89	2.05	1.89	1.37	0.29	0.02	0.56	0.96	1.91

Conclusion The effect of a stepwise ascending and descending PEEP trial on alveolar recruitment/derecruitment in porcine saline-lavage-induced lung injury could be displayed in EIT analysis and may directly be helpful in titration of PEEP.

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P9

It is possible to reduce the exposition to ionizing radiation for lung computed tomography scan analysis?

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Critical Care 2006, **10(Suppl 1):**P9 (doi:10.1186/cc4356)

Introduction The computed tomography (CT) scan can be used to measure the lung weight–volume and to determine the degree of inflation (not aerated, poorly aerated, well aerated, over aerated tissue). Nowadays to accurately study the lung, a whole thoracic CT scan must be performed, thus exposing the patient to a large dose of ionizing radiation. A possible solution could be to acquire only three CT lung sections instead of scanning the whole lung. We previously showed that in ALI/ARDS patients three lung sections are able to accurately estimate the lung inflation similar to the whole CT scan.

Objective To evaluate whether three lung sections gives comparable data to the whole lung CT analysis in patients with unilateral pneumonia.

Materials and methods Thirty-two patients with unilateral pneumonia were studied (mean age 64.2 ± 20.4 years, 18 males, BMI 25.4 ± 2.8 kg/m^2, PaO_2/FiO_2 261.1 ± 102.8, SAPS-II 35.3 ± 16.8, 14 mechanically ventilated). Each patient underwent a whole lung spiral CT scan. The lung regions of interest were manually delineated on each CT slice, using dedicated software (MALUNA; University of Mannheim, Germany). The three CT lung sections were selected at the level of the aortic arch, carina and at the mid right atrium (representing the lung apex, hilum and base). Lung quantitative analysis was performed with specific software (SOFT-E-FILM; University of Milan). The agreement between the two methods was evaluated using Bland–Altman analysis considering each compartment of lung inflation (expressed as the percentage of the total weight).

Results For the nonaerated tissue the mean of the difference ± 2SD was 0.015 ± 0.096, poorly aerated was 0.011 ± 0.056, well aerated – 0.025 ± 0.084 and over aerated – 0.001 ± 0.014.

Conclusions Our data show that a lung CT scan of only three sections can provide comparable information on the distribution of lung inflation as a whole lung CT scan.

P10

Computed tomography-based risk estimation on acute lung injury/acute respiratory distress syndrome after blunt thoracic trauma

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Objective Computed tomography (CT) is used in the diagnostic management of polytraumatized patients. Multiple trauma and pulmonary contusion are typical triggers of post-traumatic acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) [1]. Therefore, an early predictor of post-traumatic ALI/ARDS would be valuable. In this study we tested whether the mass of nonaerated lung tissue (Mnon) in admission CT could predict post-traumatic ALI/ARDS.

Methods The Mnon of 54 polytraumatized patients with pulmonary contusion was analyzed as previously described [2]. We studied the association of Mnon with physiologic variables and injury descriptors such as PaO_2/FiO_2 ratio, injury severity score (ISS) and thoracic trauma severity score (TTSS) [3] recorded on admission. To evaluate Mnon as a predictor of ALI/ARDS we used a receiver operator characteristic (ROC) curve.

Results Patients developing post-traumatic ALI/ARDS had significantly larger Mnon and significantly higher ISS and TTSS values. Literature data suggest a higher incidence of ALI/ARDS with a contusioned lung volume >20% [4]. Our results, however, indicate a higher risk of ALI/ARDS already with a Mnon of around 10%. The Mnon predicting ALI/ARDS with the highest sensitivity (81%) and specificity (87%) was 9.8%. The area under the ROC curve was 0.89 (confidence interval 0.79–0.99).

Conclusion The mass of nonaerated lung tissue on admission CT can help to predict the development of ALI/ARDS. It may thereby help to implement appropriate therapeutic options such as lung protective ventilation. The clinical use of our technique, however, is limited by the time-consuming CT analysis.

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P11

Immediate and long-lasting effects of recruitment maneuvers on the pressure–volume curve in normal anesthetized animals

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Critical Care 2006, **10(Suppl 1):**P11 (doi:10.1186/cc4358)

Introduction Recruitment plays a major role in defining the sigmoid shape of the static pressure–volume (PV) curve in ARDS. The injured lung is at risk of atelectasis due to surfactant dysfunction and due to increased superimposed pressure caused by increased lung weight. In normal lungs, however, alveoli are much more stable than in the injured lung. Therefore, it is not clear to what extent recruitment defines the shape of the PV curve in normal lungs. We hypothesized that resolving atelectasis using a recruitment maneuver leads to typical changes in the shape of the PV curve.

Methods After induction of anesthesia and oral intubation, six sheep were mechanically ventilated in a prone position. Data acquisition was performed using an Evita4Lab measurement system (Draeger Medical, Lübeck, Germany). The protocol consisted of a low flow inflation maneuver (LF1), followed by a recruitment maneuver (RM) and a second low flow inflation (LF2). Before LF1 and between interventions, animals were ventilated at ZEEP for 5 min. The shape of the static PV curves during LF1 and LF2 and the shape of the dynamic PV curves during ventilation at ZEEP were analyzed.

Results During LF1 a sudden incline (INC) in the static PV curve was observed in all animals. Due to the incline, the curves were not compatible with the sigmoid approximation according to Venegas

Figure 1 (abstract P11)

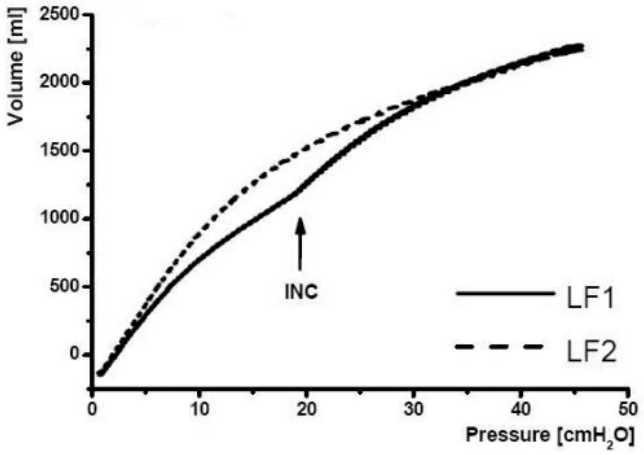
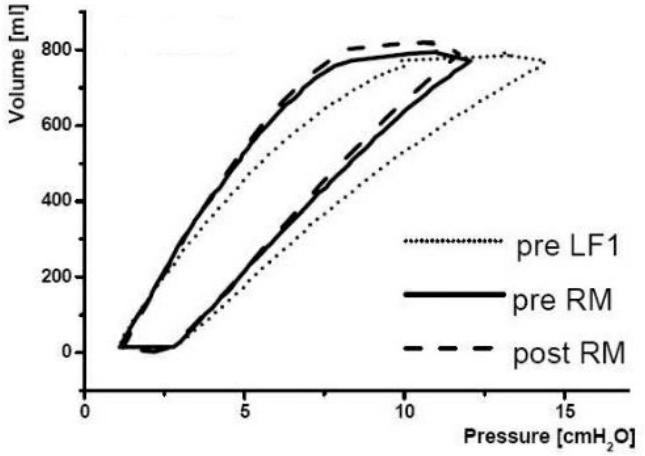


Figure 2 (abstract P11)



and colleagues. The sudden incline had disappeared in LF2 (Fig. 1). The shape of the dynamic PV curves and dynamic compliance were changed by LF1. Afterwards dynamic compliance remained unchanged irrespective of 5-min ZEEP and of the RM (Fig. 2).

Conclusion In normal sheep lungs, recruitment does influence the shape of the static PV curve. Other than in ARDS, the presence of recruitment does not generate a sigmoid PV curve. The changes in dynamic compliance after a RM were preserved for at least 5 min, indicating a long-lasting effect. The effects of recruitment on the shape of the PV curve might serve as diagnostic tool to differentiate normal patients from patients at risk of lung injury.

P12

Online SLICE: a tool for continuous monitoring of respiratory mechanics

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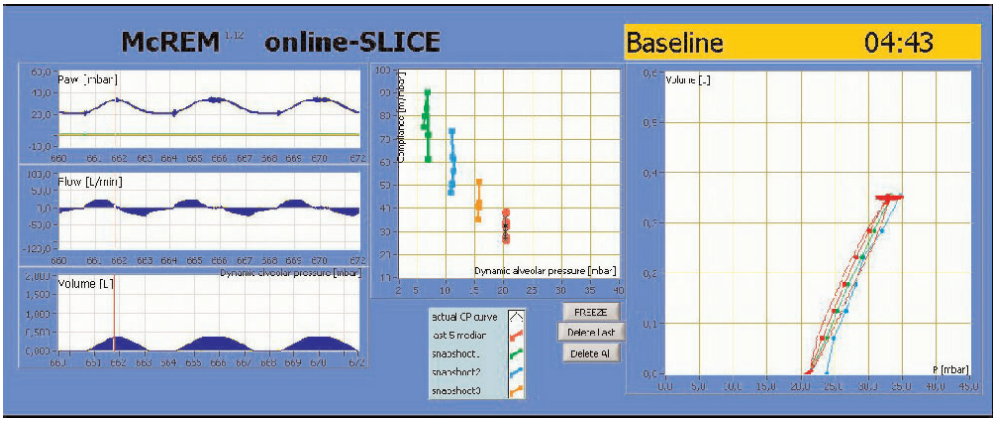
Introduction The clinical use of respiratory mechanics is limited due to complicated measurement methods and restricted bedside availability of the achievable information. For observational and interventional studies in the ICUs of the university clinics of Freiburg we developed a laptop-based tool, which provides online information about the mechanical state of the patient's respiratory system on a breath by breath basis.

Methods We developed a program in LabView (National Instruments, Austin, TX, USA) on a laptop that is able to read the internal data of a ventilator (Evita 4; Dräger Medical, Lübeck, Germany) in real time. A serial connection is established using the MEDIBUS protocol. Pressure, flow and volume provided by the ventilator are read into the laptop at 125 Hz, analyzed and visualized. The signal analysis provides dynamic compliance and resistance in dependence of alveolar pressure [1,2]. Statistics and trends are displayed on request of the user.

Active manipulations of the settings of the ventilator are possible and were used for animal experiments. With appropriate maneuvers (by controlling the volume/time or pressure/time curve) it is possible to derive mechanical properties of the respiratory system separated according to inspiration and expiration.

Results In an animal ($n = 6$) and an observational patient ($n = 30$) study at University Hospital Freiburg the system was evaluated. Figure 1 shows a screen plot of the online monitor during an experiment performed on healthy anesthetized sheep. Trends are

Figure 1 (abstract P12)



visualized by overlaying older data in different colors with actual data. The physician gets immediate feedback on whether changes of ventilator settings show the expected effects.

Conclusion Online monitoring of respiratory mechanics provides additional information about changes in the state of a patient's respiratory system. Thus the physician is enabled to evaluate the therapeutic strategy online and to base the settings of the ventilator on current trends observed in the data.

References

1. Guttmann *et al.*: *Technol Health Care* 1994, **2:**175-191.
2. Stahl *et al.*: *Crit Care* 2004, **8 (Suppl 1):**P28.

P13

Abstract withdrawn

P14

The position of the lower inflection point depends on volume history

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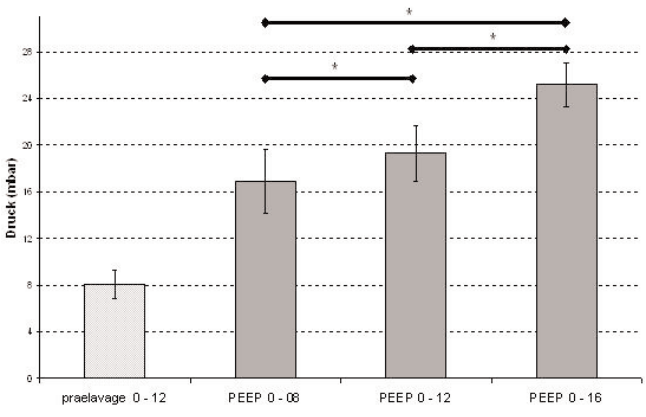
Critical Care 2006, **10(Suppl 1):**P14 (doi:10.1186/cc4361)

Introduction ARDS is a difficult to treat disease and is associated with a high mortality. For lung protective ventilation strategies the interaction of ventilator settings and respiratory mechanics is essential. In the past the static PV curve was used to determine ventilator settings in ARDS patients. Atelectasis was assumed to occur at pressures below the lower inflection point (LIP). This study was performed to investigate the influence of ventilatory patterns with different tidal volumes (Vt) on the shape of the static PV curve.

Methods After induction of anesthesia and tracheotomy, 14 surfactant-depleted piglets were ventilated at ZEEP with three different Vt (8, 12, 16 ml/kg) in a randomised order. For data acquisition a BICORE CP100 monitor (Bicore Monitoring Systems, Irvine, CA, USA) was used. The protocol consisted of a static maneuver at the end of each ventilator setting. In addition a baseline measurement (12 ml/kg) was performed before saline lavage. At the end of each setting a recruitment maneuver was performed before Vt change. After determining the LIPs their corresponding pressure values were compared using ANOVA and the Fisher PLSD post-hoc test.

Figure 1 (abstract P14)



Results Figure 1 shows the pressure belonging to the LIP (mean ± SD) prelavage and postlavage with different Vt. In healthy lungs the LIP is located at lower pressures than after surfactant depletion. Postlavage the pressure at LIP increases significantly with increasing Vt.

Conclusion The analysis of static respiratory mechanics shows interdependence between the ventilator settings prior to the static maneuver and the LIP. This could be interpreted as an effect of volume history on the relative position of the LIP. As we observed this effect despite standardisation of the maneuver itself the value of the current interpretation of static measurements has to be questioned.

P15

Assessment of the effectiveness of lung recruitment and PEEP setting by vibration response imaging

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Critical Care 2006, **10(Suppl 1):**P15 (doi:10.1186/cc4362)

Introduction Vibration response imaging (VRI) is a novel technology that measures vibration energy generated from airflow to create a real-time structural and functional image of the respiration process. Since this new imaging technique can be performed quickly and non-invasively at the bedside, it offers potential as a real time noninvasive method of adjusting ventilatory therapy.

Case A 75-year-old male patient was admitted to the ICU with acute lung injury due to acute pancreatitis and was mechanically ventilated with a PEEP setting of 5 mmHg and FiO_2 1.0. VRI recordings were obtained before and after a recruitment maneuver (40 cmH_2O PEEP for 40 s) and increasing PEEP to 10 cmH_2O. Images were taken during 20-s periods of respiration and respiratory cycles for analysis selected based on predefined selection rules. Mechanical ventilator settings were the same before and after recruitment. The total areas were measured by using the Image-J program (Table 1). Arterial blood gases were obtained immediately before and after recruitment and in close proximity (within 1 min) of VRI (Table 2). Statistical analysis was performed using a *t* test. Figures 1 and 2 show representative images before and after recruitment and PEEP elevation.

Discussion This case demonstrates a significant increase in the geographical area of vibration response images at peak inspiration after recruitment maneuver and a PEEP increase in early ARDS. This increase in VRI area correlates with improvement in oxygenation.

Conclusion Increased spatial distribution of ventilation following effective recruitment has previously been demonstrated using computerized tomography. VRI may provide a rapid bedside

Table 1 (abstract P15)

	Mean area (pixels)	Standard deviation
Pre-recruitment ($n = 5$ breaths)	47,863.8	3557.7
After-recruitment ($n = 5$ breaths)	60,888.2 *(<0.0025)	2735.7

Table 2 (abstract P15)

	FiO_2	pH	pO_2	pCO_2
Pre-recruitment	1.0	7.29	76	23
After recruitment	1.0	7.22	143	25

Figure 1 (abstract P15)

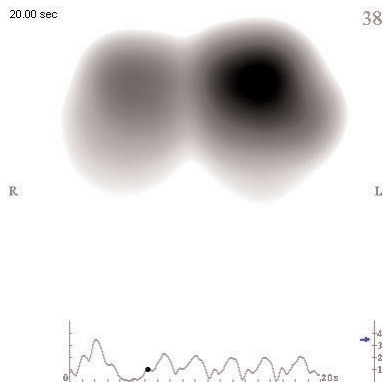
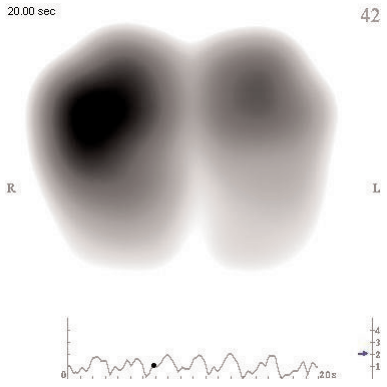


Figure 2 (abstract P15)



assessment of the effectiveness of lung recruitment and PEEP setting as an alternative to computerized tomography

P16

Influence of inertance on linearity of respiratory mechanics during mechanical ventilation in ARDS

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Aim The aim of the study is to investigate the influence of respiratory system inertance (Irs) on the linearity of respiratory mechanics during mechanical ventilation (MV) under conventional frequencies.

Methods Airway pressure (Pao), flow (V′) and volume (V) were recorded from 11 ARDS patients under MV at 10 and 20 c/min. Data were analyzed according to: Pao = EEP + Ers.V + Rrs.V′ and Pao = EEP + Ers.V + Rrs.V′ + Irs.V″, where Ers and Rrs are the respiratory system elastance and resistance, and EEP is the end-expiratory pressure. The fitness of data to models was evaluated by the standard error of the regressions (RMSD). Comparisons between all coefficients were done at 10 and at 20 c/min with the aid of the Wilcoxon rank test ($P < 0.05$).

Results and conclusions The mean values ± SD of all coefficients are presented in Table 1. Irs did not differ significantly between 10 and 20 c/min. The use of the inertive term results in a significantly higher Ers, lower Rrs and lower RMSD ($P < 0.001$) at both frequencies, but these differences are clinically irrelevant. We conclude that Irs is not negligible during MV in ARDS. Respiratory pathophysiology and the ventilator characteristics may contribute to the important role of Irs during MV.

P17

Is PEEP detrimental to splanchnic perfusion in mechanically ventilated patients?

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Objective Disturbances in splanchnic perfusion leads to insufficiency of the gut mucosal barrier. As a consequence it causes bacterial translocation that might be a trigger to septic shock and multiorgan failure. The present study was designed to assess whether mechanical ventilation with positive end-expiratory pressure (PEEP) is a factor disturbing cardiac output and splanchnic perfusion. Gastric intramucosal PCO_2 ($PiCO_2$) and pH (pHi) are currently used as indices of the accuracy of splanchnic perfusion and as end points to guide therapeutic intervention. The definition of the ideal PEEP does not include improvement in oxygen delivery and its accessibility in the splanchnic region.

Design A prospective study.

Setting Department of Anesthesiology and Intensive Care of Medical Postgraduate Education Center, Warsaw, Poland.

Patients Twenty adult ICU patients after laparotomy (hemicolectomy, colectomy) (group A) and five nonsurgical ICU patients (group B). All of them did not have serious respiratory and circulatory abnormalities, and did not need adrenergic or any circulatory support. All were mechanically ventilated under sedation with PEEP 0, PEEP 5, PEEP 10, PEEP 15. Each patient ventilated with PEEP 0 was a control for himself/herself. Each ventilation setting period lasted 1 hour. All the measurements were performed twice during that time.

Measurements and results $PiCO_2$–$PaCO_2$, pH–pHi, CI, CVP, ITBVI, EVLWI were measured using gastric tonometry and the PiCCO method (pulse contour cardiac output) after each change of PEEP value. No differences in pH–pHi and $PiCO_2$–$PaCO_2$ were observed between groups A and B. PEEP does not compromise gastric mucosal perfusion, as assessed by tonometry. Even the patient's age was not essential. A decrease in cardiac output did not result in necessity of adrenergic support. Only in one case

Table 1 (abstract P16)

	Model 1			Model 2			
c/min	Ers	Rrs	RMSD	Ers	Rrs	Irs	RMSD
10	46.9 ± 10.37	16.4 ± 4.48	1.95 ± 0.896	47.3 ± 10.31	16.4 ± 4.48	0.16 ± 0.076	1.87 ± 0.925
20	50.2 ± 10.62	13.7 ± 3.21	2.00 ± 1.083	51.6 ± 10.59	13.7 ± 3.21	0.16 ± 0.084	1.82 ± 1.124

there was a need to use it for more than 1 hour after setting PEEP 10. Mean values of CI were higher in group A compared with nonoperated group B. CI depends on the age and PEEP level. CVP was increased by PEEP in both groups, but ITBVI was almost untouched, the right ventricle preload did not decrease, and EVLWI was slightly lowered under PEEP 15. IAP did not exceed 10 mmHg in any case.

Conclusions PEEP up to 15 cmH_2O is well tolerated by the majority of ICU patients. The results of the present study indicate that incremental increases in PEEP do not impact on splanchnic perfusion as assessed by gastric tonometry in patients with adequate fluid loading. In some cases a necessity for adrenergic support might appear. Facing the fact of nonaffecting splanchnic perfusion, we cannot recommend any PEEP value as ideal for perfusing that region. More studies are needed in this area, particularly in patients receiving adrenergic support.

P18

Separate determination of inspiratory and expiratory dynamic lung mechanics using expiratory flow control

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Introduction During mechanical ventilation, the volume-dependent mechanical behaviour of the respiratory system may differ between inspiration and expiration due to expiratory collapse of small airways and due to repeated intratidal recruitment. Up to now, no method is available for separate determination of inspiratory and expiratory resistance (R) and compliance (C) during mechanical ventilation. We hypothesized that the control of the expiratory flow rate (expiratory flow control [EFC]) allows a discrete analysis of R and C.

Methods Different flow profiles were applied in two mechanical lung models. These profiles included standard ventilator and EFC modes. The volume dependency of dynamic respiratory mechanics was calculated using the SLICE method [1]. The algorithm was extended for a separate analysis of the inspiration and expiration phase. We validated the efficacy of EFC in six sheep using a modified standard ventilator (Evita 4; Draeger Medical, Lübeck, Germany) with EFC in the pressure-control mode.

Results It is mainly the passive expiration with the linear dependency of flow, volume and pressure that inhibits the separate inspiratory and expiratory analysis of respiratory mechanics. Figure 1 shows the effect of EFC on the breathing pattern in a healthy animal. At early expiration with EFC, flow is drastically reduced as compared with passive expiration (grey line). With EFC (solid line), the change in flow is independent of the change in volume, allowing the determination of R and C. Figure 2 displays the analysis of compliance in a lung model (C = 24) during constant flow ventilation without EFC. Without EFC, expiratory compliance is indeterminable (solid line). With EFC (Fig. 3) excellent agreement of inspiratory and expiratory compliance with the reference compliance was found. In six healthy sheep compliance determined during EFC was computed in inspiration and expiration. Dependent on the extent of EFC, we found a high agreement of inspiratory and expiratory compliances compared with mixed (inspiratory and expiratory) data.

Conclusion The control of expiratory flow allows the application of volume-dependent multiple linear regression analysis during inspiration respectively expiration alone. With EFC, the separate mechanical analysis reveals accurate results in well-controlled mechanical lung models and in experimental animals.

Reference

1. Guttmann *et al.*: *Technol Health Care* 1994, **2:**175-191.

P19

The course of the oxygenation index before kinetic therapy or prone ventilation is decisive for the prognosis of acute respiratory failure

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Critical Care 2006, **10(Suppl 1):**P19 (doi:10.1186/cc4366)

Introduction In acute respiratory failure (ARF), in particular acute lung injury (ALI) and respiratory distress syndrome (ARDS), an intervention in the form of rotational therapy (RT) or the prone position (PP) may improve oxygenation by recruiting alveoli situated in dorsal-dependent regions and by alteration of the ventilation/perfusion ratio. The efficacy of this interventions can be demonstrated among other parameters by the course of the oxygenation index. The aim of our study is to analyze the prognostic value of the course of the oxygenation index before and after such an intervention.

Methods We studied 112 mechanically ventilated patients (mean age 63 ± 15.6 [SE] years) with an ARF (ARDS $n = 69$; ALI $n = 43$)

Figure 1 (abstract P18)

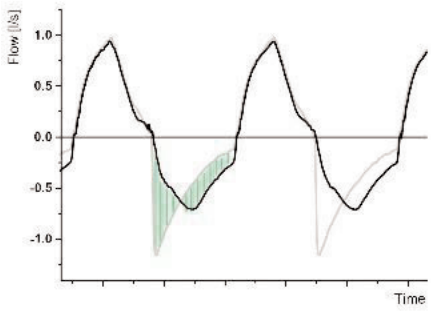


Figure 2 (abstract P18)

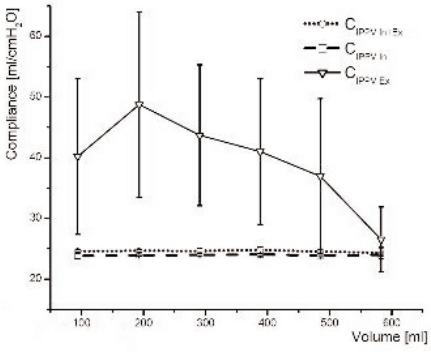
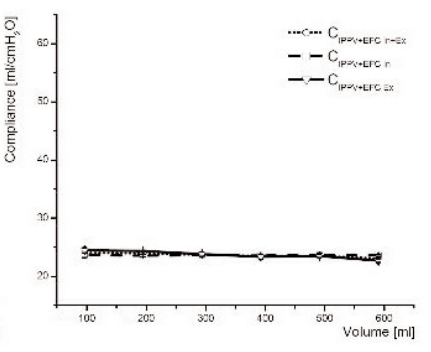


Figure 3 (abstract P18)



at a surgical ICU in a university hospital using the American–European consensus definition in a clinical follow-up design, who received supportive therapy either with RT ($n = 52$; Rotorest®) or using PP ($n = 60$; 135° left/right-side position for at least 6 hours in each position). The physicians on duty had the freedom of choice to use one or other method guided by their clinical experience and judgement. Data collection included, apart from baseline characteristics, individual PAO_2/FiO_2 of patients in the course 64 hours before and 120 hours after intervention. The individual PAO_2/FiO_2 before and after intervention was compared with linear regression analysis for each group (linear regression procedure and *t* test, SPSS®).

Results The mean PAO_2/FiO_2 decreased within 64 hours until the intervention from 230 ± 91 to 178 ± 59 mmHg in all patients (mean ± SE). Patients who died ($n = 64$) showed a more rapid deterioration of PAO_2/FiO_2 during conventional ventilation in the supine position in the interval of 64 hours prior to intervention in the form of RT or PP (slope of regression straight line: RT −5.14; PP −7.14) in comparison with patients who survived their acute respiratory failure (slope RT −3.43; PP −0.57) within the scope of the critical illness ($P < 0.05$). Nearly all patients showed a more or less marked improvement of PAO_2/FiO_2 during the first 5 days after intervention (PAO_2/FiO_2 after 120 hours: RT group 184 ± 77.28; PP group 213 ± 75 mmHg; *y* [all patients] = 3.9045**X* + 234.61], but there was no significant difference in the linear regression analysis between survivors (slope of regression straight line: RT 0.28; PP 2.48) and nonsurvivors (RT 0.61; PP 2.03) during 120 hours after the intervention.

Conclusion The course of PAO_2/FiO_2 seems to be more decisive for the prognosis of patients with an evolving ARF than the course after supportive interventions such as RT or PP. In patients with a rapid deterioration of PAO_2/FiO_2 we should be aware that this may indicate an unfavourable prognosis in the sequel. Supportive measures such as RT or PP, which aim to treat the ventilation/perfusion heterogenity, both seem to work, and therefore should be used in the early phase of ARF to reduce aggravation of lung injury and complications of mechanical ventilation.

P20

High-frequency oscillatory ventilation and prone position as early alternative therapy in adults with severe acute respiratory distress syndrome

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Critical Care 2006, **10(Suppl 1):**P20 (doi:10.1186/cc4367)

Background In the past few years there has been a resurgence of interest in high-frequency oscillatory ventilation (HFOV), as part of the search for lung-protective ventilation in acute respiratory distress syndrome (ARDS). The prone position has been used increasingly as a simple and safe method to improve oxygenation in conventional mechanical ventilation (CMV), but only occasionally as adjunctive therapy in HFOV.

Objective To evaluate safety and results when using both HFOV and the prone position in adult patients in the early phase of severe ARDS as integrated therapy for alternative lung-protective ventilation.

Methods Adult patients diagnosed with ARDS resulting from a pulmonary cause (ARDSp) and from an extrapulmonary cause (ARDSe) receiving mechanical ventilation for less than 72 hours, when it is not possible for a conventional lung-protective strategy of low tidal volumes (≤ 6 ml/kg PBW) and limited inspiratory plateau pressures (≤ 30cmH_2O), requiring $FiO_2 \geq 0.6$ to keep $PaO_2 \geq 60$ mmHg or $SpO_2 \geq 90\%$ with moderate–high levels of PEEP in CMV and the prone position. Data are presented as the mean ± SD.

Results We included in the study seven consecutive critically ill patients with early ARDS, four men and three women (five ARDSp/two ARDSe), aged 46.3 ± 20 years. APACHE-II score: 28.1 ± 4.8. LIS: 3.7 ± 0.2. OI: 35.6 ± 18.1. PaO_2/FiO_2: 88.6 ± 39.2. Patients were ventilated in the prone position and CMV with FiO_2: 0.84 ± 0.2. Tidal volume: 6 ± 0.3 ml/kg PBW. Plateau pressure: 34.3 ± 2.1 cmH_2O. Mean airway pressure: 25.9 ± 3.8 and PEEP: 17.1 ± 3.6 cmH_2O.

The patients were switched to HFOV in the prone position as alternative lung-protective ventilation. It was possible to apply higher mean airway pressures than in CMV and the prone position, to achieve significant and sustained improvements in gas exchange (PaO_2/FiO_2) and reductions in FiO_2 requirements in the first 24 hours of HFOV without hemodynamic instability or barotrauma. Patients were turned back to the supine position in HFOV (mean time in prone position: 3.1 ± 1.5 days) before transition to CMV (mean time in HFOV: 5.6 ± 3.2 days).

Two patients died in the first 2 days after being switched to HFOV, due to fulminant sepsis in Gram-negative bacteraemia and to massive alveolar haemorrhage in lupus, respectively. The other five patients were discharged alive from the ICU without ventilatory support. They are alive 3 months after diagnosis and treatment of ARDS.

Conclusions It is possible to use lung-protective ventilation using HFOV and the prone position as adjunctive therapy, with good outcomes in adult patients in the early phase of severe ARDS without significant complications. In our experience, it would be interesting to evaluate in future studies whether HFOV and the prone position is a better approach to lung protective ventilation than CMV for the most severe ARDS adult patients.

P21

High-frequency oscillatory ventilation in acute respiratory distress syndrome in adult patients

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Critical Care 2006, **10(Suppl 1):**P21 (doi:10.1186/cc4368)

Objective To evaluate the efficacy of high-frequency oscillatory ventilation (HFOV) in acute respiratory distress syndrome (ARDS) in adult patients.

Setting A 30-bed medical and surgical ICU of a tertiary care hospital.

Design A prospective clinical study over a period of 12 months.

Methods ARDS patients receiving mechanical ventilation as per the ARDSnet protocol and requiring positive end expiratory pressure (PEEP) ≥ 12 cmH_2O and $FiO_2 \geq 0.7$ to maintain oxygen saturation ≥88% were considered for HFOV. Initial settings of HFOV were selected based upon the mean airway pressure (MAP), PO_2/FiO_2 ratio, PCO_2 and oxygenation index (OI) ($OI = MAP \times FiO_2 \times 100 / PO_2$). Predetermined protocols for HFOV adjustments and weaning from HFOV were implemented. Continuous hemodynamic, plethysmographic monitoring was performed. Arterial blood gas parameters were documented at 1, 6 and 24 hours after initiation of HFOV.

Results A total of 18 patients were ventilated with HFOV for 80.82 ± 58.70 hours. Baseline characteristics before initiation of HFOV were: APACHE II score 21.11 ± 4.65, hours of conventional ventilation 61.83 ± 52.77, PEEP of 14.16 ± 3.7 cmH_2O, plateau pressure (Pplat) of 29.44 ± 4.93 cm, FiO_2 of 0.89 ± 0.11 and average ≥ 3 organs failure. There was an improvement in oxygenation status at 6 and 24 hours. The PO_2/FiO_2 ratio

increased from a baseline of 97.47 ± 27.92 to 181.26 ± 110.37 and 256.41 ± 130.85 at 6 and 24 hours, respectively. The OI reduced from a baseline of 26 ± 10.98 to 23.59 ± 16.98 and 15.95 ± 12.38 at 6 and 24 hours, respectively. Out of 18 patients 13 were 'Responders' – i.e. showed progressive and sustained improvement in oxygenation and were successfully weaned to 'T' piece oxygen (≥12 hours without any ventilatory assistance). The remaining five were 'Non Responders' and did not show sustained improvement in oxygenation and died of resistant hypoxia.

Subgroup analysis The Responder ($n = 13$) and Non Responder ($n = 5$) groups were similar in Pre HFOV baseline characteristics such as age, APACHE II score, number of organs failed, Pplat, PO_2/FiO_2 ratio and OI. The PO_2/FiO_2 ratios at 6 hours were 208.81 ± 110.96 vs 109.61 ± 77.41 ($P = 0.04$) in Responders and Non Responders, respectively. PO_2/FiO_2 ratios at 24 hours were 290.78 ± 117.43 vs 167.05 ± 132.58 ($P = 0.03$) in Responders and Non Responders, respectively. The reduction in OI in the Responder group at 6 and 24 hours was significant as compared with Non Responders: 17.27 ± 8.37 vs 40.01 ± 23.42 at 6 hours ($P = 0.003$) and 11.17 ± 4.28 vs 28.36 ±18.16 at 24 hours ($P = 0.002$). One patient developed pneumothorax and one patient had endotracheal tube displacement while on HFOV.

Conclusion HFOV is effective in adult patients with severe ARDS failing conventional ventilation. Progressive and sustained improvement in the PO_2/FiO_2 ratio and the reduction in the OI at 6 and 24 hours are strongly associated with successful response to HFOV.

P22

A registry of high-frequency oscillatory ventilation in adults

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Critical Care 2006, **10(Suppl 1):**P22 (doi:10.1186/cc4369)

Introduction High-frequency oscillatory ventilation (HFOV) theoretically provides the ideal mode of ventilation for patients with acute lung injury. By avoiding repeated recruitment and de-recruitment of lung units it has the potential to reduce ventilator-associated lung injury. In the vast majority of centres, however, it is still only used as rescue therapy for patients failing conventional ventilation (CV). In our 29-bed university hospital ITU we maintain a registry of patients receiving HFOV, and the first 25 entries are presented here.

Patients Patient demographics are presented in Table 1. Changes in gas exchange are presented in Table 2. Complications attributable to HFOV were CVS instability (4/25); pneumothorax (3/25) and ETT blockage (2/25). Two out of 25 patients died on HFOV; 5/25 died on CV post-HFOV and 18/25 were discharged alive from the ICU.

Conclusion HFOV is currently perceived as a rescue therapy in adult patients unresponsive to CV. Our experience of using HFOV in acute lung injury shows that it is an effective method of ventilation in refractory respiratory failure and is also a safe and practical alternative to CV when used early in acute lung injury.

Table 1 (abstract P22)

Age (years)	38 (22–71)
Direct:indirect ARDS	12:13
APACHE II score on admission	21 (10–38)
Duration of CV pre-HFOV (hours)	24 (8–360)
Duration of HFOV (hours)	80 (6–274)

Table 2 (abstract P22)

	CV pre-HFOV	1 hour HFOV	6 hours HFOV	12 hours HFOV
FiO_2	1.0 (0.4–1.0)	0.8 (0.4–1.0)	0.78 (0.4–1.0)	0.65 (0.4–1.0)*
PaO_2 (mmHg)	66 (56–104)	71 (42–122)	74 (51–107)	80 (61–137)
P:F ratio	88 (35–200)	93 (42–180)	109 (51–148)	122 (61–298)*
$PaCO_2$ (mmHg)	53 (35–86)	45 (29–67)	44 (28–65)	46 (36–60)

Values presented as median (range). *$P < 0.05$ compared with CV pre-HFOV.

P23

Superimposed high-frequency jet ventilation and oleic-acid-induced acute lung injury piglets: an experimental study

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Superimposed high-frequency jet ventilation (SHFJV) is a special form of combined high-frequency jet ventilation described in other studies as an effective respiratory therapy of acute lung injury (ALI) patients. We compared this technique with conventional mechanical ventilation in oleic-acid-induced ALI piglets over a study period of 5 hours. After ALI induction, 18 pigs were randomly assigned to three groups. A SHFJV group with a high-frequency (500 bpm) and a low-frequency (15–20 bpm) jet stream and a PEEP of 10 cmH_2O; a CPPV group (continuous positive pressure ventilation) presenting VT = 10 ml/kg, I:E = 1:1, PEEP = 10 cmH_2O; and a IPPV group (control group; intermittent positive pressure ventilation) VT = 10 ml/kg, I:E = 1:1, zero PEEP. SHFJV animals showed an earlier and more efficient improvement in oxygenation compared with group B (90 vs 180 min; PaO_2 70.5 ± 11.3 vs 41.2 ± 7.9 kPa) despite lower mean airway pressures applied (16 ± 1.4 vs 22 ± 1.8 mbar). CO_2 elimination was also more effective (6.0 ± 1.4 vs 8.2 ± 1.6) although peak airway pressures were the lowest (30 ± 3.8 vs 45 ± 4.6 mmHg). SHFJV may therefore be useful in ALI management.

P24

Pressure drop across neonatal endotracheal tubes during high-frequency ventilation

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Introduction High-frequency ventilation (HFV) is a concept of mechanical ventilation that is mainly used in therapy of infants. The resistance of the small neonatal endotracheal tubes (ETT) causes a noticeable difference between airway pressure (proximal end of the ETT) and tracheal pressure (distal end of the ETT). The aim of this laboratory study was to evaluate the pressure drop across the ETT

during HFV and to investigate whether tracheal pressure can be calculated from airway pressure using conventional methods.
Methods A physical model of an infant's respiratory system was connected with one of two differently sized ETTs (ID 3 mm or 4 mm; Blue Line, Portex Ltd., Hythe, Kent, UK) with the positioning of the tip inside the trachea of the model. The ETT was bent along a test fixture to approximate the *in-situ* curvature of an ETT simulating the nasal route of intubation. An infant HF-ventilator Sensormedics 3100A (SensorMedics Corp., Yorba Linda, CA, USA) was used to ventilate the model with an I/E ratio of 1:2. We varied mean airway pressure from 8 to 16 mbar (in steps of 2 mbar), the set airway pressure amplitude from 10 to 50 mbar (in steps of 10 mbar) and the frequency to 5 Hz, 10 Hz and 15 Hz, respectively. We analyzed the pressure drop across neonatal ETTs in a physical model setup during different conditions of HFV.
Results We found that depending on the ventilator's settings the relative loss of mean pressure amplitude caused by the ETT ranged from 23.8% up to 51.2% during the positive flow phase and from 3.3% up to 24.7% during the negative flow phase.
Additional to the well-described flow dependency of ETT resistance we found an increase of resistance caused by the HFV. Due to this effect, calculation of the ETT's pressure drop using the Rohrer or Blasius-Itos approach underestimated the true pressure drop significantly.
Conclusion We conclude that an increased pressure drop during HFV caused by the ETT must be considered to be dependent on the size of the ETT, the ventilation frequency and the flow rate, the latter implicating a dependency on the ventilator's performance in flow delivery. For the patient's respiratory system only that part of delivered energy that is transferred to the patient's lung is of relevance. This means that decisions for setting parameters of HFV must be made from the view of tracheal pressure. For an adequate noninvasive monitoring of tracheal pressure during HFV, new methods for calculation of the pressure drop across the ETT appear crucial.

P25

Efficacy of exogenous surfactant in adult patients with acute respiratory failure

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Introduction Acute respiratory failure and ARDS remains an important cause of mortality and morbidity in patients admitted to the ICU. Several trials were conducted to improve the survival in patients with respiratory failure. The efficacy and safety of the use of surfactant in improving the outcomes of patients with ARDS was recently evaluated in several trials.
Objective This review is primarily aimed at assessing the efficacy of surfactant in improving the survival of adult patients with acute severe respiratory failure.
Search strategy The following databases were searched for reports of trials: the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2005, Issue 4), MEDLINE (1966–November 2005), and EMBASE (1980–November 2005). In addition, bibliographies of review articles and potentially included studies were also searched.
Selection criteria Prospective randomized controlled trials comparing surfactant treatment with the standard care (or placebo and standard care) in managing adult patients with acute respiratory failure requiring intubation and mechanical ventilation were included.
Data collection and analysis Data regarding clinical outcomes including the survival at 28 days, the duration of mechanical ventilation, the duration of ICU and hospital stay, and adverse effects. The data on the methodological quality (allocation concealment, intention to treat analysis and Jadad score) of the trials were collected a using a standardized data extraction form. Wherever the data were adequate, the outcomes of interest were quantitatively pooled using a random effects model.
Main results Out of the 16 potentially eligible studies, five trials randomising a total of 1315 patients were included in the analysis. Three of these trials were pilot trials conducted to assess the safety (and efficacy) of surfactant. The other two were large trials conducted to evaluate the efficacy of surfactant. The pooled data on mortality suggested no significant effect of surfactant in reducing the mortality (odds ratio = 1.01; 95% CI = 0.81–1.26: $P = 0.9$). The data on other outcomes such as the duration of ventilation, ICU and hospital stay, and adverse events were not suitable for performing a meta analysis. The two large trials have both shown an increased incidence of adverse effects in patients where surfactant was used.
Conclusion The use of surfactant is not associated with an improvement in survival in adult patients with severe respiratory failure.

P26

Extracorporeal membrane oxygenation in the adult patient: experience in a medical ICU

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Introduction Extracorporeal membrane oxygenation (ECMO) is a technology that provides gas exchange and supports cardiac function in patients with ARDS or cardiac failure. We report on the experience with ECMO in our medical ICU, a tertiary centre.
Patients ECMO was started in 20 patients (14 males/six females) failing conservative treatment with life-threatening respiratory (13 patients), cardiac (two patients) or combined failure (five patients). Bypass surgery was performed bedside. For respiratory failure, veno-venous (v/v) access was used; for cardiac failure, veno-arterial (v/a) access was preferred. The mean age was 45.3 years. Nine apparently immunocompetent patients presented with community-acquired pneumonia (CAP). Two of these later appeared immunocompromised and had opportunistic infections. Eight other immunocompromised patients received ECMO. The remaining three patients had ARDS due to sepsis, cardiogenic shock and nosocomial pneumonia.
Results The average APACHE II score was 24.5 and SOFA score was 11.5. The Murray score before the start of ECMO averaged 3.2. The mean duration of ventilation was 32.5 hours and the average PaO_2/FIO_2 was 53.8 mmHg. In 13 patients the bypass was initially v/v, in seven patients v/a. In one patient v/v access was changed to v/a as cardiac failure developed. In another patient the v/a bypass was switched to v/v for insufficient oxygenation of the upper body. The mean duration of ECMO was 6.4 days (range 0.5–18), and mean duration of mechanical ventilation was 13.1 days (range 0.5–36). Overall survival was 50%. All patients that survived weaning from ECMO were also discharged and are still alive with a mean follow up of 804 days. Seven out of nine patients with CAP survived. Only 3/10 immunocompromised patients survived. All three are still alive after 2, 23 and 34 months. Ten out of 20 patients died. Twelve technical complications occurred, two of which were fatal (massive bleeding).
Discussion and conclusion ECMO is a potentially life-saving technology. Our overall survival was 50%. Unfavourable factors such as low pH and low pO_2/FIO_2 do not exclude a successful

ECMO intervention as our two patients with the lowest pH (6.89 and 6.95) survived, as did four out of seven patients with PaO_2 / FIO_2 < 40 mmHg. Predictive factors therefore cannot be used as exclusion criteria. Patients who develop intractable acute respiratory insufficiency due to CAP without underlying disease seem to benefit most from ECMO. Most series of ECMO reported in the literature exclude immunocompromised patients. We confirm that these patients stand a poor prognosis (survival of 30%). However, long-term and good functional survival appears to be possible in selected patients. v/a bypass seems to carry a higher risk for major and potentially fatal technical complications. v/a bypass is only indicated if cardiac support is required. Increasing experience from the ECMO team probably reduces the incidence of technical complications.

P27

Outcome of patients with congenital diaphragmatic hernia requiring ECMO: can we predict?

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Introduction In spite of the advances in pre-neonatal and neonatal intensive care including the use of antenatal steroids, foetal surgery, nitric oxide (NO), surfactant, high-frequency oscillation (HFOV), liquid ventilation and extracorporeal membrane oxygenation (ECMO), the mortality of patients with congenital diagrammatic hernia (CDH) remains high. The use of ECMO is generally reserved for patients who cannot be managed by other treatments such as HFOV, NO and surfactant. The aim of this study was to identify factors that could predict the outcome in patients with CDH requiring ECMO.
Methods This study is a retrospective review of case records, microfilms and our database between September 1991 and December 2004. All patients with CDH managed in our unit using ECMO were included. 'Pre ECMO' variables such as gestational age, sex of the patient, birth weight, age at the time of ECMO cannulation, acid–base status and blood gasses and ventilator settings before commencing ECMO, and variables during the ECMO course such as the mode of ECMO (VA vs VV), use of NO, surfactant, liquid ventilation, vaso-active agents, timing of repair of CDH, use of blood products, and complications (mechanical and patient related) on ECMO were analysed to identify predictors of outcome.
Results A total of 52 patients were managed using ECMO in our unit during the study period. All these patients were referred to our unit following the failure of maximal conventional treatment. The mean gestational age at birth was 38.9 (SD 2.74) weeks and the birth weight was 2.92 (SD 0.44) kg. The APGARS scores were 4.35 (SD 2.9) at 1 min and 5.93 (SD 2.9) at 5 min of birth. The mean age at the time of referral for ECMO was 2 (SD 3.1) days. The mean PaO_2/FiO_2 ratio was 49.7 (SD 49.8). The overall survival to hospital discharge was 58%. The mode of ECMO was venovenous in 27 patients and venoarterial in 25 patients. On univariate analysis, the mean duration of ECMO (181 ± 120 vs 317 ± 156 hours; $P = 0.001$), use of NO (6 vs 10; $P = 0.049$) and renal complications (4 vs 14; $P < 0.001$) were significantly different between the survivors and nonsurvivors. The pre ECMO variables were comparable between the survivors and non-survivors. Multiple logistic regression analysis of the variables included in the analysis revealed the duration of ECMO and renal complications developing on ECMO to be independently associated with mortality.
Conclusion Prolonged duration of ECMO and renal complications on ECMO were independently associated with mortality. None of the pre ECMO variables could be identified as predictors of mortality in patients with CDH requiring ECMO.

P28

Abstract withdrawn

P29

Respiratory variable predictors for intensive care mortality

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Introduction Nowadays it is not clear whether the level of hypoxemia is related to the outcome. It has been shown that the pulmonary dead space fraction is an independent risk factor for death in the early phase of acute respiratory distress syndrome [1].
Objective We aimed to study possible respiratory predictors for mortality in mechanically ventilated patients.
Materials and methods Consecutive patients invasively mechanically ventilated for more than 48 hours were enrolled. At ICU admission blood gas exchange and the ventilatory setting were recorded.
Results Sixty-eight patients (45 males, mean age 59.6 ± 15.5 years, weight 71.6 ± 14.1 kg) were enrolled at one ICU from October 2004 to October 2005. Thirty-seven patients presented acute lung injury or acute respiratory distress syndrome during their intensive care stay.
The overall intensive care mortality was 23% (16 patients). The blood gas analysis showed a mean PaO_2/FiO_2 ratio of 207 ± 120 mmHg, $PaCO_2$ of 37 ± 10 mmHg and pH of 7.34 ± 0.13 with the following ventilatory setting: PEEP 8.1 ± 4.6 cmH_2O, respiratory rate 17.8 ± 5.2 bpm, tidal volume 662 ± 145 ml and minute ventilation 9.1 ± 2.0 l/min. Among the respiratory variables considered only the $PaCO_2$ was associated with an increased intensive care mortality (OR 1.08, 95% confidence interval 1.021–1.152).
Conclusion The increase in $PaCO_2$, reflecting a higher degree of pulmonary impairment, was associated with intensive care mortality.
Reference
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P30

Model and clinical studies of a novel differential lung ventilation system for adults

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Introduction In clinical conditions when the mechanical properties of each lung of a patient differ very much, it is necessary to ventilate them separately. The connection of each lung with one respirator, by means of a double-lumen endotracheal tube, enables its physical separation and control of its ventilation. Generally, therefore, two synchronized respirators are required to perform

differential ventilation of lungs. It is also possible to use one respirator with a feedback-controlled variable pneumatic valve to divide the total ventilation volume from a respirator between two lungs.

Materials and methods A prototype of a flow divider based on stabilization of tidal volume measurement, according to adjustments made by an anesthesiologist, was designed. This feedback-controlled circuit can precisely keep the tidal volume division on a constant value, irrespective of lung mechanics (alveolar/chest compliance, airway resistance) and ventilatory parameter (frequency, total tidal volume and selective PEEP) changes. In order to assess the solution that was realized, one respirator with a feedback control of tidal volume division was tested using a physical model of the adult respiratory system and in clinical conditions, during thoracic surgery.

Results The physical model of respiratory system consisted of two parallel circuits of artificial lung. The model study has proved that maximal errors of tidal volume division are less than 10% in a wide range of division ratio and PEEP value, which is acceptable in clinical practice. Differential ventilation was applied to 10 patients undergoing thoracic surgery. Measurement of each lung parameter showed the stable tidal volume division (error < 10%) in all patients.

Conclusion Clinical data show that the proposed system fulfils the same function as two synchronized ventilators, with independent adjustment of volume and PEEP to each lung.

P31

Open lung ventilation does not increase right ventricular afterload in cardiac surgery patients

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Open lung ventilation (OLV) consists of recruitment maneuvers, followed by low tidal volume and elevated positive end-expiratory pressure (PEEP). Elevated PEEP is associated with an increased right ventricular (RV) afterload. We investigated the effect of OLV on RV afterload during inspiration and expiration in patients after cardiac surgery using Doppler echocardiography.

In 28 patients scheduled for cardiac surgery, two ventilation strategies were applied in a randomized cross-over design. During OLV, recruitment maneuvers were applied until $PaO_2/FiO_2 > 375$ Torr was achieved (reflecting an open lung) and were maintained by the use of sufficient levels of PEEP. The tidal volume was 4–6 ml/kg. During conventional mechanical ventilation (CMV) the ventilation was with a low tidal volume (6–8 ml/kg) with 5 cmH_2O PEEP, without recruitment maneuvers. The acceleration time (Acmean) of the pulmonary artery was measured with transesophageal echocardiography in a long-axis view of the pulmonary artery during end-inspiration and end-expiration.

The total PEEP in the OLV group was 14 ± 4 compared with 5 ± 1 cmH_2O in the CMV group. During expiration, the Acmean of both ventilation strategies was comparable. Inspiration caused a significant decrease of Acmean compared with expiration during CMV (Table 1). Surprisingly, this did not occur during OLV.

Table 1 (abstract P31)

	Expiration	Inspiration
Acmean OLV	9.6 + 2.2	10.0 + 2.9*
Acmean CMV	10.2 + 3.3	8.6 + 2.9†

Acmean = mean acceleration (m/s^2). *$P < 0.05$ OLC vs CV, †$P < 0.05$ inspiration vs expiration.

We conclude that despite the use of 'relatively' high PEEP, OLV with low tidal volume does not increase RV afterload during inspiration and expiration.

P32

Detection of expiratory flow limitation during experimental mechanical ventilation

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Introduction The present study examines the possibility of non-interventional detection of expiratory flow limitation (EFL) during experimental mechanical ventilation (MV), with the aid of nonlinear regression analysis.

Methods Eight New-Zealand rabbits under MV were included in the study. EFL was induced by the application of negative expiratory pressure (−5 to −10 hPa) and recognised by the negative expiratory pressure technique. The airway pressure (Paw) and flow (V′) were recorded and treated offline with the aid of the nonlinear model $Pao = EEP + E1.V + E2.V2 + k1.V' + k2.V'.|V'| + k3.V.V'$, which accounts for volume dependence of elastance and flow and volume dependence of resistance. The timed signal of resistive pressure (Pres) was reconstructed after subtraction of elastic nonlinear pressure from the whole pressure.

Results and conclusions The Pres signal presents two different configurations that permit one to separate between EFL and non-EFL. More specifically, in cases without EFL Pres is similar to the flow signal, while in cases with EFL expiratory Pres presents a minimum, which corresponds to the point of EFL installation. We conclude that the present technique, which combines computational and graphical parts, offers the possibility of EFL recognition and quantification at least during mechanical ventilation.

P33

Increased spatial distribution of airflow in lungs with low-level pressure support ventilation compared with maintenance ventilation

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Introduction Vibration response imaging (VRI) is a novel technology that utilizes sophisticated software and surface skin sensors placed on the back to record, analyze and display vibrations as a non-invasive measure of lung ventilation.

Hypothesis Compared with assist volume control ventilation (AVC), pressure support ventilation (PSV) will result in a greater spatial distribution of lung airflow.

Methods We performed serial VRI during maintenance AVC and immediately following initiation of a spontaneous breathing trial using low-level PSV in 26 mechanically ventilated patients. Recordings were performed over 12–20 s periods of respiration. Respiratory cycles free of noise or motion artifacts were chosen for analysis, and images at mid-inspiration were analyzed. Areas of images were calculated digitally using the program ImageJ. The areas of right and left lung measured at mid-inspiration were

summed, and compared, AVC vs PSV. Statistical analysis was performed using a *t* test and the *t* distribution.
Results The tidal volume (VT) was 534.8 ± 69.4 ml for AVC and decreased to 407.6 ± 152.1 ml for PSV ($P = 0.00015$). The mean areas of both lungs were 68.75 ± 11.06 and 71.57 ± 10.50 (mean in kilopixels ± SD) in the AVC and PSV images, respectively ($P = 0.00985$). There was a mean increase of 4.73 ± 9.09% in the areas of the lungs during PSV compared with AVC ($P = 0.039$).
Conclusions Despite a lower VT, PSV (compared with ACV) produced a greater spatial distribution of lung airflow. Possible mechanisms of this PSV-associated increase are the increase in patient-generated negative intrapleural pressure during inspiration and better synchronization of patient-negative pressure with positive pressure from the ventilator. VRI allows a non-invasive quantitation of airflow distribution during different modes of mechanical ventilation.

P34

Effects of different spontaneous breathing modes on respiratory mechanics and gas exchange

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Objective In patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) the use of spontaneous breathing modes in mechanical ventilation can be beneficial. Nevertheless the opportunity to combine different forms of assisted ventilation is not sufficiently investigated. We evaluated the effects of the combination of different modes of spontaneous ventilation on respiratory mechanics and gas exchange in patients with ALI or ARDS.
Design A prospective, interventional study.
Setting ICU of a university hospital.
Patients Seven patients who were ventilated mechanically for at least 24 hours due to acute respiratory insufficiency.
Methods Each patient was ventilated using one of four ventilation modes for a time period of 45 min, followed by a 15-min equilibration period. All four respiratory settings were applied in randomly assigned order in every patient. A: biphasic positive airway pressure (BIPAP); B: BIPAP in combination with pressure support (BIPAP + PSV); C: BIPAP in combination with automatic tube compensation (BIPAP + ATC); D: pressure support ventilation in combination with ATC (PSV + ATC). In every ventilator setting all patients had spontaneous breathing efforts in at least 30% based upon minute ventilation (VE). The settings were adjusted to achieve a tidal volume (VT) of 6–8 ml/kg body weight. Hemodynamic data were obtained every 15 min and at the end of each period blood gas analyses were obtained. The primary endpoints were the patient's work of breathing obtained by the Bicore CP-100 pulmonary monitor (Bicore, Irvine, CA, USA).
Results The mean tidal volume was 6.51 ± 0.36 ml/kg body weight. In combination with automatic tube compensation, inspiratory pressure support obtained the highest work of breathing in all tested modes (A: 0.80 ± 0.15 J/l vs B: 0.86 ± 0.17 J/l vs C: 0.96 ± 0.19 J/l vs D: 1.47 ± 0.22 J/l). Hemodynamic parameters and indices of pulmonary gas exchange did not differ between the tested modes.
Conclusions Our results show that PSV in combination with ATC obtained the highest work of breathing. A possible reason is that PSV assists every single breath and acts more like controlled ventilation than an assisting mode. The combination of different modes of spontaneous breathing has no benefit on the work of breathing the patient had to obtain when BIPAP is used as the primary ventilator mode.

P35

Vibration response imaging of the lungs in mechanically ventilated patients in chronic obstructive pulmonary disease

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Introduction Vibration response imaging (VRI) measures the vibration response energy generated from airflow to create a radiation-free, dynamic, real-time, structural and functional image of the respiration process. The characteristics of VRI in mechanically ventilated patients with chronic obstructive pulmonary disease (COPD) has not been previously studied.
Hypotheses This was an observational study to compare the VRI of mechanically ventilated (MV) patients with no known pulmonary disease with those with COPD.
Methods Five consecutive MV patients with COPD were compared with five consecutive MV patients with no known pulmonary disease. Using custom-designed software the vibration signals were fitted to a mathematical function and a gray level frame was constructed. At peak inspiration and expiration, spatial areas of the images were captured and the total area of the image calculated using Image J Software.

Table 1 (abstract P35)

Distribution of image area in patients with no pulmonary disease

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Inspiration	93,735	55,618	55,573	86,432	79,791
Expiration	85,490	50,005	38,919	82,362	73,858

Table 2 (abstract P35)

Distribution of image area in patients with COPD

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Inspiration	25,831	60,0085	51,195	72,372	24,229
Expiration	64,484	63,139	71,231	73,628	57,300

Results In patients with normal lungs, the spatial distribution of the maximal signal expiratory vibration response image was lower than the maximal signal during inspiration. The mean decrease in area was 8103 pixels + 20,606 ($P = 0.01$) (Table 1). In patients with COPD the spatial distribution of the maximal signal expiratory vibration response image during expiration was higher than the maximal signal inspiratory image. The mean increase in area was 19,214 pixels + 6552 ($P = 0.03$) (Table 2).
Discussion The increase in the image area during the expiratory phase in COPD patients may reflect increased airflow resistance causing increased vibration energy. Air trapping and auto-PEEP are other possible mechanisms accounting for the expiratory increase in image area.
Conclusion VRI provides real-time non-invasive lung imaging of airflow in the mechanically ventilated patient. Mechanically ventilated COPD patients demonstrate a dramatically different VRI pattern than normal MV patients. VRI may provide important diagnostic information in COPD patients.

P36

Effects of connecting tubes and swivels on the breathing pattern and work of breathing during pressure support ventilation: a laboratory and simulation study

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Introduction The influence of the resistance of endotracheal tubes (ETT) on the additional work of breathing (WOB) has been extensively evaluated. However, not only the ETT resistance causes additional WOB, but also the connecting tubes and swivels (CT+S) that are placed between the Y-piece and ETT. This study was performed to test the hypothesis that CT+S significantly increase the resistance of the breathing circuit with the consequence of increased WOB during PSV.
Methods Four different types of CT+S (Rüsch, Medisil, Medisize, Mallinckrodt) were ventilated using a sinusoidal flow pattern, and the flow-dependent pressure drop across the CT+S was recorded. Flow dependency of the pressure drop was determined by fitting Rohrer's equation ($\Delta P = K1*V' + K2*V'^2$). The resulting coefficients K1 and K2 were used in a mathematical simulation of PSV ventilation to calculate the influence of CT+S on breathing pattern, minute ventilation (VE) and WOB in simulated normal, obstructive and restrictive patients.
Results The resistance of the different models of CT+S widely varied. The CT+S type used in our ICU had a resistance of 3.1 mbar/l/s (at 1 l/s), comparable with a #9 ETT. Dependent on the patient's disease and muscle strength (Pmus) and on the ventilatory demand, the use of CT+S reduced minute ventilation by up to 13% (Fig. 1). If the additional WOB is accomplished by the patient, he/she has to increase the Pmus by up to 45% (Fig. 2). If the pressure support is increased instead, an additional pressure of up to 37% has to be applied (Fig. 3). In some simulated patients with pulmonary obstructive disease, this additional pressure support caused missed efforts and additional dynamic hyperinflation. Interestingly, in simulated pulmonary restriction, a paradox effect of the additional resistance on tidal volume during PSV was observed: the reduction of peak inspiratory flow led to a delayed cycling of inspiration. As the cycling criterion during PSV (flow drop to 25% of peak inspiratory flow) results in a very short inspiratory time in these patients, a delayed cycling led to an increased inspiratory time and hence to an increased tidal volume.
Conclusions The resistance of CT+S adds significant load to the respiratory system. CT+S consisting of low resistive parts should therefore be preferred. In restrictive patients, PSV without variable cycling may be an inappropriate mode.

P37

The intensive care requirements and need for early ventilatory support in patients undergoing emergency and elective spinal surgery

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Background Patients undergoing emergency or elective spinal surgery often require mechanical ventilation for prolonged periods because of their inability to protect their airways, persistence of excessive secretions, and inadequacy of spontaneous ventilation. Tracheostomy plays an integral role in the airway management of such patients; however, its timing still remains subject to considerable practice variation
Study design A retrospective review of all spinal surgery admissions to the ICU and high dependency unit (HDU) from the National Spinal Injuries Unit (NSIU) at the Mater Misericordiae University Hospital over a 4-year period ($n = 152$).
Objective To assess the intensive care requirements of a tertiary referral centre specializing in acute spinal cord injury and diseases of the spine, and to identify risk factors associated with respiratory compromise in the spinal surgery patient.
Methods A retrospective review of all spinal surgery admissions from the NSIU to the ICU and HDU at the Mater Misericordiae University Hospital between 1 January 2002 and 30 September

Figure 1 (abstract P36)

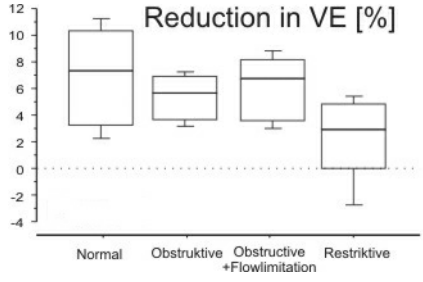


Figure 2 (abstract P36)

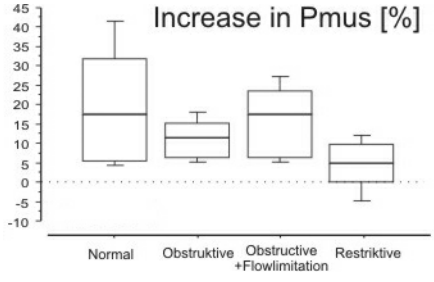
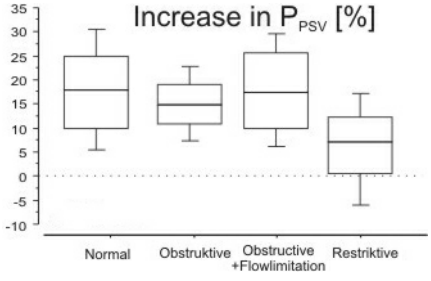


Figure 3 (abstract P36)



2005 ($n = 152$). The Hospital Inpatient Enquiry System, NSIU and ICU databases were used to identify our study cohort. The medical records, ICU records and the computerized hospital inpatient system were utilized to gather all relevant data. Parameters evaluated included demographics, vertebral level, APACHE II score, forced vital capacity, tracheostomy placement, pneumonia, premorbid pulmonary disease, smoking history, evidence of direct thoracic/lung trauma, operative intervention, associated appendicular trauma, and pre-existing medical comorbidities.

Results There were 152 spinal admissions to the ICU between 1 January 2002 and 30 September 2005. The average length of stay was 6.6 days (range 1–35 days). Ninety-eight patients were subsequently admitted to the HDU for further intensive management. The average stay for the HDU admissions was 6.5 days (range 1–58 days). Tracheostomies were performed in 36 of these 152 patients (24%). The percentage of high cervical spinal cord injuries was 35% (54/153). We found a significant correlation between high cervical spinal cord injury and respiratory compromise warranting tracheostomy placement, with a relative risk ratio of >1.0.

Conclusion Several risk factors were identified corresponding to frequent tracheostomy placement in patients undergoing major spinal surgery. Early tracheostomy may be considered in patients with multiple risk factors to reduce the duration of stay in the ICU and facilitate the weaning of ventilatory support.

P38

Effect of inspiration rise time on work of breathing and patient comfort during pressure support ventilation

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Introduction Pressure support ventilation is widely used in patients in the ICU. Matching the patient's respiratory needs with adequate ventilator settings is necessary to ensure a low work of breathing (WOB) and maximal patient comfort. The inspiratory rise time (IRT) determines the time to reach the selected airway pressure. A short IRT results in a high peak inspiratory flow and a short time to reach that peak, but is also associated with the development of turbulent flow, resulting in increased WOB. The aim of this study was to investigate the effects of different IRT settings on WOB and patient comfort during pressure support ventilation.

Methods We performed a prospective, single-blind cohort study in patients on pressure support ventilation. Ten healthy adult patients admitted to the ICU after elective facial or neck surgery were included. All patients were ventilated in the pressure support mode using a Servo 300 ventilator (Siemens, Elema, Solna, Sweden), with a positive end expiratory pressure (PEEP) of 5 cmH_2O, a pressure support level of 12 cmH_2O above PEEP and an inspiratory oxygen fraction of 0.40. Patients were awake and cooperative (Ramsay 2). WOB was measured with an esophageal balloon and a miniature flowmeter (Bicore system). Breathing comfort was evaluated using a visual analogue scale (VAS) ranging from 1 to 10. WOB and patient comfort was measured (in random order) at 0, 5, and 10% IRT. For statistical analysis, two-way analysis of variance was used. $P < 0.05$ was considered statistically significant.

Results An interim analysis was performed after four of a total of 10 patients. The WOB increased from 0.25 ± 0.11 J/l at 0% IRT to 0.48 ± 0.01 J/l at 5% IRT and 0.59 ± 0.21 J/l at 10% IRT (values expressed as mean ± SD). At the same time the patients comfort as analysed by the VAS decreased from 5.5 (4.0–7.75) at 0% IRT to 4.5 (3.0–6.5) at 5% IRT and 2.0 (1.0–3.75) at 10% IRT (values expressed as median [IQR]). Analysis of all patient data with a complete statistical analysis will be available soon.

Conclusions With increasing IRT the WOB increases and patient comfort decreases. In this category of patients we therefore suggest using the shortest IRT (0%).

P39

Effects of change in the expiratory trigger during pressure support ventilation in COPD

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Critical Care 2006, **10(Suppl 1):**P39 (doi:10.1186/cc4386)

Introduction During pressure support ventilation (PSV) the ventilator cycles from inspiration to expiration when the inspiratory flow reaches a given percentage of the peak inspiratory flow 'expiratory trigger' (ET). On the most recent available ventilators it is possible to modify the percentage of the ET.

Objective We evaluated in a group of COPD patients during PSV the change of ET (high 40% and low 5% of the peak inspiratory flow, respectively) in terms of the pattern of breathing and inspiratory effort (pressure time product [PTP]).

Materials and methods Nine COPD patients were studied during respiratory failure (PaO_2/FiO_2 295 ± 108, PEEP 6.2 ± 1.7 cmH_2O, mean age 70 ± 2 years, and BMI 25.4 ± 4.3). PSV was set at 5 cmH_2O without PEEP while the oxygen fraction remained constant during the study. Airway, esophageal, gastric pressures and airflow were measured.

Results See Table 1.

Table 1 (abstract P39)

	Respiratory rate (bpm)	Tidal volume (ml)	Cycling flow (l/s)	PTP (cmH_2O*s*min)
Low ET	26.6 ± 7.5	361 ± 118	0.04 ± 0.01	313 ± 81
High ET	26.4 ± 8.1	352 ± 93	0.17 ± 0.04†	284 ± 85

†Statistically significant.

Conclusions The change of percentage of ET at a low level of PSV did not modify the inspiratory effort and pattern of breathing.

P40

Effects of different spontaneous breathing modes on hemodynamics in patients after coronary artery bypass graft surgery

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Critical Care 2006, **10(Suppl 1):**P40 (doi:10.1186/cc4387)

Objective During mechanical ventilatory support the use of spontaneous breathing modes can be beneficial. Nevertheless the opportunity to combine different forms of assisted ventilation is not sufficiently investigated. We evaluated the effects of the combination of different modes of spontaneous ventilation on global end-diastolic volume and cardiac output in patients after elective coronary artery bypass graft surgery.

Design A prospective, interventional study.

Setting ICU of a university hospital.

Patients Eight postoperative patients who underwent elective coronary artery bypass graft surgery.

Methods After admission to the ICU each patient was ventilated using one of three ventilation modes for a time period of 30 min, followed by a 15-min equilibration period. All three respiratory settings were applied in randomly assigned order in every patient. A: biphasic positive airway pressure (BIPAP); B: BIPAP in combination with pressure support ventilation (BIPAP + PSV); C: pressure support ventilation (PSV). In every ventilator setting, all patients had spontaneous breathing efforts in at least 30% based upon minute ventilation (VE). The settings were adjusted to achieve a tidal volume (VT) of 6–8 ml/kg body weight. At the end of each 30-min period bolus thermodilution-derived cardiac output was obtained from thermodilution curves detected in the femoral artery. Three intermittent consecutive boli consisting of 10 ml ice-cold saline were randomly injected over the ventilatory cycle. The primary endpoints were the global end-diastolic volume and the cardiac output obtained by the PICCO monitor (Pulsion Medical AG, Munich, Germany).
Results The mean tidal volume (VT) was 7.81 ± 0.31 ml/kg body weight. The mean airway pressure was A: 8.80 ± 1.36 mbar vs B: 8.72 ± 0.90 mbar vs C: 8.33 ± 1.73 mbar (P = not significant). No differences were found for GEDV (P = 0.99), stroke volume (P = 0.23) and cardiac output (P = 0.35). Respiratory parameters and indices of pulmonary gas exchange did not differ between the tested modes.
Conclusions The combination of different modes of spontaneous breathing has no different effects on hemodynamic parameters of patients after elective coronary artery bypass graft surgery when the mean airway pressure did not change.

P41

Streamlining the weaning process within a UK critical care network

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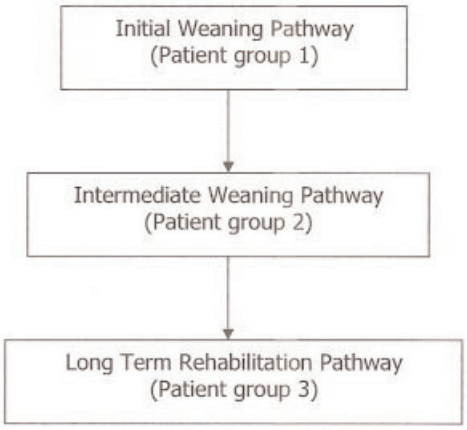
Critical Care 2006, **10(Suppl 1):**P41 (doi:10.1186/cc4388)

Current UK practice demonstrates that weaning from mechanical ventilation (MV) is an ad-hoc process, where weaning is not valued and there is a paucity of research related to weaning compared with North America and other European countries. Evidence exists outside the United Kingdom that proactive approaches to weaning yield benefits to service and coordination form a dedicated, experienced practitioner within a systematic framework generates positive outcomes.
The Surrey Wide Critical Care Network (SWCCN) comprises four district general hospitals with a total of 30 level-3 critical care beds. A weaning audit was undertaken by the SWCCN Nurse Consultant across all four ICUs over a 3-month period in 2003. The audit demonstrated that the process of weaning was often inconsistent and at times haphazard, especially in relation to those patients who have difficulty in weaning from MV. This often led to an unnecessary increase in ICU length of stay (LOS). The audit also established that patients weaning from MV can be identified into three groups: (1) those patients who will wean from MV within 24–72 hours; (2) those patients who will wean from MV within 3–21 days; and (3) those patients who will have a prolonged stay in ICU and a complex weaning process greater than 21 days.
In order to streamline and coordinate the whole weaning process and effectively manage the three groups of weaning patients across the SWCCN, a systematic evidence-based framework with three distinct pathways was developed and implemented within in all four ICUs by the Network Nurse Consultant (Fig. 1).
Following 1 year of implementation the framework was audited and demonstrated the following:

Figure 1 (abstract P41)



Weaning pathway.

- The process of weaning all three patient groups within all four ICUs was much more systematic and consistent.
- A reduction in ITU LOS in patient groups 1 and 2.
- Quicker identification and placement onto the rehabilitation pathway of those patients who would require a prolonged ITU stay and have complex weaning problems. Their management and care was much more coordinated.
- Symbiosis of ventilation care bundle and weaning framework.
- Identification for the need of a specialist regional weaning unit.

P42

Weaning from mechanical ventilation using pressure support and T-tube induces ventricular arrhythmia in cardiac patients

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Critical Care 2006, **10(Suppl 1):**P42 (doi:10.1186/cc4389)

Introduction Weaning from mechanical ventilation (MV) can be associated with cardiac arrhythmias. Few studies are found comparing their occurrence during weaning with pressure support ventilation (PSV) and T-tube (TT) in patients with and without heart disease.
Objective To evaluate the occurrence of arrhythmias in these groups of patients during PSV and TT.
Methods Patients without (group 1) and with (group 2) heart disease, under mechanical ventilation for at least 48 hours, were observed during 30 min of PSV or TT, in a random order. Variables analyzed were: age, APACHE score, length of stay in the ICU (LOS), and cardiorespiratory variables including respiratory rate, rapid shallow breathing index (f/VT), maximum inspiratory (PImax) and expiratory (PEmax) pressure. A continuous ECG was recorded by the Holter method. For statistical analyses, repeated-measures ANOVA or ANOVA on ranks was used.
Results Twenty-two patients were studied, 13 in group 1 and nine in group 2. Comparisons between groups 1 and 2 showed: no differences in APACHE score (23 ± 4; 23 ± 8, not significant), PImax (32 ± 19; 28 ± 12 cmH_2O, not significant) and PEmax (24 ± 10; 20 ± 7 cmH_2O, not significant); f/VT was greater in cardiac patients during TT (PSV: 48 ± 25 versus 41 ± 18; TT: 42 ± 18 versus 57 ± 20, ANOVA, $P < 0.05$), as well as the

respiratory rate (PSV: 21 ± 6 versus 20 ± 5; TT: 22 ± 6 versus 25 ± 6, ANOVA, $P < 0.05$). The occurrence of ventricular arrhythmias (median and interquartile ranges), respectively, in PSV and TT in group 1 were 1 (0–13) vs 1 (0–5.5) and in group 2 were 3 (0.5–87) vs 21 (4–61) (ANOVA, $P < 0.05$).
Conclusions During weaning from MV, cardiac patients showed a higher respiratory rate and higher f/VT during TT when compared with PSV, as well as a greater occurrence of ventricular arrhythmias in both methods when compared with noncardiac patients.

P43

Non-invasive mechanical ventilation can be useful during difficult weaning from invasive ventilation

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Critical Care 2006, **10(Suppl 1):**P43 (doi:10.1186/cc4390)

Introduction Non-invasive mechanical ventilation with positive pressure (NPPV) has been investigated in several acute respiratory failure situations. There are some doubts considering its benefits during weaning from invasive mechanical ventilation (IMV).
Objective To evaluate the use of NPPV in patients with difficult weaning characterized by failure in a spontaneous breathing trial (SBT).
Methods All patients under IMV for more than 48 hours from June 2003 to February 2005 were submitted to a SBT. Those that failed during the first 30 min of a T-piece trial, and without contraindications to NPPV, were randomized back to IMV (conventional treatment) or changed to NPPV. Contraindications to NPPV included patients with facial trauma or cranial surgery, recent gastric or esophagic surgery, tracheostomy, respiratory secretion excess, agitation and noncooperative behaviour that were excluded from the experiment. Inclusion in the experiment was authorized by signed informed consent. Previous to subjecting the patient to SBT we collected a sample of arterial blood gases and we measured the maximal inspiratory pressure (PImax). During spontaneous ventilation in the T piece, in the 1st and 30th min measurements of tidal volume (VT), minute ventilation (Ve), respiratory rate (f), rapid shallow breathing index (f/VT), heart rate and peripheral oxygen saturation were taken. After randomization to IMV or NPPV, patients were followed clinically and evaluated concerning the time of ventilation, length of stay (LOS) in the ICU and in the ward, complications and the mortality rate.
Results Out of 156 patients, 65 (42%) failed in the T-piece trial, of which 28 were submitted to NPPV and 37 were maintained under IMV. The average ages of the NPPV and IMV groups were 67.6 ± 15.5 and 59.7 ± 17.6 years, respectively. Chronic pulmonary disease aggravation, heart diseases and postoperative respiratory failure were the most frequent causes of IMV use. Ventilation time previous to SBT was 7.3 ± 4.1 days for both groups. Cardiac and respiratory parameters were similar for both groups, either at 1 or 30 min of SBT as well as during their follow-up. The percentage of complications in the NPPV group was lower than in IMV (28.6% vs 75.7%), with lower incidence of pneumonia and tracheostomy. Death occurred in 29% in the NPPV and 22% in the IMV group (not significant). LOS in the ICU was similar for both groups (10.3 ± 9.4 for NPPV vs 11.8 ± 9.1 days for IMV) and LOS in the ward was lower for the NPPV group (9.6 ± 12.7 vs 15.0 ± 18.6 days, not significant).
Conclusions NPPV can be used as a good ventilation procedure for patients with difficulties during weaning from mechanical ventilation. It is related to a lower incidence of ventilation-associated pneumonia and a lower need for tracheostomy.

P44

Echocardiographic assessment during weaning from mechanical ventilation: pressure support ventilation versus T-tube

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Critical Care 2006, **10(Suppl 1):**P44 (doi:10.1186/cc4391)

Introduction Physiologic changes occurring during transition from mechanical ventilation (MV) to spontaneous ventilation can overload the cardiorespiratory system and cause difficulties in the weaning process. There are few reports studying myocardial function during weaning from MV.
Objective To evaluate cardiorespiratory parameters and cardiac function during weaning from MV.
Methods Patients under MV for more than 48 hours and prone to weaning were observed during 30 min of pressure support ventilation (PSV) and T-tube, in a random order, and with a rest period of at least 30 min between methods. Variables analyzed were: age, APACHE score, underlying disease, period of MV, length of stay (LOS) in ICU and hospital, basal ventilatory parameters, cardiorespiratory parameters in the first and 30th min, ECG, echocardiogram and blood gas analysis in the 30th minute in both methods. Echocardiographic parameters, obtained at the end of expiration with the patient in a position offering the best window, included: measurements of heart cavities; ejection fraction; acceleration of the E wave of mitral inflow (MI); deceleration of the E wave of MI; duration of the A wave of MI; isovolumetric relaxation time (IRT); mitral E/A ratio and myocardial performance index (MPI). Values obtained during PSV and T-tube were compared using a *t* test.
Results Sixteen patients (mean age 53 ± 20 years and APACHE score 17 ± 6) have been analyzed up to now. The majority of patients had neurologic diseases. The period of MV was 25 ± 25 days and the LOS in the ICU was 35 ± 35 days. Twelve patients were extubated and four failed during the T-tube trial. Comparisons between PSV and T-tube showed similar results concerning cardiorespiratory parameters as well as echocardiographic measurements. The difference between patients that failed and those successfully extubated was a lower level of PaO_2 as well as a higher value of rapid shallow ventilation index during T-tube.
Conclusions In our preliminary results in this group of patients under weaning from mechanical ventilation, echocardiographic assessment of cardiac function showed no differences when comparing PSV with T-tube.

P45

Predictors of early extubation (within 4 hours) in adult cardiac surgical patients

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Critical Care 2006, **10(Suppl 1):**P45 (doi:10.1186/cc4392)

Background The extubation time after cardiac surgery and its impact on outcome have been extensively studied recently. Many studies reported that early extubation (within 8 hours) appears to be safe without an increased incidence of morbidity. Some intraoperative and preoperative factors may have an important influence in predicting early extubation and determining strategies to optimize postoperative therapy.

Objective To investigate predictors of early extubation.
Design A prospective cohort study.
Setting A 19-bed medico-surgical ICU in a private hospital.
Patients All 104 patients admitted after cardiac surgery.
Measurements and results One hundred and four cardiac surgical patients were admitted to our ICU from March to November 2005; 63 (60.6%) were male; 85 (81.7%) were submitted to coronary artery bypass grafts, 17 (16.3%) to valvular replacement and 23 (2%) to combined surgery. The mean extubation time was 8.9 ± 21.96 hours. Patients were divided into two groups: early extubation (EE – within 4 hours) (n = 56 [53.8%]) and late extubation (LE – after 4 hours) (n = 48 [46.2%]). Mean extubation times for EE and LE were 2.52 ± 1.49 hours and 16.52 ± 30.7 hours ($P < 0.001$), respectively. Multivariate logistic regression analysis showed that the use of peridural anesthesia was the best independent predictor of early extubation (OR = 9.37, 95% CI 2.19–40.17). The presence of acute coronary syndrome and the Ontario score were also independent predictors of early extubation (OR 7.17 with 95% CI 1.99–25.77 and OR 0.648 with 95% CI 0.5–0.84, respectively). The Ontario score had an area under the receiver operating curve of 0.731 (95% CI 0.635–0.826), with the best cutoff value of ≤5 points.
Conclusions In this cohort, use of peridural anesthesia was the best predictor of early extubation after cardiac surgery. The presence of acute coronary syndrome and a low Ontario score also were independent predictors of successful early extubation. This conclusion raises the hypothesis that patients with an elevated Ontario score could benefit from peridural anesthesia to be extubated earlier.

P46

Norepinephrine use at the time of extubation was not associated with weaning failure from mechanical ventilation in septic patients

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Critical Care 2006, **10(Suppl 1):**P46 (doi:10.1186/cc4393)

Background Weaning may represent 40% of the time spent by patients on mechanical ventilation (MV). A stable cardiovascular system and minimum dose of vasopressor medication is required to withdraw from MV in current guidelines. We found no evidence to support this practice, and this can lead to an unnecessary prolonged time of MV.
Objective To evaluate whether the use of norepinephrine (NE) interferes with weaning success (WS) in septic patients.
Design A prospective observational clinical study.
Methods All patients were on MV for more then 48 hours. Patients able to be weaned according to the institutional protocol were submitted to a spontaneous breathing trial (SBT) during 30 min and followed for 48 hours after extubation. All patients had blood gas analyses, hemodynamic (heart rate [HR], mean arterial pressure [MAP]) and ventilatory parameters (respiratory rate, tidal volume, f/Vt, maximal inspiratory pressure [MIP]) recorded. The outcome was a return to MV within 48 hours after extubation. Data are expressed as mean ± SD and were compared by two-way t test and chi-squared; $P < 0.05$ was considered significant.
Results Sixty-three septic shock patients were included from January to September 2004. Mean age was 59.6 ± 17.6 years and APACHE II score was 20.3 ± 6.5. The reintubation rate was 19% and mortality was 15.9% overall. Clinical, hemodynamic and ventilatory variables were not related to weaning outcome. During acute illness, the maximal NE dose was 0.52 ± 0.29 and 0.12 ± 0.10 μg/kg/min at SBT. Neither the maximal NE dose during septic shock nor the NE dose during SBT were different between weaning failure (WF) and weaning success (WS) patients (Table 1).
Conclusion NE use was not a contraindication to weaning and extubation from MV in patients recovering from septic shock.

Table 1 (abstract P46)

Parameters	WS (n = 51)	WF (n = 12)	P
Age (years)	58.7 ± 18.4	63.1 ± 13.6	ns
Gender (male/female)	31/21	9/3	ns
MV (days)	9.8 ± 6.2	8.0 ± 3.9	ns
Glasgow score	14 ± 1.7	14.9 ± 0.3	ns
APACHE II score	19.8 ± 6.5	22.3 ± 5.9	ns
PaO_2/FiO_2	285 ± 178	296 ± 131	ns
RR (rpm)	24.5 ± 6.9	29.4 ± 6.4	0.03
MIP (cmH_2O)	40.6 ± 13.7	44.2 ± 16.8	ns
CROP index	40.1 ± 25.1	33.2 ± 22.6	ns
f/Vt	62.1 ± 38	79 ± 45	ns
MAP (mmHg)	90 ± 13	93 ± 13	ns
HR (bpm)	96 ± 18	93 ± 22	ns
Maximal NE	0.51 ± 0.27	0.59 ± 0.39	ns
SBT NE	0.14 ± 0.11	0.11 ± 0.10	ns

ns, not significant.

P47

Outcome predictors of non-invasive positive pressure ventilation in hypoxaemic acute respiratory failure

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Critical Care 2006, **10(Suppl 1):**P47 (doi:10.1186/cc4394)

Objective To determine outcome predictors of non-invasive positive pressure ventilation (NIPPV) in patients with hypoxaemic acute respiratory failure (HARF).
Design Retrospective analysis.
Method One hundred patients with HARF treated with NIPPV in a 30-bed tertiary care hospital were analysed. A successful outcome of NIPPV was avoiding endotracheal intubation, and failure was considered if intubation was needed. We classified the patients into three etiological subgroups: (1) acute cardiogenic pulmonary edema (ACPE), (2) acute respiratory distress syndrome (ARDS) secondary to sepsis, and (3) miscellaneous group including pulmonary embolism, bronchial asthma exacerbation, postoperative respiratory failure, status post-extubation, etc. We compared various patient variables and parameters among successful and failure groups.
Results The overall success rate of NIPPV was 56% in avoiding intubation. The success rate in the ACPE, sepsis-related ARDS and miscellaneous subgroups were 71.79%, 29.26% and 80%, respectively. Logistic regression analysis exhibited duration of NIPPV (OR 4.137, $P = 0.02$), number of organ failures besides the respiratory system (negative coefficient −1.4193) and post-NIPPV PO_2/FiO_2 ratio ($P = 0.0342$) as significant predictors of outcome of NIPPV. In subgroup analysis of ACPE, left ventricular ejection fraction >30% was a predictor of successful outcome. In subgroup analysis of sepsis-related ARDS, a lower PO_2/FiO_2 ratio and a higher number of organ failures were associated with unfavourable outcome ($P = 0.02$ and $P = 0.0184$).
Conclusion In HARF, ACPE as a cause of ARF, shorter duration of NIPPV, higher post-NIPPV PO_2/FiO_2 ratio and fewer organ failures

were associated with a favourable outcome of NIPPV. In subgroup analysis of ACPE, left ventricular ejection fraction >30% was a predictor of successful outcome of NIPPV. In subgroup analysis of sepsis-related ARDS, a lower PO_2/FiO_2 ratio and higher number of organ failures were associated with poorer outcome.

P48

The learning, introducing and effects of a non-invasive respiratory support programme with the infant-flow method in newborns: Polish 2-year experience

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Introduction Mechanical ventilation results in an increased risk of pulmonary complications in the newborns treated for respiratory failure in NICUs.
Aim This abstract reports on our 2-year experience with the application programme of the infant flow (IF) method in infants (in 67 neonatal centres in Poland between 1 August 2003 and 30 April 2005).
Methods We reviewed collected data of 1321 newborns (male/female 799/522; range of gestational age 22–45 weeks; birth weight 480–4950 g).The indications for treatment were categorized into three classes: RDS, weaning and other.
Results The IF method enabled us to avoid intubation in these groups in 77.8%, 61.2% and 77.9%, respectively. The lowest rate of complications compared with the two other groups was in the RDS group (Table 1). Low gestational age was associated with a statistically significantly lower rate of successes than higher gestational age: 62.7 and 83%. A similar effect was seen while comparing success rates of newborns by weight: 60.7 and 82.4%. The incidence of pneumothorax was 1.1%. Among extrapulmonary complications PDA occurred in 12.8%; ROP 11.9%; IVH 7.4%; PVL 3.6% of infants. Occurrence of local complications was infrequent, as shown in Table 2.

Table 1 (abstract P48)

Indication	BPD	CLD	ROP	IVH	PVL	PDA
RDS	7.6%	3.5%	4.4%	3.7%	1.8%	4.0%
Weaning	42.2%	26.9%	25.6%	15.3%	7.6%	29.1%
Other	35.1%	16.5%	19.7%	9.2%	4.6%	21.1%

Table 2 (abstract P48)

Year	RDS	Weaning	Other
2003	4/64 (6.2%)	8/97 (8.2%)	3/23 (13.0%)
2004	43/386 (11.1%)	18/129 (14.0%)	5/69 (7.2%)
2005	47/318 (14.8%)	18/81 (22.2%)	2/62 (3.2%)

Conclusions The results strongly suggest that the IF method is effective and clinically valuable. Some typical problems consistent with the 'learning curve' phenomenon were observed during the study.

P49

Non-invasive ventilation in trauma patients: is there a role?

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Critical Care 2006, **10(Suppl 1):**P49 (doi:10.1186/cc4396)

Background In the ICU non-invasive ventilation (NIV) allows one to reduce the complications related to endotracheal intubation and mechanical ventilation (e.g. increased infections), and it could improve the outcome of patients in certain clinical conditions. Actually only few trials support the use of NIV in trauma patients and its use is limited in this clinical setting.
Methods We performed a retrospective evaluation of 29 patients with major trauma admitted to our ICU over a 2-year period from January 2004 to December 2005 (ISS 25.97 ± 10.29, SAPS II 25.31 ± 9.38). All patients had thoracic trauma, and four patients had associated head trauma. Twenty-four patients have been treated with CPAP delivered by helmet, two patients were ventilated with PSV by face mask, two with PSV by TotalFace Mask®, and one with both PSV by TotalFace Mask® and CPAP by helmet. The indications for NIV have been: in 21 cases traumatic pulmonary contusion, in four cases atelectasis, in three cases pneumonia and in one case reduction in chest wall compliance. In 18 patients NIV has been employed for weaning from invasive mechanical ventilation, and in the other 11 patients NIV was the first mode of ventilatory assistance. We evaluated the ability of NIV to improve oxygenation (P/F ratio).
Results Patients have been treated with NIV for 4.41 ± 2.33 days. Twenty-five patients (86.2%) significantly improved oxygenation after NIV (Table 1) (*t* test; $P < 0.001$) and were discharged from the ICU. Four patients failed the NIV and were intubated (in two patients NIV had been used for weaning): in this subgroup of patients two died of septic shock from pneumonia. In the subgroup of intubated patients the duration of mechanical ventilation was 7.17 ± 5.02 days and the length of stay in the ICU was 14 ± 5 days. Mortality in the NIV group was 13.8%.

Table 1 (abstract P49)

ISS	25.97 ± 10.29
SAPS II	25. 31 ± 9.38
P/F before NIV	200.6 ± 50.9
P/F after NIV	284.4 ± 88.5

Conclusions NIV has proved to ensure adequate oxygenation and to be successful in respiratory assistance of patients with thoracic trauma. It could be considered a valid alternative to endotracheal intubation in trauma patients requiring ventilatory support. Further investigations are needed to evaluate the incidence on outcome and to define indications.
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P50

In vitro comparison of the standard and the Cole endotracheal tubes with an endotracheal tube of new design

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Aim To assess *in vitro* the usefulness of three paediatric uncuffed endotracheal tubes of various shapes: a standard (one-diameter) tube, a Cole tube and the newly designed cone tube, use of which is not associated with an increased risk of periglottic trauma.
Methods The flow (0–30 lpm) resistance (RETT) was measured across the length of each tube and repeated for similar tubes of internal diameters 3, 3.5 and 4 mm. The imposed work of breathing (WOBI), necessary to overcome the tube resistance, the patient's resistive work of breathing (RWOB) and the pressure–time product (PTP) were determined from the computer simulation of a spontaneous breathing, intubated infant.
Results The resistance of the 3.5 mm ID cone tube to 10 lpm air flow was 44% and 6% lower when compared with the resistance offered by the standard and the Cole tubes, respectively. The WOBI necessary to overcome the cone tube resistance was approximately 44% and 6% lower than with using the standard and the Cole tubes, respectively. The RWOB and PTP of the virtual infant intubated with the cone and with the Cole tubes were similar; however, the values of both parameters decreased by 18% and 8%, respectively, in comparison with the situation when a standard tube was used.
Conclusion Replacement of a standard endotracheal tube with the cone or Cole tubes resulted in a significant decrease of RETT, WOBI, RWOB and PTP.
Acknowledgement The study has been supported by the Foundation for Polish Science.

P51

Influence of rhDNAse on the duration of mechanical ventilation in intensive care patients: interim analysis of the LUFIT trial

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Background rhDNAse is effective in the treatment of children with cystic fibrosis [1]. A significant reduction of the duration of ventilation by rhDNAse has been reported in children following cardiac surgery [2].
Objective To investigate whether rhDNAse is able to reduce the duration of ventilation in adult mechanically ventilated intensive care patients.
Methods After approval of the local ethics committees we conducted a double-blind, placebo-controlled, randomised, multicentre national trial. Patients were stratified into two subgroups depending on their status as surgical or nonsurgical. The trial was started within 48 hours after the start of mechanical ventilation and lasted until weaning was successful. Patients in the active treatment group received 2.5 ml rhDNAse endotracheally twice a day. Patients in the placebo group received the same amount of normal saline. This interim analysis reviewed 98 nonsurgical patients. Data from 85 patients were included in the analysis.
Results Forty-four patients in the study group and 41 patients in the placebo group were analysed. Factors such as gender, weight, smoking habit, chronic pre-existing diseases and prevalence of COPD were distributed equally in both groups. Three patients died in the rhDNAse group versus eight in the placebo group. The median duration of ventilation was 140 hours (CI 120–200 hours) in the rhDNAse and 324 hours (CI 178–442 hours) in the placebo group.
Discussion This interim analysis suggests that rhDNAse may have the potential to reduce the duration of ventilation in adult nonsurgical intensive care patients. This confirms results obtained in paediatric patients [2]. Data from surgical patients will be presented as soon as the interim analysis in that group is completed.
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P52

The efficacy of intratracheal rhDNase therapy in the treatment of severe hypercapnoeic respiratory acidosis in ventilated children with status asthmaticus and bronchiolitis

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Objective Successful rescue therapy with intratracheal recombinant (rh) DNAse has been documented in case reports of severe status asthmaticus with life-threatening mucus plugging [1]. Benefit may occur via its mucolytic properties or enhancement of mucociliary transport. The aim of this study was to report the efficacy of rhDNAse in terms of CO_2 clearance in a cohort of ventilated children with severe airflow obstruction secondary to either status asthmaticus or viral bronchiolitis unresponsive to conventional therapy.
Method We reviewed retrospectively the case notes of 19 ventilated patients admitted to a tertiary paediatric ICU with a clinical diagnosis of asthma or bronchiolitis who received rhDNAse therapy for severe persisting hypercarbic acidosis ($pCO_2 > 10$ kPa, pH $<$ 7.2) despite optimising conventional ventilation (peak inspiratory pressure $>$ 28 cmH_2O, pressure control mode). One millilitre per kilogram of rhDNAse (0.25 mg/ml concentration in 0.9% saline) was instilled bronchoscopically ($n = 4$) or blindly ($n = 15$) into the trachea followed by percussive physiotherapy with adequate patient sedation and muscle relaxation. Ventilator settings (Servo 300) and arterial blood gases were recorded pre-DNAse and at 4 and 8 hours after therapy according to our standard DNAse protocol. Tidal volumes were not measured due to known inaccuracy of the Servo 300 ventilators. Data were analyzed using two-way, repeated-measures ANOVA. Significance levels for group (asthma vs bronchiolitis), time (0, 4 and 8 hours) and interaction effects are reported.
Results Patient demographics are presented in Table 1. There was a significant fall in arterial pCO_2 in both groups over the 8 hours after DNAse therapy (time effect $P = 0.01$, group effect $P = 0.03$; Fig. 1), which was mirrored by a rise in pH (time effect $P = 0.002$). This was associated with a reduction in peak inspiratory pressure (time effect $P = 0.03$; Fig. 2) which was more pronounced in asthma (interaction effect $P = 0.004$; Fig. 2). Patients with bronchiolitis were ventilated at a higher rate than asthma (group effect $P = 0.001$), which did not change with time (time effect $P = 0.4$), suggesting the reduced pCO_2 was a function of improved tidal volumes.
Conclusion Intratracheal DNAse with percussive physiotherapy may offer an effective method to improve ventilation in status asthmaticus and bronchiolitis patients with severe hypercarbic acidosis. Further studies are warranted.

Table 1 (abstract P52)

	Asthma ($n = 8$)	Bronchiolitis ($n = 11$)
Age (months)	72.6 (48–104)	4.2(2.5–7)
Days of ventilation	3.4(2.6–5.5)	5.55(3.8–9.9)
Hours pre-DNAse	2.28(1.0–2.9)	4.67(3.1–5.9)

Figure 1 (abstract P52)

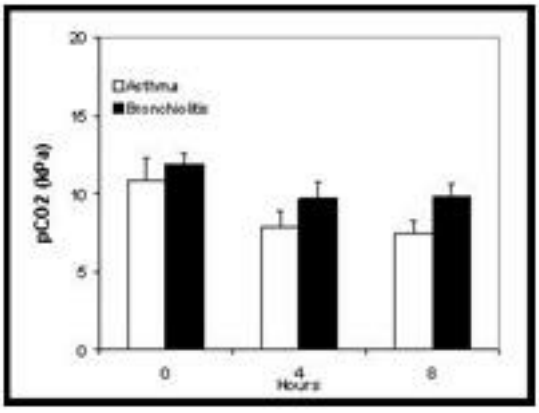
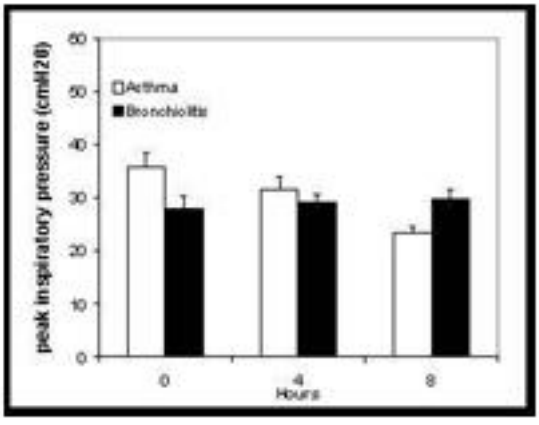


Figure 2 (abstract P52)



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P53

The use of the laryngeal mask airway during percutaneous dilatational tracheostomy

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Introduction Percutaneous dilatational tracheostomy (PDT) is a widely used and accepted method of long-term ventilation of critically ill patients in many ICUs.

Aim To study the use of the laryngeal mask airway (LMA) during PDT for controlled ventilation in critically sick patients and compare its complications and duration procedure in relation to the ETT.

Methods and materials A prospective, randomized clinical trial performed in the seven-bed general ICU of a training and research hospital of the Ministry of Health. The bedside PDT was performed in 73 critically ill patients in a period of 3 years. Patients were randomly assigned to ventilation via LMA ($n = 31$ patients) and to ventilation via ETT ($n = 42$). The duration of the procedure and complications were compared in the two groups.

Results The ETT group and the LMA group did not differ regarding age. There was no significant difference in the operating time between the two groups. We found that the incidence of complication was 26.2% in the ETT group and 25.8% in the LMA group (Table 1).

Table 1 (abstract P53)

Complication	ETT (n [%])	LMA (n [%])	$P = 0.971$
(+)	11 (26.2)	8 (25.8)	
(–)	31 (73.8)	23 (74.2)	

Conclusion The LMA is an effective and successful ventilatory device during percutaneous dilatational tracheostomy. For PDT, the LMA has an advantage over the ETT of lying remote from the operating field. The LMA does not cause the difficulties associated with the use of an ET such as cuff puncture, tube transection by the needle, and accidental extubation.

P54

How early is enough in lactate monitoring?

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Background In ARF patients treated with non-invasive ventilation (NIV) a low pH value not improving within 2 hours greatly increases the risk of NIV failure. In relation to the high diaphragm lactate production, we tested the hypothesis that the lactate clearance (LC) was more predictive of the risk of NIV failure in comparison with the difference in pH (DpH) in patients with cardiac pulmonary edema (PE) and metabolic or mixed acidosis.

Methods Forty-seven consecutive patients observed in the Emergency Room with PE were treated with pharmacological therapy (FiO_2 0.5, morphine, inotropes, diuretics, vasodilators if hypertensive) and CPAP (10 cmH_2O) by helmet if they had metabolic acidosis, or BIPAP (IPAP 14 cmH_2O – EPAP 6 cmH_2O) by face mask if they had mixed acidosis. The mean inspiratory airway pressure was the same in the two ventilatory treatments. Blood gas analysis were performed at admission and every 30 min for 2 hours. Clearance of lactate was calculated as: lactate start – lactate (30 min, 1 hour, 1.5 hour, 2 hour) / lactate start × 100 (%).

Results Significant results were obtained after 2 hours of NIV. In Table 1 the pH value at admission and after 2 hours of NIV and lactate clearance at 2 hours are reported in 35 patients responding to NIV and 12 patients who failed NIV. The higher proportions predicted to fail were with DpH < 0.01 and LC < 25% at 2 hours (OR 3.4 and 5.1, respectively). In another 15 similar patients we compared the predicted risk of failure of NIV related to DpH < 0.01 and LC < 25%, selecting an arbitrary probability of failure equal to 50% between expected and observed failures: the C statistics

Table 1 (abstract P54)

	NIV responders	NIV nonresponders
pH at start	7.25 ± 0.09	7.24 ± 0.07
pH at 2 hours	7.34 ± 0.07*†	7.24.± 0.06
Lactate clearance at 2 hours (%)	51 (41, 57)†	13 (12, 22)

*,† $P < 0.0001$ between admission and 2 hours of NIV, and responders vs nonresponders.

(area under the ROC curve) of LC < 25 and DpH < 0.01 were 0.85 and 0.73, respectively ($P < 0.001$).

Conclusions Lactate clearance is a reliable indicator of the response of patients with PE to NIV. LC < 25% is more sensible than DpH < 0.01, perhaps because it does not take into account confounder factors related to previous metabolic acidosis. It could be considered a cost-effective method for early triaging of patients to be admitted to the ICU for invasive ventilation.

P55

Early tracheostomy in acute lung injury: who could benefit?

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Introduction Early tracheostomy has been associated with improved outcome in patients with high likelihood of death or ventilator dependency. While a significant number of patients with acute lung injury (ALI) require prolonged mechanical ventilation and could potentially benefit from early tracheostomy, lack of an accurate prediction limits its utilization in this group of patients.

Methods From the database of the second international study of mechanical ventilation we selected patients with ALI who were alive and invasively ventilated on the third day post intubation. From a broad range of risk factors prospectively collected during the first 3 days of mechanical ventilation, univariate and multivariate logistic regression identified variables associated with increased risk of death or ventilator dependency.

Results From 372 patients meeting inclusion criteria, 281 reached a composite outcome of either death or ventilator dependency of more than 2 weeks. One hundred and ninety-nine (53%) died in the ICU, 104 (28%) were ventilated >14 days and 76 (20%) underwent tracheostomy, median 12 (IQR 8–18) days after the intubation. A score based on age and day 3 values of oxygenation index, VE 40 (minute ventilation needed to bring $PaCO_2$ to 40 mmHg) and shock predicted death or ventilator dependency better (area under receiver operating characteristic curve [AUC] 0.71) than SAPS II (AUC 0.51) or day 3 SOFA (AUC 0.54) scores.

Conclusion If confirmed in an independent sample, this score may be a useful tool to identify patients with ALI who might benefit from early tracheostomy

P56

Comparison of four methods to calibrate respiratory inductive plethysmograph in premature infants

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Introduction Respiratory inductive plethysmography (RIP) is a widely used method providing important information on the breathing pattern. This non-invasive technique is particularly interesting in infants and newborns. However, the different calibration methods developed in adults to allow the measurement of volume have not been validated in premature infants, even if they are frequently used. We developed a calibration method using the least square method to identify the coefficients (α; β) to calculate the reconstructed volume from the RIP signals ($V = \alpha$ ribcage + β abdomen) with a pneumotachograph (PNT) signal as reference, and using an individually adapted filter to suppress heart artefacts.

Objectives To compare the accuracy of this calibration method with three frequently used calibration methods: a simple fixed-coefficients method with either equal weight attributed to the abdomen and rib cage (method 1:1) or with a higher weight attributed to the abdomen (i.e. $\beta = 2\alpha$; method 1:2); and an equivalent of the qualitative diagnostic calibration method, using coefficients proportional to the standard deviation of abdomen and ribcage signals ($\beta / \alpha =$ SD(abdomen) / SD(ribcage)) (method SD).

Methods Twelve premature infants breathing spontaneously were studied. Birth weight was (mean ± SD) 1528 ± 340 g; gestational age 31.2 ± 0.6 weeks; age 6 ± 2 days. A specially adapted RIP jacket was installed 15 min before the study. RIP signals were recorded continuously. A face mask connected to a PNT was applied during two 30-s periods. The most regular 15 PNT cycles were identified and served as reference period, during which the coefficients (α; β) were calculated with each method. The four reconstructed flows were then recalculated, and we estimated the distance R2 between reconstructed flows and the PNT reference signal for the entire period of PNT; with R2 = 1 − (mean square difference between the normalized flows / variance of PNT); that is, a R2 value closer to 1 represents a better reconstruction of the signal.

Results The mean distance R2 was 0.62 ± 0.22 with method 1:1, 0.63 ± 0.22 with method 1:2, 0.62 ± 0.23 with method SD, and 0.70 ± 0.17 with the least square method ($P = 0.02$; repeated-measure ANOVA with a significant difference between the last method and the three others). The ratios β/α were 2.1 ± 1.5 and 2.9 ± 4.3 with the two last methods, respectively.

Conclusions This new RIP calibration method using the least square method with a short period of PNT as reference and an individually calculated filter gives a better reconstructed flow as compared with three other calibration methods. This method attributes a higher weight to the abdominal signal.

P57

Safety of percutaneous tracheostomy in coagulopathic patients

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Critical Care 2006, **10(Suppl 1):**P57 (doi:10.1186/cc4404)

Aim To determine whether percutaneous tracheostomy is safe in coagulopathic patients.

Study design A prospective, observational study.

Setting A 450-bed tertiary cancer referral center with a nine-bed ICU and 10 HDU beds.
Patients and methods One hundred and ninety patients underwent percutaneous tracheostomy between November 1996 and September 2001, using the Griggs technique. Of these, 23 patients were deemed to be coagulopathic (platelet count $< 70{,}000$ or PT > 18, PTT > 60). We determined the incidence of bleeding and other complications in these patients.
Results Only one patient had major bleeding, requiring surgical intervention and conversion to surgical tracheostomy. This patient also had a difficult tracheostomy complicated by pneumothrorax. Twenty patients required perioperative transfusion of platelet concentrates or fresh frozen plasma. Five patients received single donor platelets (average 1 ± 0), eight patients received random donor platelets (average 3.6 ± 1.30), and 15 patients received fresh frozen plasma (average 3.8 ± 2.7). Minimal blood loss was observed in the 22 other patients. Of the 167 patients without coagulopathy, four patients had significant bleeding. There was no difference in the incidence of hemorrhagic complications between coagulopathic and noncoagulopathic patients ($P > 0.05$, chi-square test).
Conclusion Percutaneous tracheostomy is a safe procedure in coagulopathic patients with adequate coagulation factor replacement.

P58

Do sleep studies effectively predict postoperative ventilatory requirements in patients undergoing bariatric surgery?

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Introduction Preoperative identification of obstructive sleep apnea (OSA) may help in the selection of patients who require ventilatory support. This study investigates the value of sleep studies in predicting the requirement for postoperative continuous positive airway pressure ventilation (CPAP) and high-dependency unit (HDU) admission.
Methods During the development of our service since 2001, 34 consecutive patients, mean age 42 years (29–61), mean weight 146 kg (100–210), mean BMI 54 (39–75), all underwent preoperative assessment by a respiratory physician before laparoscopic adjustable gastric banding, based on which 28 had sleep studies while six did not. The decision to provide CPAP was determined by sleep study results: patients with moderate or severe OSA were electively prescribed CPAP preoperatively and postoperatively.
Results Sleep studies were normal in 19 patients (NSS) and abnormal in nine patients (ABSS). In ABSS, OSA was severe in four patients, moderate in one patient, and mild in four patients. Preoperative and postoperative CPAP was prescribed electively for the five patients with moderate and severe OSA. Postoperatively, 3/19 of the NSS patients required CPAP and were admitted to the HDU. Another NSS patient was admitted to the HDU because of her age (61 years). The duration of operation, stay in recovery, and timing of extubation were comparable for NSS and ASS. The mean BMI was 63 and 53 in ASS and NSS patients, respectively ($P = 0.05$).
Conclusion Postoperative CPAP and HDU admission was required in 21% of NSS patients. Although ABSS was associated with higher BMI, sleep studies do not reliably predict postoperative CPAP or HDU requirements.

P59

Inhaled nitric oxide improves pulmonary functions following massive pulmonary embolism

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Objectives Acute pulmonary embolism increases pulmonary resistance and may lead to acute right ventricular failure and cardio circulatory collapse, possibly resulting in substantial morbidity and mortality. Inhaled nitric oxide (NO) dilates pulmonary blood vessels and has been used to reduce pulmonary vascular resistance in patients with chronic thromboembolic pulmonary hypertension and acute respiratory distress syndrome. This case series describes our experience with inhaled NO administered to four patients suffering from acute massive pulmonary embolism following abdominal surgery.
Results The four described patients were recovering from small bowel resection, pancreatoduodenectomy, hemipelvectomy or recent gastrointestinal bleeding and presented with severe respiratory and hemodynamic deterioration due to pulmonary embolism. Each received inhaled NO (20–25 ppm) via the inspiratory side of the breathing circuit of the ventilator. Pulmonary and systemic blood pressures, heart rate and gas exchange levels improved in all the patients within minutes after the initiation of NO administration.
Conclusions Inhaled NO may be useful in treating acute massive pulmonary embolism. This potential application warrants further investigation.

P60

Management of severe adult respiratory failure: evidence-based?

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Critical Care 2006, **10(Suppl 1):**P60 (doi:10.1186/cc4407)

Introduction The management of severe respiratory failure (SRF) remains a challenging problem. With the availability of many options with variable results, the management of patients with SRF is likely to vary between different ICUs and these practices may not necessarily be evidence-based. In this study we aimed to define the respiratory and the general management of the patients with SRF, and to identify the treatment practices that are evidence-based in the surveyed ICUs in the UK.
Methods This study is a questionnaire survey of the ICUs that were participating or were willing to participate in CESAR (www.cesar-trial.org), an ongoing randomised controlled trial (RCT) comparing ECMO with conventional intensive care for SRF. Although participating ICUs are free to use any modality of treatment at their discretion, the CESAR trial recommends a low tidal volume ventilation strategy according to the ARDS Network group. The collaborators of all 87 participating ICUs (out of a total of 262 ICUs in the United Kingdom) were requested to complete a postal questionnaire between February 2002 and May 2004. The response rate was 100%. A literature search for RCTs and meta-analyses of RCTs was performed to identify practices studied in this survey that were proved to improve survival in patients with SRF.
Results The practices in the surveyed ICUs are shown below, with the percentages of the ICUs in parentheses. Practices that were

Figure 1 (abstract P61)

	Baseline	Healthy lung				Injured lung				
Hours / Value (Units)	0	1	2	3	4	5	6	7	8	P
Pao_2 (mmHg)	73.25	73.85	71.58	73.68	67.15	74.15	67.33	69.90	77.75	0.866
$Paco_2$ (mmHg)	32.10	26.25	25.50	26.13	26.70	24.05	26.68	23.85	24.48	0.11
Pvo_2 (mmHg)	32.34	33.58	33.63	32.93	34.23	36.93	35.98	35.03	35.20	0.05*
$Pvco_2$ (mmHg)	37.40	28.33	28.43	29.88	29.58	24.98	22.40	23.98	23.65	0.00068*
Sao_2 (% Sat)	94.74	96.03	95.50	95.43	93.08	94.20	93.53	94.13	94.68	0.398
Svo_2 (% Sat)	60.69	67.23	67.28	63.35	65.33	68.18	68.95	69.15	66.93	0.158
$AaDO_2$ (mmHg)	26.03	32.78	35.99	33.11	38.92	35.23	38.77	39.73	31.10	0.287
Pao_2/Fio_2 (%)	348.99	351.67	340.83	350.83	319.76	353.10	320.60	332.86	370.24	0.866
Cao_2 (mL/100mL)	11.36	12.29	11.89	11.52	11.37	13.16	11.85	11.88	11.46	0.733
Cvo_2 (mL/100mL)	6.98	8.44	8.19	7.51	7.82	9.34	8.56	8.51	7.95	0.327
$a\text{-}vo_2$ (mL/100mL)	4.38	3.85	3.71	4.01	3.55	3.82	3.29	3.37	3.51	0.12
Do_2 (mL/min/m²)	42.05	50.72	43.60	40.78	44.68	54.18	44.89	40.87	39.50	0.909
Vo_2 (mL/min/m²)	16.52	16.03	13.59	14.19	13.90	15.52	12.25	11.62	12.13	0.202
Compliance (mL x cmH_2O^{-1})	22.06	22.51	22.38	21.18	20.42	18.93	19.40	19.92	19.21	0.032*
PCWP (mmHg)	9.38	10	9.75	9	9.75	8	8.25	7.75	8.5	0.153

* P<0.05

Oxygen indexes and values before and after lung injury with oleic acid.

proven to improve survival by at least one RCT are highlighted with an asterisk.

- Preferred mode of ventilation: pressure controlled (82%), PRVC (6%), volume controlled (7%), HFOV (5%).
- PEEP strategy: above lower inflection point (28%), best PEEP against SPO_2 (61%), other (e.g. empirical high PEEP 10–15, Best PEEP against SPO_2 and tidal volumes) (11%).
- Peak plateau pressure limitation: <30* (48%), >30 (37%).
- Practice of ARDS network group approach* (ventilation with low tidal volumes) (69%).
- Use of nitric oxide (10%); prone ventilation (91%).
- Timing of tracheotomy: within 48 hours (16)*, within 7 days (51%); percutaneous* (95%), surgical (3%).
- Routine cardiac output monitoring (63%): PA catheter (38%), oesophageal monitor (44%), other (18%); resuscitation fluid: colloids (82%).
- Target Hb: 7–9 gm*% (69%), 9–10 (14%) >10 gm% (17%).

Conclusion Although there are variations of practices in the management of adult patients with SRF, most of the ICUs evaluated in this survey are following evidence-based practices. This should improve the survival of patients managed conventionally in the CESAR trial compared with historical results.

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P61

Supplemental systemic oxygen support with peritoneal oxygenation using a continuous low-pressure oxygen flow system (PEROX)

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Background In a continuous peritoneal oxygen flow model, we studied its influence on hemodynamic stability, arterial and mixed venous gases, comparing its effects in normal and in oleic-acid-induced ARDS lungs.

Methods Four pigs were anesthetized, mechanically ventilated and invasively monitored with a Swan–Ganz and femoral catheter. A continuous infusion of dobutamine (2 µg/kg/hour) was maintained. Arterial pressure, cardiac output, pulmonary compliance, PCWP, and arterial and mixed venous gases were measured every hour. Baseline measures were taken and three laparoscopic trochars were introduced in the abdomen. A continuous oxygen flow of 5–6 l/min was maintained for 8 hours with a sustained intra-abdominal pressure of 5–6 mmHg using a continuous low-pressure flow system (PEROX). At the fifth hour an oleic acid (OA) dose (0.2 mg/kg) was injected into the pulmonary circulation. Afterwards, lungs were histopathologically studied to evaluate the presence of ARDS. A two-way ANOVA with replication was used for the sequential analysis of data.

Results PEROX demonstrated efficiency to maintain normal oxygenation indexes even though the presence of ARDS after the injection of OA was confirmed with a histopathological study and a significant difference in the pulmonary compliance ($P = 0.032$).

This is evident because no statistical difference was observed in oxygen indexes and variables during the 4 hours posterior to the injection of OA (Fig. 1).

Conclusions This experimental model demonstrated that peritoneal oxygenation could be an effective gas interchange-supporting alternative in ARDS. The mechanism of action could be an increase of the mixed venous oxygenation.

P62

Oxford Miniature Vaporiser for halothane in ventilated asthmatics

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Introduction Critically ill asthmatics that require mechanical ventilation may benefit from halothane and other inhalational agents. Various methods of administration of halothane have been tried. Anaesthetic machines are commonly used but are resource-expensive.

Methods We used a simple in-line Oxford Miniature Vaporiser (OMV), as part of the inspiratory limb of a Servo 300 (Siemens) mechanical ventilator. We employed this device in three patients for a total duration of 120 hours without adverse effects.

Results The OMV is a small and portable thermally buffered vaporiser used to speed the induction of anaesthesia (Fig. 1). 'Draw over anaesthesia' is simple in concept and entails drawing a carrier gas over a volatile liquid, thus entraining its vapour to the gaseous carrier. 'Draw over' systems operate at less than, or at, ambient pressure, and flow through the system is intermittent, varying with different phases of inspiration, and ceasing in expiration. A one-way valve prevents reverse flow in the circuit. This is different to 'plenum anaesthesia' in which a carrier gas is pushed through the vaporiser at a constant rate. In 'draw over' systems the carrier gas is drawn through the vaporiser either by the patient's own respiratory efforts or by a self-inflating bag or manual bellows with a one-way valve placed downstream from the vaporiser.

Conclusion We used the OMV as part of a regular positive pressure ventilatory circuit. The OMV was specially calibrated for halothane and was robust and reliable. Halothane delivery was controlled and in steady fashion; a simple wall-suction unit scavenged the exhaled halothane. Staff acceptance and user-friendliness were high. We recommend the OMV for regular ICU use for halothane in asthma.

Figure 1 (abstract P62)

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Assessment of oxygen consumption from standard E cylinders by fluidic, turbine, and compressor style portable mechanical ventilators

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Background Gas consumption of portable ventilators is an important variable when considering ventilation in mass casualty events. We evaluated the oxygen consumption from standard E cylinders of fluidic (IC-2A; BioMed Devices, CT, USA), turbine (LTV-1000; Pulmonetic Systems, MN, USA), and compressor (Impact 754; Impact Instrumentation, NJ, USA) style transport ventilators.

Methods Each ventilator was connected to a Training Test Lung (TTL) (Michigan Instruments, MI, USA) in Assist Control (A/C) with tidal volume (VT) 750 ml at a rate of 12 breaths per minute (bpm), providing a minute ventilation (VE) of 9.0 l/min. The positive end expiratory pressure (PEEP) was set at 0 and 10 cmH_2O, and the fraction of inspired oxygen (FiO_2) at 1.0 and 0.5. Ventilators used either compressed gas (IC-2A) or electricity (LTV-1000 and Impact 754) as power sources. All oxygen sources were standard E cylinders beginning with 2200 psi (680 l) connected to ventilators with standard regulators. Ventilators were connected to TTL by manufacturer-provided corrugated tubing. FiO_2 and VE were continuously monitored during each run and the time of operation was recorded. Three runs were conducted at each ventilator setting. The time of operation was recorded and the ventilator oxygen consumption was calculated.

Results Each run delivered 9 l VE on A/C ventilation to the TTL. With FiO_2 1.0 and PEEP 0 cmH_2O, times to complete E cylinder gas consumption for the IC-2A, LTV-1000, and Impact 754 ventilators, respectively, were 34.3 (±1.2), 43.3 (±0.6), and 69.0 (±1.7) min. With FiO_2 1.0 and PEEP 10 cmH_2O, run times were 34.0 (±1.0), 41.8 (±1.6), and 69.3 (±1.2) min. For the LTV-1000 and the Impact 754 with FiO_2 0.5 and PEEP 0 cmH_2O, respective run times were 105.8 (±13.0), and 144 (±11.6) min. For each run the oxygen consumption in addition to the delivered VE for the IC-2A, LTV-1000, and Impact 754 was 10.8 (±0.7), 6.7 (±0.2), and 0.9 (±0.2) l/min with FiO_2 1.0 and PEEP 0 cmH_2O, and was 11.0 (±0.6), 7.3 (±0.6), and 0.8 (±0.2) l/min with FiO_2 1.0 and PEEP 10 cmH_2O. For the LTV-1000 and Impact 754, oxygen consumption was 3.2 (±0.8) and 1.4 (±0.4) l/min on settings of FiO_2 0.5 and PEEP 0 cmH_2O.

Conclusions Our initial runs to assess E cylinder oxygen consumption of various types of ventilators demonstrate that fluidic and turbine style ventilators consume more oxygen than compressor style ventilators. The turbine ventilator tested uses a continuous flow of 10 l/min, which is gas inefficient. PEEP has little effect on oxygen consumption. Use of the internal air source and lower FiO_2 significantly increased the length of operation from an E cylinder. If oxygen E cylinders are a scarce resource, our data suggest that compressor style transport ventilators may currently be the transport ventilators of choice.

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Prehospital endotracheal intubations in vitally comprised children in The Netherlands

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Introduction The reason for the study was to evaluate prehospital endotracheal intubations of vitally compromised children. The data studied were collected by a Dutch Helicopter-transported Medical Team (HMT) that provides advanced medical care in the eastern part of The Netherlands. The HMT consists of a specially trained physician and paramedic transported to the incident location by helicopter in day-time. The Dutch HMT is activated together with the emergency medical service (EMS) by the dispatch centre, or by the EMS paramedics from the incident location. Activation of the HMT is according to a structured list of incident situations and/or the medical condition of the patient.
Design Retrospective analysis of 297 HMT calls for prehospital vitally comprised children (<16 years) from 2001 to 2005 by the HMT-Netherlands-East. Registered data included age, sex, physiological parameters, prehospital treatment given, and survival until hospital discharge.
Endotracheal intubation was performed by either the EMS paramedic or the HMT physician. Intubation was confirmed by the HMT physician with auscultation and capnography. For descriptive analysis, the Fischer exact test and relative risk were used on SPSS. $P \leq 0.05$ was considered significant.
Results The EMS on scene cancelled the paediatric HMT calls before the landing of the helicopter in 36% ($n = 107$) – reasons: no serious injury 82% ($n = 88$), deceased 10% ($n = 11$), other 8% ($n = 8$). The HMT examined and treated 190 children on scene.
The EMS paramedic attempted an endotracheal intubation in 33 patients before the arrival of the HMT, and the HMT physician performed 89 endotracheal intubations. The success rate of endotracheal intubation for EMS paramedics was 70% ($n = 23$) and for the HMT physician 100% ($n = 89$) ($P < 0.001$).
The HMT physician checked the endotracheal intubation and ventilation on arrival by auscultation and capnography; an emergency correction had to be performed by the HMT physician in 10 out of 33 patients. Four patients had an oesophageal intubation, four patients had an inappropriate sized endotracheal tube making ventilation impossible, and two patients had lethal ventilator settings. Two of these 10 patients were discharged from the hospital in good condition, the others died at the incident scene or in the hospital.
Thirty-three per cent ($n = 65$) of all patients had an initial prehospital Glasgow Coma Scale (GCS) of 3 or 4. The overall survival rate until hospital discharge with an initial GCS of 3 or 4 was 23% ($n = 14$). The survival rate until hospital discharge with a GCS of 3 or 4 was 6.5% ($n = 2$) for the EMS-intubated group, and 40% ($n = 12$) for the HMT-intubated group (Fischer exact $P = 0.007$).
Conclusion Successful endotracheal intubation is a difficult task for EMS paramedics; 30% of all recorded endotracheal intubations resulted in potentially lethal complications. Mask-balloon ventilation is to be preferred to a failed intubation effort; prehospital endotracheal intubation of children calls for an experienced physician.

P65

Transit care of the ventilated critically ill in commercial airliners

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Air ambulances and customized military aircraft are established modes of transporting critically ill patients. Defence services and aid agencies even have flying hospitals, replete with operating theatres and ICUs. With burgeoning travel by an increasingly elderly population, a growing number of travelling Australians suffer critical illnesses overseas. Transcontinental air ambulances are prohibitively expensive and many American and European commercial airlines ban travel by seriously ill patients.
Transit intensive care on board commercial airline flights poses complex physiological and logistic challenges. We have transported hundreds of critically ill patients and report on 10 episodes of aero-intensive care with IPPV on board scheduled passenger services. These were from the Philippines, the USA, the United Kingdom, Thailand, France, Norway and Austria on Qantas, Singapore Airlines, Thai Airways and Malaysia Airlines.
The aviation environment imposes a bewildering array of electronic, safety and security related issues to be overcome. The entire mobile ICU weighs 100 kg. A vacuum-mattress on a stretcher fitted to the cabin floor at the rear of the economy-class cabin and screened off from the other passengers ensures patient privacy (Fig. 1). Oxygen is scarce and extremely expensive during flight. We employed the 'circle system' with a CO_2 absorber and in-line oxygen analyser. Mobile suction, infusion pumps, transit-care monitors and portable blood gas analysers were all adapted for use in commercial aircraft.
Australia and New Zealand lead the world in transit care of the critically ill in commercial airliners.

Figure 1 (abstract P65)

P66

Nosocomial pneumonia in ICU patients after surgical and percutaneous tracheostomy

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Introduction The aim of this clinical trial was to study the incidence of nosocomial pneumonia (NP) in ICU patients after surgical (SGT) and percutaneous (PCT) tracheostomy.
Methods We studied retrospectively 108 patients, 79 men and 29 women, who underwent tracheostomy. Mean age: 52.4 ± 21.4 years, mean stay in ICU: 27.9 ± 11.6 days. All patients were mechanically ventilated. Underlying diseases: multiple trauma 69 patients, complicated surgery 23 patients, other 16 patients. Timing of procedure was determined by the ICU doctors, while the method of tracheostomy was determined by both the ICU and the Ear Nose and Throat (ENT) doctors. The patients were divided into two groups: group A (60 patients) who had a PCT and group B (48 patients) who had a SGT. The mean time of hospitalisation from admission to tracheostomy was 10.2 ± 3.1 days. PCT were performed by ICU doctors at the bedside, while SGT were performed by ENT doctors (32 at bedside and 16 in the surgery room–theater).
Results In group A NP was diagnosed in 23 patients (38.3%), mean time to tracheostomy from infection: 4.1 ± 2.1 days. In group B NP was diagnosed in 18 patients (37.5%), 3.5 ± 2.4 days after tracheostomy. The types of invading microorganisms were similar in both groups. The mortality rate in group A was 20/60 = 33.3% and in group B was 18/48 = 37.5%. We noticed one tracheal infection in group A (1.7%) and three in group B (6.2%); this difference was not statistically significant.
Conclusion There is no significant difference in incidence of NP between patients receiving PCT and SGT. The type of infection and pathogens are similar. Tracheal infections are very rare in both groups.

P67

Too few, too late: submission patterns of bronchoalveolar lavage fluid samples obtained under the suspicion of the diagnosis of ventilator-associated pneumonia

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Introduction At our hospital, ventilator-associated pneumonia (VAP) is diagnosed by microbiological and cytological analysis of bronchoalveolar lavage (BAL) fluid. Opening hours of the inhouse microbiological laboratory are between 8.00 a.m. and 5.00 p.m. During off-hours a laboratory technician is on call for urgent samples including BAL fluid. The total laboratory workup of the BAL fluid including the differential cell count takes 2 hours. The present study aimed to analyse the day and hour submission patterns of BAL fluid samples.
Materials and methods During a 58-month period (January 2000–October 2005), the day and hour of submission of all consecutive BAL fluid samples obtained from patients suspected of VAP were recorded. The diagnosis of VAP was made if quantitative cultures reached $\geq 10^4$ colony forming units/ml and/or if ≥2% infected cells were enumerated on May–Grunwald Giemsa stained cytocentifuged preparations.
Results A total of 433 BAL fluid samples was included. On week days, a total of 69.8 ± 5.8 samples for each day were submitted, compared with 38 and 46 samples on Saturday and Sunday. For nearly one-half (199, 46.0%) of the samples, the onduty laboratory technician was required: 99 (23.0%) samples arrived within 1 hour before closing, and an additional 100 (23.0%) were submitted after closing. VAP was diagnosed in 168 (38.8%) samples, 92 (54.8%) of these diagnoses were made after closing hours. VAP was diagnosed in 76/220 (34.5%) of samples submitted during opening hours, and tended to be diagnosed proportionally more after closing hours during weekdays (54/129 41.8%) and during weekends (38/84 samples, 45.2%; $P = 0.09$).
Discussion and conclusions The high number of BAL fluids processed after laboratory opening hours is of concern because of the suboptimal working conditions (fatigue, lack of supervision). Technician time spent on these samples puts a strain on the laboratory in terms of costs and absence of the technicians because of legal recuperation. The low number of BAL fluids submitted during the weekends combined with the higher proportion of VAP in these samples points to poor compliance with inhospital guidelines for the diagnosis of VAP and could suggest that we missed a number of (unconfirmed) episodes of VAP.

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Criteria of the systemic inflammatory response syndrome in patients with community-acquired pneumonia

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The absence of a single approach to the determination of severe pneumonia troubles the objective evaluation of the patients' state. It is proposed that the disease's severity reflects the apportionment of patients with pneumonia with systemic inflammatory response syndrome (SIRS). This study was planned to demonstrate how the clinical laboratory criteria of SIRS in pneumonia reflect the systemic inflammatory response of the organism.
We examined 46 patients aged 36–58 years. Twenty-two patients had the middle–severe type (first group) and 24 patients (second group) had the severe type of pneumonia. We determined the cytokine concentrations (IL-6, IL-8, TNF-α) and LPS-binding protein (LPS-SP) in the blood serum using the immunochemo-luminescent method on the immunochemoluminescent analyzer 'IMMULITE One' (USA) 1, 3, 10 and 17 days after the treatment's onset. The C-reactive protein concentration was appreciated by the latex-agglutination method.
Digital material was treated using the Student *t* criterion.
Analysis of the clinical signs in patients with community-acquired pneumonia demonstrated the expressed changes in patients with severe pneumonia, which manifested in increased tachycardia, respiratory failure, and decreased values of the systolic and diastolic arterial pressures. The temperature reaction in the second group remained during all the observation period.
The patients of the first group revealed segmentary infiltration, whereas the patients of the second group had changes of the pulmonary lobar lesion and polysegmentary changes.
The LPS-SP level in the severe type of pneumonia group exceeded 2.4 times as large as ($P < 0.01$) the one in the middle–severe type of pneumonia group at admission to the hospital. By the 10th day of observation the LPS-SP concentration in the blood decreased in

both groups, remaining significantly high in the second group as compared with the first group (five times as large, $P < 0.01$), which suggests the continuing stimulation of the LPS bacteria of the monocytic macrophagal link cells and cytokine synthesis induction. Patients of the second group demonstrated hypercytokinemia the most expressed from the first to 10th observation day. At admission the IL-6 and IL-8 concentrations exceeded 13 and 18.4 times as large as ($P < 0.05$) the values of the first group. The maximal differences in the TNF-α levels between the groups were observed on the third day.

An elevated level of C-reactive protein was registered in patients of both groups. At the same time the C-reactive protein concentration in the patients with severe type pneumonia exceeded four times as large as ($P < 0.05$) the values of the compared group, which suggested continuous induction of the protein synthesis by cytokines. The LPS-SP, IL-6, IL-8, and TNF-α concentrations in the blood of patients with pneumonia therefore reflect the activity of the systemic inflammatory process and make an important contribution to the development of the whole complex of clinical symptoms causing the state's severity. The analysis of these values' levels will allow one to use them as the laboratory criteria of SIRS appreciation in further studies.

P69

Correlation between GCS and the risk of aspiration pneumonia in self-poisoning patients

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Introduction Self-poisoning is a common cause of nontraumatic coma, especially in young people. The management of these patients aims to protect the airway in order to prevent aspiration pneumonia (AP). Some author recommend to intubate when GCS < 8. However, only few studies have examined the relation between GCS, the caught reflex and the frequency of AP in self-poisoning patients (SPP). The aim of our study is to evaluate the relation between GCS and the risk of developing this complication.
Materials and methods We conducted a retrospective study during 2004 including all admitted SPP in our ICU. GCS was noted on admission or immediately before intubation. The diagnosis of AP was performed according to the usual criteria. Two groups were compared: G1 (without AP) and G2 (with AP). Data were expressed as a mean ± SD and percentage. Tests used for comparisons were the Q square and Student *t* tests. The ROC curve was used to determinate the cutoff value of GCS associated to high risk of AP.

Table 1 (abstract P69)

	G1 ($n = 446$)	G2 ($n = 78$)	*P*
Age	27.8 ± 12.9	31.1 ± 12.8	0.036
Gender, female (%)	67.2	55.1	0.04
IGS II	18 ± 11	33 ± 11	<0.001
APACHE II score	6.8 ± 5.1	14.3 ± 4.8	<0.001
SBP	112 ± 19	105 ± 22	0.05
GCS	12.7 ± 3.2	8.1 ± 3.2	<0.001
MV (%)	22	87	<0.001
LOS (hours)	44 ± 69	67 ± 71	0.006
Mortality (%)	1.6	2.6	0.8

Results Five hundred and twenty-four SPP were included. Seventy-eight (14.9%) had developed AP. The characteristic of the two groups are presented in Table 1. GCS was significantly lower in G2. The cutoff value on the ROC curve was 12 with a sensitivity of 86%, a specificity of 70% and an area under the curve of 0.816.
Conclusion Criteria used for intubation in SPP must be more rigorous. According to our study, patients with GCS < 12 should be considered for intubation.

P70

Bronchoalveolar lavage in mechanically ventilated patients with suspected pneumonia: a descriptive study

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Objective To describe etiologic agents, the antibiotic use and the clinical outcome of pneumonia patients who require mechanical ventilation
Methods Seventy-three consecutive mechanically ventilated patients with suspected pneumonia and BAL recruited between November 2003 and December 2005 were registered. The ICU length of stay, time on mechanical ventilation (MV), mortality, isolated bacteria, and antimicrobial susceptibility were collected.
Results Twelve inmunocompromised patients were excluded. A total of 61 cases of suspected pneumonia were recruited (Table 1), including eight (13.1%) cases of community-associated pneumonia (CAP), 20 (32.7%) cases of early-onset ventilator-associated pneumonia (VAP < 5 days), and 33 (54.09%) cases of late-onset ventilator-associated pneumonia (VAP ≥ 5 days).
Twenty-eight patients (84.8%) with late-onset VAP received antibiotics before performing BAL, as compared with 12 (60%) with early-onset VAP and five patients (71.4%) with CAP.
BAL was positive (>10,000 ufc/ml) in 36.4%, 60% and 14.3% of late-onset VAP, early-onset VAP and CAP, respectively. The ICU length of stay was significantly longer for patients with CAP and late-onset VAP than for early-onset VAP patients. Mortality was 24.2%, 35% and 28.6% due to late-onset VAP, early-onset VAP and CAP, respectively. CAP and early onset VAP were mostly caused by antibiotic sensitive bacteria, while late-onset VAP were caused more frequently by multiple pathogens with an inadequate prior antibiotic treatment.
Conclusions The low incidence of positive BAL in the CAP group underwrites the use of BAL only for particularly severe, selected cases. Although there was a difference in the isolated bacteria and antibiotic susceptibility among different kinds of pneumonia, the mortality was the same. Inadequate prior antibiotic therapy was more frequent in the late-onset VAP group.

Table 1 (abstract P70)

	CAP	Early-onset VAP	Late-onset VAP
Cases (*n*)	8	20	33
APACHE II score	21.8 ± 5.7	18.6 ± 7	21 ± 8.3
Days of MV	14.5 ± 9.2*	6.7 ± 5.4*	16.6 ± 10.8*
Length of stay	16.8 ± 9.4*	9.6 ± 6.9*	23.2 ± 13.4*
Mortality (%)	28.6	35	24.2
Inadequate AB (%)	0	16.7	50

*$P < 0.001$.

P71

Bronchoalveolar lavage cytology in the diagnosis of ventilator-associated pneumonia

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Introduction Ventilator-associated pneumonia (VAP) is a common nosocomial infection in intensive care patients. The most accurate diagnosis relies on the quantitative culture results of bronchoalveolar lavage (BAL) fluid. In our hospital, BAL fluid quantitative culture and cytology analysis are performed routinely in patients suspected of VAP. In this study, we assessed the value of the combination of various BAL fluid cytology findings for the diagnosis of VAP.
Study design All BAL fluid samples obtained from patients suspected of VAP were collected. VAP was defined as BAL fluid cultures with $\geq 10^4$ colony forming units/ml BAL fluid. BAL fluid cytology included the total cell count/ml, the differential cell count on 500 nucleated cells including the percentage of polymorphonuclear neutrophils and the percentage of infected cells containing phagocytised organisms (intracellular organisms [ICOs]). Areas under the curve (AUCs) of receiver operating characteristic curves were calculated and plotted for various cytologic parameters and their combinations.
Results Over a 61-month period (January 1999–February 2004), a total of 335 BAL fluid samples were included from 287 patients. In 126 (37.6%) patients VAP was confirmed by positive culture. Highest AUCs were as follows: total cell count: 0.65, percentage polymorphonuclear neutrophils: 0.71 and percentage ICO: 0.90. The combination of percentage ICO with any other cytological parameter did not increase the AUC. At a threshold of 2%, the percentage ICO had an 86.2% positive predictive value and a 88.1% negative predictive value for VAP.
Conclusion Among all cytologic parameters analysed in BAL fluid obtained under the suspicion of VAP, the percentage of ICOs was the parameter most predictive of VAP. Combination with other cytological parameters did not improve its predictive value.

P72

Community-acquired pneumonia treated on the ICU

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Introduction Little is known about ICU use in severe community-acquired pneumonia (SCAP). The aim of our study was to examine epidemiological data, prognostic factors and treatment of adult patients admitted to the ICU for SCAP in the industrial region of Western Macedonia.
Methods Cases of SCAP admitted to the five general hospitals covering the health services needs in the region were identified retrospectively for the period April 2002–February 2005 using the hospital admission forms. Data concerning SCAP treated on the ICU were extracted by ICU records review over the same period. Variables assessed included characteristics at presentation, underlying risk factors, microbiological diagnosis, main therapies and evolution during the ICU stay. Prognostic factors were determined by comparison of the above variables between ICU survivors and nonsurvivors.
Results Over this 3-year period 839 patients with SCAP were admitted to the hospital, and the mean incidence of SCAP in Western Macedonia was found to be 93 cases per 100,000 population. Of all patients admitted 45 (5.36%) needed intensive care. Thirty-seven (84%) of those patients had comorbidity and 38 (84.9%) received early (<12 hour) intubation. The average age was 60.48 (SD 16.46) years and the average APACHE II score, PSI points and CURB-65 score were 23.1 (SD 8.9), 161.24 (SD 1.1) and 3.75 (SD 41.28), respectively. A microbiological diagnosis was made in 11 patients (24,4%). Mortality was not increased in those in whom a bacterial diagnosis was not made. A total 4.4% of the strains were drug-resistant and the pathogens most frequently identified were *Acinetobacter baumanii*, *Pseudomonas aeruginosa* and *Klembsiella*. ICU mortality was 33.3%. Prognostic factors on and during ICU admission were confusion ($P = 0.004$), bilateral chest X-ray involvement ($P = 0.001$), admission through the Emergency Department ($P = 0.023$), active oral steroid treatment ($P = 0.026$), ineffective initial antimicrobial therapy ($P = 0.01$), a longer median mechanical ventilation period (13.66 days vs 6.26, $P = 0.01$), sepsis-related complications ($P = 0.001$), ICU-related complications ($P = 0.005$) and acute renal failure ($P = 0.01$).
Conclusion SCAP treated on the ICU carries a high mortality, which is related to underlying diseases, ineffective initial antimicrobial therapy, requirements for mechanical ventilation, bilateral disease and complications during ICU stay. The importance of the admission to ICU at an early time point is underlined. The approach to empirical therapy must take into account local infecting organisms and susceptibility.

P73

Multinational, observational study of procalcitonin in ICU patients with presumed or confirmed pneumonia and requiring mechanical ventilation

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Objectives Respiratory tract infections requiring mechanical ventilation account for more than 50% of all infections treated in the ICU and prolonged hospital stay and high ICU mortality [1-3]. Procalcitonin (PCT) may help to identify patients at increased risk of worsening organ dysfunction associated with severe sepsis. The goal of this study was to assess whether maximum PCT concentrations are associated with deterioration of organ function.
Method PCT-7 is a multicenter, multinational, observational study of the association of PCT levels with acute organ dysfunction and 28-day outcome in ICU patients with presumed or confirmed pneumonia and requiring mechanical ventilation. Procalcitonin was determined daily by LUMItest® (BRAHMS AG, Germany).
Results One hundred and ninety-seven patients (62.4% males) were enrolled from January 2003 to November 2004 in eight centers in Europe, the USA, and Canada. The mean age was 61.4 years (range 19–99); the mean APACHE II score was 23.7. Patients with high PCT levels had higher mortality rates (PCT cutoff: 2 ng/ml: odds ratio: 3.0 [95% CI: 1.4–6.4], $P = 0.006$; PCT

cutoff: 4 ng/ml: odds ratio: 3.7 [95% CI: 1.8–7.8], $P < 0.001$). There was a significant correlation between the maximum SOFA score and the maximum PCT during the ICU stay ($r = 0.57$; 95% CI: [0.45–0.66]; $P < 0.001$; $n = 175$). Both SOFA score and PCT elevations at any day had an area under the curve >0.7 in the receiver operator characteristic curve.

Conclusions In this first multicenter study on patients with pneumonia, high levels of PCT identify patients with organ dysfunction and a high risk of death.

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P74

Procalcitonin: analysis of diagnostic specificity and effectivity in comparison with other markers of inflammation in the critically ill

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Aim To evaluate diagnostic specificity and sensitivity of procalcitonin (PCT) in comparison with C-reactive protein (CRP) and other markers of inflammation phase reactants in relation to clinical status and microbiology examinations.

Materials and methods A prospective study in ICU patients. One hundred and sixty-four examinations of PCT, CRP, orosomucoid, prealbumin, fibrinogen, INR, leukocyte and platelet count were evaluated in 43 patients. The APACHE II score was calculated on admission, the SOFA daily. SIRS, MODS, positivity of bacteriology, hemoculture and apparent infection were also assessed. Statistical methods comprised the chi-square test, Wilcoxon unpaired test, nonparametric Kruskal–Wallis test, ROC analysis and comparison of area under the curve (AUC).

Results AUC is given for the following variables (only AUC > 0.6 is mentioned). MODS: temperature 0.700, PCT 0.683, platelets 0.657. SIRS: temperature 0.852, leukocytes 0.761, PCT 0.694, fibrinogen 0.612. SOFA: PCT 0.756, platelets 0.711, temperature 0.654, leukocytes 0.646. Hemoculture: albumin 0.703, fibrinogen 0.686, orosomucoid 0.666, temperature 0.649. APACHE II score: platelets 0.685, PCT 0.605, leukocytes 0.602. Bacteriology: temperature 0.653, PCT 0.627. Apparent infection: temperature 0.694, fibrinogen 0.680. There was a significant difference between survivors and nonsurvivors with respect to ICU stay for PCT ($P = 0.00$), platelets ($P = 0.00$), leukocytes ($P < 0.03$) and temperature ($P < 0.05$).

Conclusions PCT was a more effective marker of sepsis-related complications in ICU patients than CRP or other acute phase reactants. ROC analysis was a suitable tool for confirmation of these relations.

P75

Procalcitonin serum levels in patients after liver, pancreas and simultaneous kidney–pancreas transplantations

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Introduction Procalcitonin (PCT) is a reliable measurable marker of the clinical course in patients with infectious complications. Nonspecific elevation of PCT concentrations may occur after major surgeries or multiple trauma. Elevated concentrations of PCT were detected after administration of some immunosuppressive drugs. The aim of our study was compare PCT serum levels in patients after liver, pancreas or simultaneous kidney–pancreas transplantations without any complications.

Patients and methods PCT serum levels were examined still before induction of anesthesia, at 4 and 8 hours following graft reperfusion, and daily until postoperative day 4. The patients were divided into a group receiving polyclonal antibody ATG Fresnius (21 patients with liver and 10 patients with simultaneous kidney–pancreas transplantation) and one without it (seven patients with liver and three patients with pancreas transplantation). PCT was also determined in 12 patients undergoing liver resection. PCT levels were evaluated using an imunoluminometric assay (ILMA) with a LUMItest PCT kit (Brahms Diagnostics, Berlin, Germany) with monoclonal antibodies against calcitonin and katacalcin sequences, part of the PCT molecule.

Results PCT serum levels were slightly elevated (up to 13.90 ng/ml) in several patients after liver transplantation without ATG therapy. PCT was strongly induced in most cases in patients after liver transplantation with ATG administration (up to 249.10 ng/ml). The mean value of the maximum PCT concentration on the first postoperative day was 4.49 ± 1.63 ng/ml in patients after liver transplantation without ATG therapy and 59.08 ± 12.60 ng/ml in patients with ATG therapy ($P < 0.001$). In addition, both groups are compared with 12 patients undergoing liver resection, whose mean serum PCT levels did not exceed 1.41 ± 0.29 ng/ml. Low PCT serum concentrations (0.46 ± 0.10 ng/ml) occurred in patients after pancreas transplantation without ATG treatment. A very marked increase (139 ± 49.08) in serum PCT levels was recorded in patients with simultaneous kidney–pancreas transplantation with ATG administration.

Conclusion Polyclonal antibody administration to patients with liver and simultaneous kidney–pancreas transplantation is associated with a very marked increase in serum PCT levels, with peak values on postoperative day 1. However, this is without a clinical correlate in the form of a severe inflammatory response. The possible PCT release following ATG therapy should be taken into account when using this inflammatory parameter in transplant patients.

P76

Immediate postinjury procalcitonin levels related to final survival

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Introduction Procalcitonin (PCT) levels have been proved to be a very useful marker not only in severe microbial sepsis but also in

SIRS and MOFS. Severe polytrauma is one typical example of SIRS without microbial infection, at least during the first days. High PCT levels are often seen in multiple trauma, sometimes higher than that seen in septic shock. The prognostic meaning of these high PCT levels is practically unknown and has to be further investigated.

Objective To assess the PCT levels during the first post-traumatic days and correlate them with: the final outcome of the patient, the injury severity score (ISS) and the expected mortality, and lactic acid as a marker of tissue perfusion.

Materials and methods Over a period of 12 months (2003–2004) 42 consecutive patients older than 18 years who were admitted to the ICU of the KAT General Hospital for an expected stay > 24 hours were prospectively included in the study. The study protocol was approved by the local ethics committee. Informed consent was obtained from the next of kin of unconscious patients. All patients (mean age 27 years old) were intubated and mechanically ventilated. From each enrolled patient blood was withdrawn at the end of the first, second and third day to assess the PCT and lactic acid levels. The modified ISS to predict mortality, the kind and the severity of the injuries, and their final outcome were also registered. The patients were divided into group A, 23 patients who survived, and group B, 19 patients who finally died.

Results The patients of group A had a mean ISS of 32.87 with expected mortality 30.77%, and group B had ISS 35.45 with expected mortality 34.57%. In group A the mean PCT levels of the first day were 5.62 ng/dl, the second day 3.69 ng/dl and the third day 2.13 ng/dl. There was a smooth decrease of the PCT over the days and the difference was statistically significant ($P = 0.05$). In group B the first day mean values were 3.03 ng/dl, the second day 3.65 ng/dl and the third day 1.12 ng/dl. There was a sudden increase over the second day and a statistically significant decreased over the third day ($P = 0.01$). There were no correlations between the PCT levels, the lactic acid levels, the ISS and the expected mortality.

Discussion As seen in the literature, the patients who die from trauma have higher PCT levels. But there are no comments on the possible meaning of the value fluctuation during the first post-traumatic days. In our study it seems that the initial PCT levels were lower in the patients who died than in the patients who survived. In group A the decrease of the PCT was linear over all three days. But in the patients who died the PCT increased suddenly the second day followed by a steep decrease on the third day much lower than that seen in group A.

There is no known explanation of this phenomenon. One could suggest that this is due to an immunity system malfunction that allows patients to die late after a severe trauma. That has to be proved.

Conclusion It seems that the high initial levels of PCT do not have such a great prognostic value as has the alteration of the PCT levels seen later during the next days.

P77

Low sensitivity of procalcitonin in cerebrospinal fluid in adult patients with bacterial meningitis

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Aim To compare the diagnostic accuracy of procalcitonin (PCT) for early diagnosis and the discrimination of bacterial and viral meningitis.

Methods A prospective, observational study involving 59 adults (25 women, 34 men) who were hospitalized for acute meningitis. The diagnosis of meningitis was based on compatible clinical features and cerebrospinal fluid analysis. At admission the serum and cerebrospinal fluid PCT levels were measured simultaneously with a specific immunoluminometric assay (LUMItest Procalcitonin; BRAHMS Diagnostica, Berlin, Germany). Fifteen patients had bacterial meningitis, 44 viral meningitis, based on the detection of pathogenic bacteria and the analysis of cerebrospinal fluid.

Results PCT levels in patients with viral meningitis were not significantly different in serum and cerebrospinal fluid (0.20 ± 0.22 ng/ml, resp. 0.22 ± 0.25 ng/ml). PCT levels in patients with bacterial meningitis were higher in serum and cerebrospinal fluid compared with patients with viral meningitis (1.04 ± 1.41 ng/ml, resp. 0.75 ± 0.46 ng/ml, $P < 0.0001$; resp. $P < 0.0005$). PCT levels were not statistically different in serum and cerebrospinal fluid in patients with bacterial meningitis. We did not find a correlation between PCT levels and an impaired cerebrospinal fluid–blood barrier. PCT levels were false negative in five patients with bacterial meningitis (sensitivity of 66%). PCT levels were correlated with the number of activating monocytes in cerebrospinal fluid.

Conclusion PCT is of limited diagnostic value in patients suffering from bacterial meningitis.

P78

C-reactive protein on the fourth day of ICU admission predicts mortality and organ failure in critically ill surgical patients

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Background Plasma C-reactive protein (CRP) levels increase rapidly after various inflammatory conditions, including surgery. Although CRP measurements are used frequently in the ICU setting, their relation to the development of sepsis, organ failure and mortality is not well known.

Objective To correlate plasma CRP levels with prognosis and hospital mortality in the postoperative period.

Design A prospective cohort study.

Setting A 19-bed medico-surgical ICU in a private hospital.

Patients All surgical patients admitted to the ICU over a period of 4 months.

Measurements and results In 2005, from September to November, 527 patients were admitted to the ICU. Of them, 435 (82.5%) patients were admitted for postoperative care, and 219 (50.3%) were male. The mean age of the whole group was 62.02 ± 16 years. Nine (2.06%) patients died during the post-operative period. Among the patients who died, the mean APACHE and SAPS 2 scores were 17.67 ± 9.40 and 52.4 ± 18.31, respectively. Among those who survived, the mean APACHE and SAPS 2 scores were 12.11 ± 6.35 and 24.66 ± 13.03, respectively. Plasma CRP levels during the first 3 days of the ICU stay were not statistically different between patients who survived and those who died. On the fourth day, the plasma CPR level was significantly higher in the group who died, compared with those who survived (28.133 ± 4.77 vs 13.849 ± 10.4; $P = 0.037$). Of interest is the fact that, on admission, the APACHE and SAPS 2 scores were higher in the group who survived. The area under the ROC curve for the analysis of plasma CRP levels on the fourth day of the ICU stay was 0.86 (95% CI 0.76–0.96) with 100% sensitivity and 75% specificity to predict death in surgical patients. The best cutoff point was 22.7 mg%. The mortality in the groups

with fourth-day PCR <22.7 mg% and ≥22.7 mg% was 0 and 25%, respectively ($P = 0.011$).
Conclusion In this cohort, a plasma CPR level higher than 22.7 mg% on the fourth day of ICU admission was a good tool to discriminate between patients who died and those who survived. Plasma CRP levels appear to be better at predicting mortality than the APACHE II and SAPS 2 scores at the time of ICU admission.

P79

High C-reactive protein and low cholesterol levels are prognostic marker in severe sepsis

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Introduction Additional biomarkers in severe sepsis are needed to tackle the challenges of determining prognosis and optimizing selection of high-risk patients for application of therapy. The use of serum cholesterol as a prognostic indicator of infection and multiple organ dysfunction syndrome, and as a biologic marker for resolution of systemic inflammation is less well defined. Proposed explanations for the development of hypocholesterolemia include downregulation of hepatic synthesis, dilutional effects with resuscitation, loss of apoproteins in burns after blister formation, and metabolic utilization. A number of inflammatory cells and mediators involved in the inflammatory response have been assessed for their role as potential markers of the presence and severity of the inflammatory response and organ failure. Serum levels of C-reactive protein (CRP), an acute-phase protein synthesized by the liver following stimulus by various cytokines including tumor necrosis factor and IL-6, markedly increase within hours after infection or inflammation.
Objective To evaluate serum CRP and cholesterol as a prognostic factor for survival in patients with severe sepsis.
Methods Ninety-six patients meeting the criteria for severe sepsis. A prospective study of mortality in patients with severe sepsis whose serum levels of CRP and cholesterol were measured on admission to an ICU, 2 days later and on the day of discharge from the ICU or on the day of death.
Results The median cholesterol levels were significantly lower in the nonsurvivor patients (first day 92.2 mg/dl [25.1], second day 92.1 mg/dl [21.7], died/discharge day 92.2 mg/dl [21.7]) than the survivor patients (first day 175.1 mg/dl [38.6], second day 173.0 mg/dl [39.3], died/discharge day 171.8 mg/dl [39.6]; $P < 0.001$). The median CRP levels were significantly higher in the nonsurvivor patients (first day 32 mg/dl [20.5–64.5], second day 33 mg/dl [22–74.5], died/discharge day 30 mg/dl [22–57]) than the survivor patients (first day 10 mg/dl [6–14], second day 9 mg/dl [5–10], died/discharge day 6 mg/dl [3–9]; $P < 0.001$).
Conclusion Serum CRP and cholesterol are a predictor of survival in patients with severe sepsis. Low cholesterol and high CRP levels appear to be a valuable tool for individual risk assessment in severe sepsis patients and for stratification of high-risk patients in future intervention trials.

P80

Urinary and plasma cytokines in the critically ill

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Introduction We have previously demonstrated changes in circulating cytokines during the evolution of severe illness in ICU patients. This pilot study aimed to measure changes in circulating and urinary cytokines in critically ill patients receiving normal and high-nitrogen enteral feeds.
Methods Patients ($n = 40$) were recruited from an adult, medical/surgical ICU; urine and blood samples were obtained over three consecutive days. TNF-α, IL-6, IL-8, MCP-1 and leptin were measured by monoclonal antibody sandwich kit (ELISA). SIRS criteria were applied using the white blood cell count, heart rate, temperature and respiratory rate.
Results Urinary cytokine concentrations (u[…]) were significantly raised in ICU patients relative to controls (at least $P < 0.005$). In addition, higher u[TNF-α] (74%, $P < 0.048$) and u[IL-8] were observed in the highest SIRS index group ($n = 8$). There was a significantly higher u[IL-6] in the surgical group ($n = 24$) compared with sepsis and trauma patients ($P < 0.0005$). Plasma leptin levels (p[Lep]) increased with the duration of ICU stay. Urinary leptin was readily detectable in ICU patients: this has not been reported before. There was a marked elevation of u[Lep] (3.5-fold) in SIRS relative to non-SIRS patients ($P < 0.001$). The mean u[IL-6] was significantly decreased (45%, $P < 0.01$) in patients given a high protein diet. There was a strong inverse correlation between u[MCP-1] and dietary intake.
Conclusions Urinary measures have potential in monitoring the ICU patient immune status noninvasively; urinary IL-8 and leptin may be markers of SIRS; a high-protein diet appears to reduce u[IL-6]; u[MCP-1] may be a marker of dietary delivery.

P81

Attempt at simultaneous quantitative determination of multiple cytokines and chemokines in peripheral blood with a suspension array system

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Purpose Blood cytokine and chemokine values have been examined in pathological analyses of surgical invasion, but making multiple simultaneous measurements has been difficult from the standpoint of cost, measurement time, specimen size, etc. Microbead suspension arrays have been developed in recent years, and they have made quantitative determination of multiple substances possible.
Subjects and methods The subjects were 16 surgical patients with severe septicemia secondary to peritonitis. The patients were divided into groups according to whether their preoperative leukocyte count was below 4000/μl (LW group) or 4000/μl or greater (HW group) and changes between before and after surgery, and the changes between before and after performance of postoperative endotoxin adsorption therapy (PMX) were investigated.
The specimens consisted of frozen plasma, and the measurements were made in 25 μl samples by Bio-Plex assays (Bio-Rad Laboratories). The Wilcoxon test was used to perform the statistical analysis.
Results There were five cases in the LW group, and 11 in the HW group. There were no significant differences in age, interval between onset of symptoms and arrival at the hospital, or APACHE II scores, and the differences between groups in the operation time and blood loss were not significant either. The difference between groups in TNF-α was not significant, but the IL-1β, IL-4, IL-5, IL-6, IL-8, IL-10, and IL-13, G-CSF, GM-CSF, INF, MCP-1, and MIP-1β values were significantly higher in the LW group both preoperatively and postoperatively ($P < 0.05$). In the HW group IL-12 and IL-17 tended to be higher before surgery. Before surgery the Th1/Th2 ratio (INF/IL-4) was higher in the LW group, but after

surgery it was higher in the HW group. Comparisons between before and after PMX therapy showed a significant decrease in endotoxin values ($P = 0.03$), but there were no significant changes in cytokine or chemokine values.

Conclusion A decreased leukocyte count in peritonitis appeared to reflect a state of increased cytokine response, especially an increased response of the Th1 system. Postoperatively, however, Th2 tended to predominate. PMX therapy had no effect on cytokines. It appeared that this type of analysis will elucidate the indications and optimal timing for PMX therapy and G-CSF and INF administration in severe pathological states.

P82

A novel biomarker panel with a Multimarker Index™ value for the diagnosis of sepsis in the Emergency Department

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Objective To define a panel of biomarkers to aid in the assessment and diagnosis of patients presenting to the Emergency Department (ED) with suspected sepsis.

Population Patients presenting to the ED of 10 tertiary hospitals. The inclusion criteria were: 18 years or older, and two or more SIRS criteria with confirmed or suspected infection and/or lactate > 2.5 mmol/l. The exclusion criteria were: cardiac arrest; Do Not Resuscitate order; pregnancy.

Methods Blood samples were collected upon enrollment and the plasma was frozen at −70°C within 1 hour. Measurement of biomarkers was performed in a blinded fashion by immunoassay (Biosite). The final diagnosis was determined based on standard definitions. A search engine based on the optimization of the area under the receiver–operator curve (ROC AUC) for diagnosis of sepsis was used to select a panel of six biomarkers and to optimize a Multimarker Index (MMX). The MMX combines the individual marker values into a single index value for the sample, which is reported as the test result.

Results The ROC AUC (95% CI) for the sepsis panel MMX for differentiating patients with SIRS ($n = 73$) from those with various sepsis conditions ($n = 224$), SIRS from all sepsis with positive blood culture ($n = 41$), SIRS from severe sepsis ($n = 43$) and SIRS from septic shock ($n = 14$) are, respectively, 0.76 (0.70–0.82), 0.85 (0.79–0.92), 0.89 (0.83–0.95) and 0.95 (0.91–0.99). For comparison, the ROC AUCs obtained with CRP are 0.62 (0.54–0.70), 0.69 (0.59–0.79), 0.63 (0.53–0.74) and 0.71 (0.57–0.85); for IL-6 the values are 0.64 (0.57–0.71), 0.69 (0.59–0.80), 0.66 (0.55–0.77) and 0.63 (0.45–0.82).

Conclusion The biomarker panel MMX shows clinical utility in identifying sepsis as an underlying cause in patients presenting with SIRS. Because this level of accuracy is attained based on the first blood draw, these results suggest that it may be useful in the rapid assessment and diagnosis of patients presenting to the ED. These results need to be confirmed in additional populations.

P83

The association of early lactate clearance with inflammatory biomarkers in severe sepsis and septic shock

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Introduction Patients presenting to the hospital with sepsis with evidence of hypoperfusion have a greater risk of developing organ dysfunction and higher mortality [1]. Early recognition of hypoperfused states and implementation of strategies to resolve global tissue hypoxia as reflected by early lactate clearance correlate with improved outcome and mortality [2]. This study is a secondary analysis comparing early lactate clearance with serum biomarkers among a cohort of patients collected during the Early Goal Directed Therapy Trial (EGDT).

Methods Lactate levels were drawn on patients presenting with severe sepsis and septic shock upon hospital presentation and at 6 hours after resuscitation. Lactate clearance was defined as the decrease in blood lactate concentration from the baseline to the 6-hour value, expressed as a percentage of the baseline value [2]. Biomarkers were examined at baseline, 6, 12, 24, 36, 48, 60 and 72 hours after hospital presentation. Biomarkers were determined by immunoassay independently performed by Biosite®, Inc. (San Diego, CA, USA). The Kruskal–Wallis statistic was used to detect differences in mean (0–72 hours) biomarker levels among patients stratified by lactate clearance quartiles. Chi-square analysis and Kaplan–Meier mortality estimation were used to compare outcome among the lactate clearance quartiles. The Student two-sample *t* test, Wilcoxon rank sum test, chi-square and Kruskal–Wallis statistics were employed to compare hospital survivors versus nonsurvivors. A two-tailed probability level < 0.05 was accepted as statistically significant.

Results Two hundred and forty-three patients were stratified into quartiles by their level of lactate clearance after 6 hours. There was a statistically significant inverse relationship between patients' lactate clearance and the mean levels of each biomarker (TNF-α, IL-1 receptor antagonist and caspase-3) over the first 72 hours of hospitalization ($P < 0.035$). There was also a statistically significantly higher hospital 28-day and 60-day mortality for each quartile of decreasing lactate clearance ($P < 0.010$).

Conclusions Early resolution of global tissue hypoxia or greater lactate clearance is associated with a corresponding decrease in inflammatory mediators and mortality. The exact mechanism by which early hemodynamic optimization modulates inflammation requires further study.

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P84

Newly developed plasma soluble E-selectin rapid assay predicts prevalence of acute respiratory distress syndrome in critically ill patients

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Background Plasma levels of soluble E-selectin (sES) have been shown to reflect the production of TNF, a proinflammatory cytokine critically involved in the pathogenesis of various types of organ failure in sepsis. We examined whether a newly developed rapid immunoassay method for plasma sES is able to predict the prevalence of organ failure including acute respiratory distress syndrome (ARDS) in critically ill patients.
Methods Plasma samples were obtained from 50 critically ill patients showing systemic inflammatory response syndrome (SIRS) on admission to the emergency unit. Plasma levels of sES were determined using a latex agglutination method.
Results The normal range of the plasma sES level was 4.8–29.7 ng/ml with this method. Among the patients examined, 22 patients showed elevated sES levels (D_AE group) and 28 patients normal sES levels (D_AN group). The prevalence of ARDS was significantly higher in the D_AE group (15/22, 68.2%) than in the D_AN group (4/28, 14.3%) ($P < 0.001$) and that of cardiovascular system failure, renal failure, and coagulation system failure was also significantly higher in the D_AE group than in the D_AN group in the first 5 days after admission. The mortality rate at 28 days after admission was significantly higher in the D_AE group (27.3%) than in the D_AN group (0%) ($P < 0.05$).
Conclusion Determination of sES levels by this new rapid assay method might be useful for prediction of the prevalence of organ failure including ARDS and the outcome in critically ill patients showing SIRS, a pathologic condition that has the potential risk for development of multiple organ failure.

P85

TLR2, TLR4, CD14, CD11b and CD11c expression on monocyte surfaces and cytokine production in septic patients

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Bacterial recognition and induced cellular activation is fundamental for the host control of infection, yet the limit between protective and harmful response is still inexact. Forty-one patients were enrolled in this study: 14 with sepsis, 12 with severe sepsis, and 15 with septic shock. Seventeen healthy volunteers (HV) were included as controls. The expression of TLR2, TLR4, CD14, CD11b and CD11c was analyzed on monocyte surfaces in whole blood. sCD14 was measured in serum and TNF-α, IL-6 and IL-10 cytokine levels were measured in PBMC supernatants following LPS, IL-1β and TNF-α stimuli by ELISA. An increase in sCD14 and a decreased mCD14 were found in patients as compared with HV ($P < 0.001$). However, no differences in the expression of TLR2, TLR4 and CD11c were found among the groups. A trend towards differential expression of CD11b was observed, with higher values found in patients with sepsis as compared with HV. A negative regulation of the inflammatory cytokine production was observed in severe sepsis and shock septic patients in relation to the sepsis and HV, regardless of the stimulus. No significant difference in IL-10 production was found among the groups. In this study we show that the inflammatory response is associated with the continuum of clinical manifestations of sepsis, with a strong inflammatory response in the early phase (sepsis) and a refractory picture in the late phases (severe sepsis and septic shock). Correlation between cell surface receptors and cytokine production after IL-1β and TNF-α stimuli and the observation of a single and same standard response with the different stimulus suggest a pattern of immunology response that is not dependent only on the expression of the evaluated receptors and that is likely to have a regulation in the intracellular signaling pathways.

P86

Increased leukocyte oxidative metabolism in severe sepsis and septic shock correlates with organ dysfunction and mortality

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Introduction Sepsis is the leading cause of mortality in the ICU. Sepsis morbidity and mortality are increasing through the years. Infection control depends on adequate microbe recognition and satisfactory cell activation. Paradoxically it has been seen that in sepsis cell activation can be both good and harmful to the host.
Objectives To evaluate neutrophil activation in the continuum of sepsis measuring cell surface receptors and oxidative metabolism; to evaluate monocyte activation measuring oxidative metabolism; and to evaluate the correlation between cell activation and organ dysfunction.
Methods Regarding the 1992 ACCP/SCCM consensus, 41 patients were included: 14 with sepsis, 12 with severe sepsis and 15 with septic shock. Seventeen healthy volunteers were included as the control group. TLR2, TLR4, CD11b, CD11c and CD66b expression on the neutrophil surface using whole blood were measured using flow cytometry. Reactive oxygen species formation due to DCFH oxidation was also measured by flow cytometry. Organ dysfunction was characterized and measured using the SOFA score.
Results Diminished TLR2 and TLR4 expression was observed in septic shock compared with healthy volunteers ($P = 0.05$ and $P = 0.06$, respectively). There were no differences found in CD11b and CD11c expression. CD66b expression was increased when comparing the whole group of patients and the control group ($P = 0.01$). The neutrophil oxidative burst was increased in the whole group of patients compared with the control group at baseline and under PMA, fMLP, LPS and *S. aureus* stimulation ($P < 0.001$ for all conditions tested). The monocyte oxidative metabolism was also significantly increased in the whole patient group compared with the control group in all conditions tested ($P < 0.01$). Neutrophil and monocyte oxidative metabolism due to PMA, LPS and *S. aureus* stimulation in severe sepsis were diminished compared with sepsis and septic shock. A strong correlation was observed between neutrophil and monocyte oxidative metabolism. The SOFA score discriminated patients between survivors and nonsurvivors (ROC curve was 0.78; $P = 0.02$). A positive correlation was observed between organ

dysfunction and oxidative metabolism in neutrophils and monocytes considering severe sepsis and septic shock. However, despite an oxidative burst in sepsis as high as in septic shock, no organ dysfunction was found in sepsis.
Conclusions Neutrophils and monocytes are activated in the continuum of sepsis considering reactive oxygen species formation. Nonetheless, in the onset of sepsis increased oxidative metabolism was probably involved in resolution of the infectious course, but in the late stages of sepsis it was associated with tissue damage and, consequently, organ dysfunction and death.

P87

A priming endotoxin bolus amplifies the inflammatory response in low-dose human endotoxemia

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Introduction The response to an inflammatory stimulus is highly variable in critically ill patients and may differ from that of healthy volunteers. One of several distinguishing characteristics between the two groups is an elevated plasma level of cytokines in patients. We hypothesized that an acute elevation in TNF-α, as evoked by a priming dose of purified *Escherichia coli* endotoxin (LPS), would enhance the inflammatory response to LPS, and we investigated this hypothesis in healthy volunteers in a randomized, double-blind, crossover design.
Methods Following approval by the local Human Ethics Committee, 13 volunteers underwent three interventions each, receiving two bolus injections, spaced 90 min apart and consisting of either saline + LPS (0.2 ng/kg) (LPS-0.2), saline + LPS (0.4 ng/kg) (LPS-0.4), or LPS (0.2 ng/kg) + LPS (0.2 ng/kg) (LPS-0.2+0.2). Physiological variables were monitored throughout until 8 hours after the last dose; blood samples were drawn for measurement of plasma TNF-α, IL-6, C-reactive protein (CRP), white blood cell (WBC) and differential counts. Interventions were spaced at least 1 month apart. A repeated-measures multivariate ANOVA (intervention-by-time) with Bonferroni corrections was performed. $P < 0.05$ was considered significant.
Results Flu-like symptoms occurred during all three interventions; the frequency was increased in groups LPS-0.4 and LPS-0.2+0.2 as compared with LPS-0.2. The heart rate, body temperature, CRP, WBC, and the neutrophil count increased more, and the lymphocyte count was more reduced, during LPS-0.2+0.2 compared with both LPS-0.2 and LPS-0.4. Levels of TNF-α and IL-6 were higher during LPS-0.2+0.2 (mean peak TNF-α ±, 44.6 [95% CI, 25.8–63.3] mg/l) compared with LPS-0.4 (28.0 [16.8–39.3] mg/l) and LPS-0.2 (12.7 [6.1–19.3] mg/l) ($P < 0.001$), as well as during LPS-0.4 compared with LPS-0.2.
Conclusion In healthy humans, induction of a low-grade inflammatory response by a priming bolus injection of LPS amplifies the clinical and paraclinical inflammatory response to a subsequent LPS injection. This may explain the potent proinflammatory response seen in some critically ill patients.

P88

The effect of systemic iNOS inhibition during human endotoxemia on the development of TLR-tolerance *in vitro*

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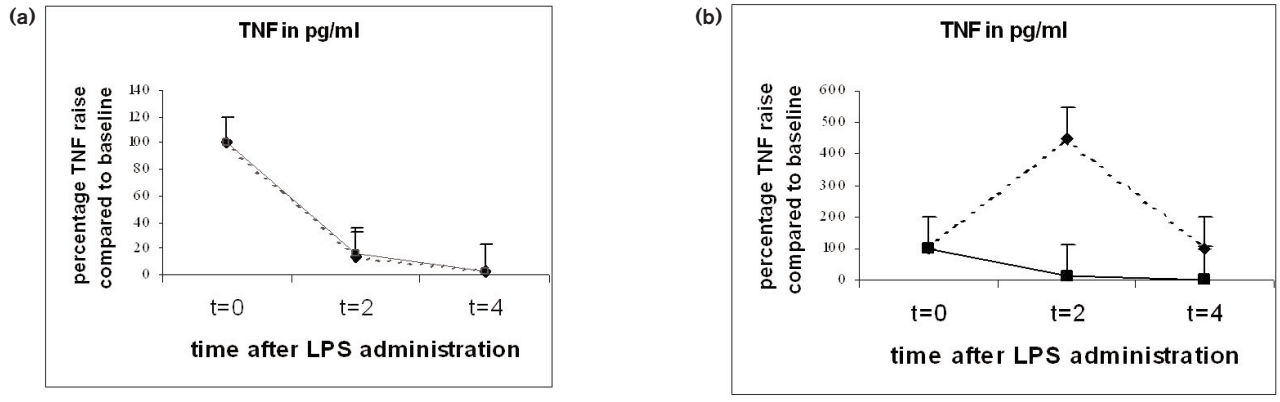
Introduction The phenomenon of repeated exposure to endotoxin resulting in diminished release of proinflammatory cytokines is called endotoxin tolerance. After receiving a low-dose pretreatment with endotoxin, tolerant animals survive a challenge with a 'lethal dose' of endotoxin. Recent studies suggests a pivotal role for NO arising from iNOS in the development of tolerance. Toll-like receptors (TLRs) are receptors that recognize specific pathogen-associated molecular patterns. Ten members of the so-called TLR family have been identified in humans, and several of them appear to recognize specific microbial products, including LPS (TLR-4), peptidoglycan (TLR-2) and flagelline (TLR-5). Recognition leads to activation of intracellular signaling pathways, which upregulate a wide array of inflammatory modulators that contribute to the early host cell response. The aim of this study was to test whether administration of the selective iNOS inhibitor aminoguanidine during human experimental endotoxemia influences the development of tolerance to several TLR-agonists *in vitro*.
Methods Seventeen healthy volunteers (age 22.2 ± 1.8 years) were treated with an i.v. bolus injection of 2 ng/kg *Escherichia coli*

Figure 1 (abstact P88)



TNF response to **(a)** TLR-4 and **(b)** TLR-5 agonist stimulation *in vitro* in the absence (straight line) and presence (dotted line) of *in-vivo* treatment with iNOS inhibitor aminoguanidine.

LPS in the absence ($n = 10$) or presence ($n = 7$) of the selective iNOS inhibitor aminoguanidine (bolus of 370 mg and continuous infusion 1 mg/min 1 hour after administration of LPS). Whole blood was stimulated *in vitro* with different TLR agonists before, and 2 and 4 hours after LPS treatment. The TLR agonists used were Pam 3 Cys, 1 μg/ml (TLR-2); Poly I:C, 50 μg/ml (TLR-3); *E. coli* LPS, 1 ng/ml (TLR-4); Flagelline, 10 ng/ml (TLR-5); and Loxoribine, 50 μg/ml (TLR-7). The samples were incubated at 37°C for 24 hours, after which cell-free supernatant was obtained (centrifugation at 2000 × *g* at 4°C for 15 min) and stored at −80°C until ELISAs were performed.

Results *In-vitro* incubation with the different TLR-agonists resulted in release of cytokines in blood samples taken prior to the LPS administration *in vivo*. The cytokine release was attenuated 2 and 4 hours after LPS administration *in vivo* (see Fig. 1a). This development of tolerance occurred in TLR-3, TLR-4, TLR-5 stimulated whole blood. *In-vivo* administration of the iNOS inhibitor aminoguanidine had no significant effect on the development of tolerance in TLR-3 and TLR-4 stimulated whole blood, but TLR-5 agonist stimulated whole blood showed that tolerance was inhibited ($P < 0.05$; see Fig. 1b).

Conclusions LPS administration *in vivo* attenuates the *in-vitro* cytokine response on various TLR-agonists. Inhibition of iNOS *in vivo* had no effect on the development of tolerance in TLR-3 and TLR-4 stimulated whole blood, but tolerance diminished in TLR-5 agonist stimulated whole blood. This suggests that NO is involved in the development of tolerance to flagelline.

P89

G-CSF is an endothelial survival factor in LPS-induced inflammatory conditions

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Background Granulocyte-colony stimulating factor (G-CSF) may induce stem cell mobilization and stimulates myelopoiesis. Functionally, G-CSF upregulates myeloid cell survival and effector function (e.g. phagocytosis, Fc-mediated killing, etc.). G-CSF has been discussed to play a role in the protection of endothelial cells and anti-apoptosis via bcl-2 family protein, caspase 9 and cIAPs. We were therefore interested to test the effect of G-CSF on endothelial cell viability in the presence and absence of granulocytes (PMN) with and without activation by bacterial endotoxin (LPS).

Methods Endothelial monolayers were established from bone marrow and layers were preincubated with rhG-CSF (filgrastim, 3000 U/ml) for 24 hours. PMN isolated from patients with septic shock or healthy donors were incubated with or without LPS (*E. coli* 0111:B4, 100 ng/ml); or were preactivated with LPS, then washed before being cocultured with the endothelial layer for another 24 hours. As a measure for cell viability, we quantified ATP contents by luciferin-based chemiluminescence. The inflammatory response by endothelial cells and/or PMN was studied by measuring IL-8, IL-6, IL-1β and TNF-α released into the culture supernatant.

Results In G-CSF treated endothelial/PMN co-cultures as well as in G-CSF substituted cultures of PMN alone, the ATP content in cell lysates was upregulated. This G-CSF effect was independent from the addition of exogenous LPS. PMN as well as LPS stimulated the cytokine release by endothelial cells. We found IL-6 levels ranging between 1 and 1054 pg/ml being exclusively secreted by endothelial cells, and IL-8 levels originating from PMN and endothelial cells between 55 and 3278 pg/ml, respectively. G-CSF had no effect on IL-6 levels but downmodulated IL-8 in all endothelial/PMN co-cultures as well as PMN cultures alone. All IL-1β levels were close to detection levels and TNF-β levels were in the range of 5–20 pg/ml. This indicates that PMN preparations were not significantly contaminated by monocytes or macrophages. This was confirmed by morphological examination.

Conclusion G-CSF increases the ATP content in both endothelial/PMN co-cultures and PMN cultures alone even if LPS or LPS-treated PMN are added, to mirror an inflammatory response. Moreover, G-CSF attenuates levels of the inflammatory cytokine IL-8, but does not modulate IL-6.

P90

Effects of naloxone on phagocyte functions

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Introduction Naloxone has been proposed to treat septic shock. We assessed by flow cytometry its effect *in vitro* on phagocytose (PH) and burst oxidation (BO) of neutrophils and monocytes after various stimuli in 10 healthy volunteers.

Methods Whole blood was incubated with or without naloxone at a range of concentrations used in septic shock (2×10^{-4}, 2×10^{-5}, 2×10^{-6}, 2×10^{-7} M). We added dihydrorhodamine 123 to mark H_2O_2 production. We stimulated the cells by either propidium iodide stained *S. aureus*, *E. coli* or *C. albicans*, or by phorbol-myristate-acetate (PMA). We used an index of PH and an index of BO. As H_2O_2 production depends on PH and on BO, we defined a global index (GI) of its final production taking those two parameters into account.

Table 1 (abstract P90)

	Naloxone			
	2×10^{-4} M	2×10^{-5} M	2×10^{-6} M	2×10^{-7} M
Neutrophils:*S. aureus*: GI(BO/PH)	−72**(−9°/−69**)	−51**(+31°/−56**)	−24**(+20*/−39*)	−14(+29*/−37**)
Neutrophils:*E. coli*: GI(BO/PH)	−90**(−30°/−90°)	−72**(+11°/−80**)	−25**(+5°/−43*)	−18**(+109°/−40**)
Neutrophils:*C. albic*: GI(BO/PH)	−51**(−46**/−10*)	−35**(−31**/−7°)	−23°(−10*/−2°)	−8°(+2°/−12°)
Monocytes:*S. aureus*: GI(BO/PH)	−58**(−75**/+55*)	−51**(−57**/27°)	−32**(−24*/−10°)	−35*(−13°/−18*)
Monocytes:*E. coli*: GI(BO/PH)	−22°(−73**/+158**)	−45**(−65**/+43**)	−35*(−31*/−4°)	−25°(−19°/−22°)
Monocytes:*C. albic*: GI(BO/PH)	−58**(−63**/+1300°)	−34**(−37**/+833°)	−3°(−10*/+21°)	+8°(+5°/+14°)
Neutrophils/monocytes: PMA: BO	−70*/−83*	−61*/−61*	−44*/−43*	−49*/−44*

*$P < 0.05$; **$P < 0.01$; ° not significant.

Results See Table 1: percentage of change in GI, BO and PH with naloxone compared with no naloxone after stimulation (Wilcoxon signed rank test).
Conclusion Naloxone inhibits significantly in a dose-dependant manner the production of H_2O_2 in both neutrophils and monocytes at concentrations used in septic shock, but its influence on PH and BO is different according to the applied stimulus.

P91

A lack of Toll-like receptor 4 expression variability in the immediate preoperative period: a pilot study of elective surgical patients

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Toll-like receptor 4 (TLR-4), a receptor of innate immunity, provides the site for the lipopolysaccharide shell of Gram-negative organisms to bind and initiate the inflammatory cascade in sepsis. Its expression has been studied in various disease states (sepsis, asthma, atherosclerosis, immunodeficiencies), ethnic groups (Chinese, Irish, Scottish, Gambian), ages, level of physical training, gestational status, and trauma. The expanding body of evidence in regard to TLR signaling is demonstrating the importance between such signaling and human disease. A translational research project between the Departments of Anesthesiology and Medical Microbiology and Immunology was initiated to determine any difference in the amount of TLR-4 expression in elective preoperative patients in regard to height, weight, age, sex, and body surface area (BSA), body mass index (BMI), hypertension, and diabetes. Race was not analyzed. After institutional research board approval, a prospective study of the blood specimens of 52 consecutive, elective, preoperative patients was performed. The blood was directly decanted into a PAXgene Blood RNA tube (Qiagen) designed for the stabilization of RNA from whole blood. Whole blood RNA was extracted using the PAXgeneTM Blood RNA System (PreAnalytiX, Hombrechitikon, Switzerland), including treatment with DNase I to prevent genomic DNA contamination. Quantification of TLR-4 expression levels in human lymphocytes was by RT-PCR and results compared with standard curves. Pearsons's correlation coefficient was use for statistical analysis of the continuous variables and *t*-testing was used in the analysis of the categorical variables. The TLR-4 concentration varied from 0.211 to 2.490 fmol/µl per cDNA; however, there was no statistical significance between the concentration of TLR-4/cDNA expressed by RT-PCR and the continuous variables (height, weight, BMI, BSA, and age) nor the categorical variables (hypertension, diabetes, and sex) (Table 1). None of the patients had postoperative infections. This was an initial attempt to quantify the TLR-4 receptor expression by elective patient variable preoperatively. It provided an opportunity for anesthesiologists to take their practice to the laboratory to explore the immunologic basis of their actions.

Table 1 (abstract P91)

Var		Mean	SD	*P* value
HTN	0	0.55	0.35	0.48
	1	0.49	0.32	
DM	0	0.51	0.34	0.48
	1	0.59	0.31	
Sex	0	0.48	0.32	0.63
	1	0.55	0.34	

P92

Gene expression in sepsis is independent of the center-associated effects and indicates a tight regulation of the inflammatory process

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Background Sepsis remains the leading cause of death in noncardiologic ICUs. Genetic predispositions of patients play an important role in the control of inflammatory response. We have recently reported that cDNA microarrays can be used to identify typical gene expression profiles in patients with severe sepsis despite strong interindividual differences. The aim of the present study was therefore to evaluate whether center-dependent effects on the gene expression pattern exist, whether diagnostically relevant gene expression profile can be identified, and which genes are important during the systemic inflammatory response.
Materials and methods Twenty-nine patients were enrolled from one German and three Czech hospitals. The ACCP/SCCM consensus conference definition was applied to predict the severity of sepsis in ICU patients. As controls we used 18 post spinal or bypass surgery patients, respectively, without signs of inflammation. Gene expression was measured using the inhouse research microarray of SIRS-Lab GmbH Jena (Germany), which comprised probes for 5226 human genes relevant to inflammation, immune response and related processes. The experiments were performed according to MIAME guidelines.
In order to reveal genes differentially expressed during sepsis and to assess the effects sample collection from different centres have on the data, we applied, gene by gene, the two-way analysis of variance to the normalised expression data. Furthermore, the q-value was estimated, thus controlling the false discovery rate (FDR) occurring in multiple comparisons.
Results A set of 213 genes was obtained, for which the gene expression significantly varied between sepsis and control patients, similarly in both centers (FDR < 0.1). In this set, 88 genes were upregulated and 125 genes were downregulated in sepsis patients compared with the controls.
Conclusions The present data indicate that microarray technology is suitable for systematically identifying those genes that underlie the attenuated inflammatory response in sepsis. Gene expression profiles were able to distinguish between infectious and non-infectious systemic inflammatory response, despite a magnitude of center-associated effects. The participation of genes involving in the control of inflammatory response indicated a necessity of tight control of inflammatory response and has a potential impact for future diagnosis and treatment of sepsis.

P93

Ketamine improves survival in burn followed by sepsis in rats

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Objective Ketamine was previously reported to decrease cytokine production and improve survival after *E. coli*-induced sepsis. The

present study examined whether ketamine decreased cytokine production and improved survival after burn or after burn combined with sepsis.

Methods In groups 1–4, rats sustained burn injury at time 0, and were given ketamine (10 mg/kg) or saline at 1 or 24 hours post burn. In groups 5–8 we created a 'two hit' model of burn followed by sepsis. Rats that sustained burn at time 0 were given *E. coli* (0.2×10^9 CFU) at 24 h. The animals received ketamine or saline at 1 or 24 hours post burn. In all the above groups mortality was recorded for 7 days and IL-6 was measured in serum at 6 and 30 hours post burn.

Results Ketamine given at 1 hour (but not 24 hours) after burn injury decreased serum IL-6 concentrations compared with saline (430.0 ± 36.71 vs 106.5 ± 3.403 pg/ml [mean ± SEM], $P < 0.0001$) without altering survival. After burn followed by sepsis, ketamine given at 1 hour tended to improve survival and decrease IL-6, and when given at 24 hours (i.e. immediately after *E. coli* inoculation) significantly improved survival (46.1% vs 13.3%, $P = 0.008$) and decreased IL-6 (72,640 ± 40,990 vs 332,300 ± 32,300 pg/ml, $P = 0.0079$).

Conclusion We conclude that ketamine therapy improves survival in burn followed by sepsis. This beneficial effect probably is achieved by interfering with the inflammatory cascade, as evidenced by attenuation of cytokine concentrations.

P94

Role of calcium regulation in vascular hyporeactivity induced by peritonitis-associated septic shock

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The norepinephrine (NE)-induced contraction contains two components: Ca^{2+} release from the sarcoplasmic reticulum (SR) as the fast (F) phase, and Ca^{2+} influx via a voltage-dependent calcium channel on the membrane as the slow (S) phase. This study was to evaluate the role of Ca^{2+} handling in vascular hyporeactivity to NE using functional isometric tension recording experiments in isolated septic rat aorta and mesenteric artery. The sepsis was induced by cercal ligation and puncture (CLP) and the vascular tissues were removed at the late phase of sepsis (i.e. 18 hours after CLP). Our results showed that rats which received CLP for 18 hours manifested severe hypotension and vascular hyporeactivity to NE *in vivo*. In addition, *in-vitro* studies showed that the vascular hyporeactivity to NE was not only observed in the aorta but also in the mesenteric artery obtained from the CLP-induced sepsis rat, and is more severe in the small resistance artery. Both the F phase and S phase of NE-induced contraction were reduced in aortas and mesenteric arteries from sepsis rats. The addition of 2.5 mM Ca^{2+} into Ca^{2+}-free solution restored the NE-induced contraction in aortas to the level of that in normal Krebs' solution in both groups, while a delayed contraction occurred in the mesenteric artery from the CLP group. In order to clarify what possible mechanisms contribute to the abnormal calcium handling in sepsis, inhibitors of calcium channel and release were used. The inhibition of 2-aminoethoxy-diphenyl borate (2-APB), ryanodine, and cyclopiazonic acid (CPA) on the NE-induced contraction in Ca^{2+}-free solution were greater in the aorta from septic rats, and inhibitions of CPA and ryanodine, but not of 2-APB, were attenuated by nitric oxide (NO) synthase inhibitor N^{ω}-nitro-L-arginine methyl ester. In addition, the attenuation of NE-induced contraction by nifedipine in the aorta was also greater in the CLP group. Our results therefore suggest that vascular hyporeactivity to NE in the CLP-induced sepsis is caused by a major decrease of SR function and a minor impairment of voltage-dependent Ca^{2+} channels on membrane to Ca^{2+} handling in aortas and mesenteric arteries of rats, and this could be attributed to the overproduction of NO in sepsis.

P95

Microcirculatory hyporesponsiveness in lipopolysaccharide-induced inflammation is endothelial cell dependent but calcium independent

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Critical Care 2006, **10(Suppl 1):**P95 (doi:10.1186/cc4442)

Background Two hallmarks of sepsis are decreased vascular resistance and hyporeactivity to vasoconstrictor agents in the microcirculation. Whether the impairment in vasoreactivity is caused by defects in the signal transduction pathway inherent to endothelial cells or smooth muscle cells remains unclear.

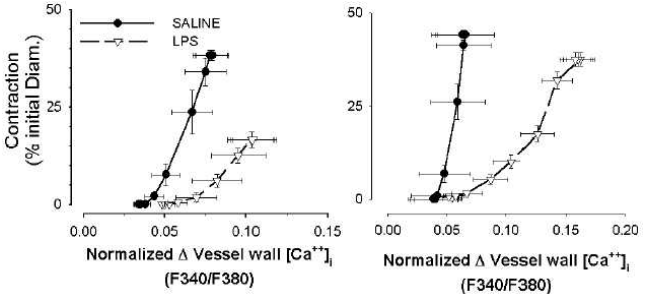
Objective The aim of this study was to determine whether impaired vasoreactivity during LPS-induced inflammation is associated with altered Ca^{2+} sensitivity of contractile proteins in small mesenteric resistance arteries (SMRA).

Methods LPS (15 mg/kg) or sterile water was injected intraperitoneally into mice. SMRAs were harvested 18 hours after injection. The arterioles (~190–220 μm) were mounted on a pressure myograph, superfused with MOPS buffer at 37°C, and loaded with fura-2. The arteriolar diameter and global intracellular Ca^{2+} were measured concurrently using light microscopy and a photomultiplier system. Concentration–response curves to phenylephrine (PE) (10^{-9} to 10^{-4} M) were conducted. In all experiments, $n = 4–6$; $^*P < 0.05$ indicates statistical significance.

Results LPS treatment resulted in hyporesponsiveness to PE as demonstrated with an increase in EC_{50} (0.7 ± 0.2 μM vs 1.9 ± 1.0 μM*), a decrease in maximal contractile response (E_{max} 35 ± 6% vs 19 ± 9%*) and a reduction in Ca^{2+} sensitivity (Fig. 1, left). Removal of the endothelium resulted in a near-normal response to PE in LPS-treated mice (EC_{50} 0.9 ± 0.2 μM vs 1.0 ± 0.6 μM and E_{max} 43 ± 2% vs 38 ± 5%). Interestingly, Ca^{2+} sensitivity remained decreased in SMRAs from LPS-treated mice (Fig. 1, right).

Conclusions In small resistance arteries, LPS-induced inflammation results in endothelial cell dependent hyporesponsiveness to vasoconstrictors in association with, but independent of, a decreased Ca^{2+} sensitivity within the smooth muscle cells. This suggests that, in the microcirculation, endothelial cells moderate contractility function without affecting calcium sensitivity within the smooth muscle cells.

Figure 1 (abstract P95)



P96

Microdialysis study of imipenem distribution in muscle and lung extracellular fluids of infected rats

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Critical Care 2006, **10(Suppl 1):**P96 (doi:10.1186/cc4443)

Background Imipenem is frequently used in ICUs to treat nosocomial infections. As infections mainly occur in tissue extracellular fluid, unbound antibiotic concentrations in this compartment are responsible for the antimicrobial effect. Microdialysis allows the measurement of unbound antibiotic concentrations. The aim of this study was to investigate the imipenem distribution in the blood, muscle and lung by microdialysis in a rat model of *A. baumannii* pneumonia, by comparing unbound concentrations between tissues and blood.
Method Three days before the pharmacokinetic experiment, seven rats were rendered neutropenic by cyclophosphamide intraperitoneal administration (150 mg/kg body weight). The day before the experiment, under isoflurane anaesthesia, rats were equipped with a femoral vein catheter, an internal jugular vein and a muscle microdialysis probe. At the end of this surgery, animals were infected intratracheally with an *A. baumannii* suspension (10^7 CFU/ml). The day of the experiment, after tracheotomy and thoracotomy under isoflurane anaesthesia, the lung microdialysis probe was inserted. The study was conducted under inhaled anaesthesia and mechanical ventilation. Imipenem recoveries in the three media were determined in each rat by retrodialysis by drug before imipenem administration (30 mg/kg over 30 min intravenously), then microdialysis samples were collected during 150 min. At the end of experiment, after euthanasia, the lungs were removed and a quantitative bacteriological study was performed to confirm pneumonia.
Results Decay of free concentrations in the blood, muscle and lung over time were monoexponential and the concentration profiles in these three media were virtually superimposed (Fig. 1). Accordingly, AUC tissue (muscle and lung) to AUC blood ratios were virtually equal to 1. Compared with values previously determined in non-infected rats, a higher interindividual variability was observed in these three media for all the pharmacokinetic parameters, probably due to the immunodeficiency and/or infection [1].
Conclusion In this rat model of *A. baumannii* pneumonia, the imipenem distribution in the lung and muscle could be predicted from unbound blood concentrations since unbound blood, muscle and lung concentrations were superimposed.
Reference
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P97

Antibacterial therapy in ovine model of sepsis

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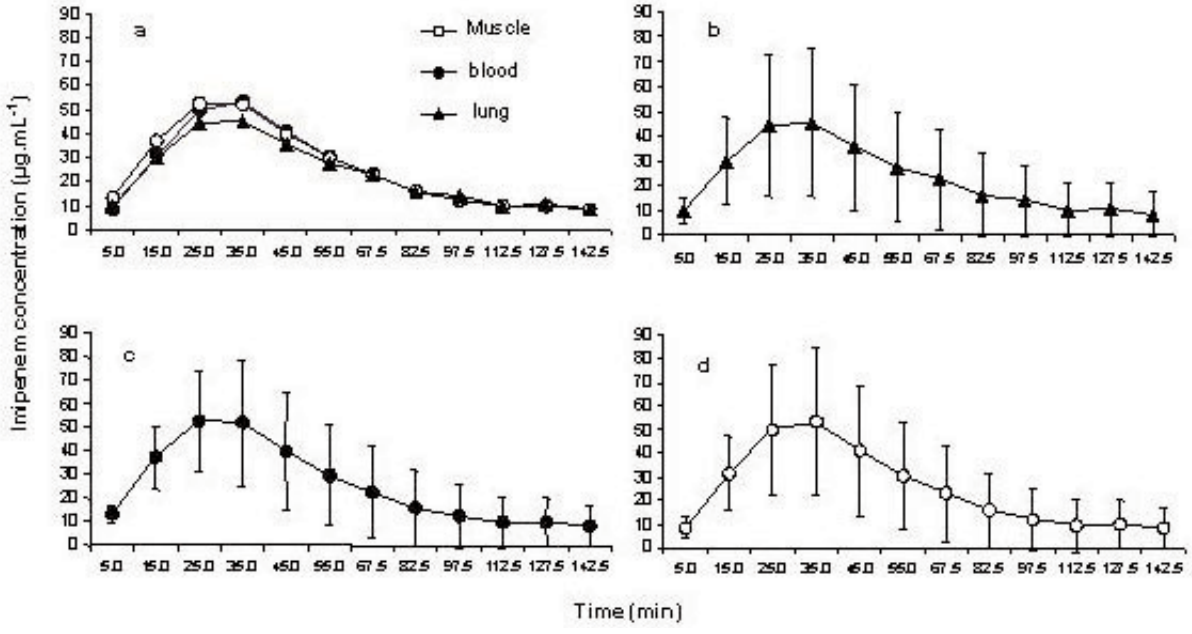
Objective Sepsis increases morbidity and mortality of burn victims with smoke inhalation. Since septic patients are usually on an antibiotic, we felt that antimicrobial therapy was appropriate to make our model clinically relevant. Because *P. aeruginosa* is a frequent cause of pneumonia/sepsis, we hypothesized that a combination of potent antipseudomonas antibiotics, such as ciprofloxacin and piperacillin, would improve the outcome of septic shock in sheep.

Figure 1 (abstract P96)



Unbound imipenem concentrations: **(a)** mean concentrations in blood, muscle and lung; mean ± SD concentrations in **(b)** lung, **(c)** blood and **(d)** muscle.

Methods Sixteen sheep were surgically prepared for study. After a tracheotomy, acute lung injury/sepsis was induced by 48 breaths of cotton smoke inhalation and instillation of *P. aeruginosa* (2–5 × 10^{11} CFU) into the lung. After the injury all sheep were awakened, mechanically ventilated, and resuscitated with Ringer's lactate solution. Animal groups: sham (n = 6, non-injured, nontreated); control (n = 5: injured, untreated); treated (n = 5: injured, treated with ciprofloxacin [0.4 g, every 12 hours] plus piperacillin [3 g, every 6 hours]). Antibiotics were intravenously administered starting 6 hours after the insult. The animals were sacrificed if they matched the termination criteria or survived over 96 hours. Statistical analysis was performed by ANOVA, significance was $P < 0.05$ *within group, †between groups. Data are the mean ± SEM.
Results Cardiopulmonary variables were stable in the sham group and the survival rate was 100%. All injured sheep reached criteria for sepsis 6 hours postinjury. The mean survival time was significantly improved in the treatment group compared with the injured group (23 hours in control group vs 83 hours† in treatment group). The control group showed a significant decrease in PaO_2/FiO_2 (P/F) ratio and mean arterial pressure (MAP, mmHg), left ventricular stroke work index (LVSWI, g × m m^{-2} $beat^{-1}$), and systemic vascular resistance index (SVRI, dynes sec cm^{-5} m^{-2}). The treatment group also showed a fall in the P/F ratio, MAP, LVSWI, and SVRI that was significantly improved after 18 hours compared with control (Table 1).

Table 1 (abstract P97)

	0 hours	18 hours
P/F ratio – control	529 ± 9	67 ± 8*
P/F ratio – treatment	543 ± 12	218 ± 44*†
MAP – control	107 ± 6	60 ± 5*
MAP – treatment	106 ± 4	95 ± 7†
LVSWI – control	66 ± 5	32 ± 8*
LVSWI – treatment	89 ± 12	56 ± 7†
SVRI (%)– control	100	47 ± 2*
SVRI (%)– treatment	100	77 ± 9†

Conclusions The delayed therapy with ciprofloxacin and piperacillin was effective as a treatment strategy for *P. aeruginosa*-induced pneumonia/sepsis. This therapy increases the validity of our sepsis model.

P98

Characterization of an experimental model of septic shock induced by fecal peritonitis in pigs

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Introduction Pathophysiological human studies in sepsis are difficult to perform due to ethical and methodological concerns. In this context, animal models of severe sepsis can be useful to better understand this condition and to test new therapeutic interventions.
Objective The purpose of this study was to describe and characterize a clinically relevant experimental model of septic shock in pigs that could be useful to test different therapeutic interventions.
Methods Five White Large pigs (35–45 kg) were anesthetized and instrumented with arterial and Swan–Ganz catheters. A splenectomy was performed and sepsis was induced by peritoneal instillation of 1.5 g/kg fecal content. Several biochemical indicators of organ dysfunction as well as infectious parameters were measured. The animals were followed until death, when fragments of the heart, small bowel, liver and kidney were removed for pathology. Three nonseptic animals served as controls.
Results The animals survived 17 hours on average (range 16–18 hours). Septic shock was characterized as a significant increase in heart rate (102 ± 27 baseline vs 139 ± 16 bpm before death, $P < 0.001$) and a decrease in mean arterial pressure (111 ± 9 vs 62 ± 9 mmHg, $P = 0.009$). Septic pigs developed a nonsignificant decrease in cardiac output (109.4 ± 54.5 vs 71.2 ± 20.1 ml/min/kg, $P = 0.221$) and mixed venous oxygen saturation (74 ± 2 vs 34 ± 13%, $P = 0.110$) during the study period. These animals were fully resuscitated (mean 12.2 ± 2.4 l Ringer lactate) as evidenced by stable values of central venous pressure (12.8 ± 2.4 vs 20.4 ± 7.4 mmHg, $P = 0.905$) and wedge pressure (11.4 ± 6 vs 19.0 ± 3.6 mmHg, $P = 0.903$). *E. coli* was recovered from blood cultures of all the septic animals. Although biochemical data did not demonstrate important organ dysfunction, some pigs developed clinical signs of organ injury, such as oliguria. Histology depicted only focal or minor abnormalities. Control animals were sacrificed 24 hours after surgery without developing significant changes in hemodynamic, respiratory or metabolic variables.
Conclusion Fecal peritonitis in pigs is a reliable and clinically relevant model of sepsis that can be useful to test several different therapeutic interventions.

P99

Early and late onset nosocomial infections in ICU patients with head injury

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Introduction The aim of this clinical study was to evaluate the incidence of nosocomial infection (NI) in ICU patients with head injury (HI) and to analyse the main characteristics of these infections.
Methods We studied retrospectively 58 ICU patients with HI (48 men, 10 women) who developed NI. Mean age: 41.4 ± 13.8 years. Mean stay: 31.2 ± 18.4 days. These patients developed 74 episodes of NI diagnosed according to CDC criteria. Early-onset (EO) NI occurred within the first 96 hours of the ICU stay (14 episodes) and late-onset (LO) NI occurred later than 96 hours from admission (60 episodes). Mean APACHE II score at admission: 15.1 ± 10.2. All were mechanically ventilated.
Results We diagnosed the following NI: 46 pneumonias (11 EO and 35 LO), 22 central venous catheter-related infections (CVC-RI) (all LO), one urinary tract infection (LO) and five central nervous system infections (CNSI) (three EO and two LO). The main pathogens were: *P. aeruginosa* 38%, *A. baumannii* 31%, MRSA 18%, *K. pneumoniae* 9%, MSSA 4%. In 10 episodes of NI (13.5%) two microbes were isolated. There was no difference between pathogens isolated in EO and LO pneumonias. Mortality rates (MR): 18/58 = 31%.
Conclusion The most frequent NI in ICU patients with HI was pneumonia (62.2%). We noticed an important increase in CVC-RI (29.7%) especially during the last 2 years; all were LO NI with

good prognosis. The most common pathogens were *P. aeruginosa*, *A. baumannii* and MRSA (totally 87%); during the last years the incidence of MRSA-NI increased significantly. *A. baumannii* was isolated especially in younger patients and almost never in the elderly. Pneumonias ($P < 0.05$) and CNSI ($P < 0.05$) increased MR, while no difference was seen between EO and LO pneumonias.

P100

Efficacy and safety of colistin in the treatment of infections in the ICU caused by multidrug-resistant Gram-negative organisms

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Background The treatment of infections caused by multidrug-resistant (MDR) Gram-negative organisms poses a therapeutic challenge. With a diminishing armamentarium of effective new chemotherapeutic agents, there has been renewed interest in the polymyxins, which had fallen out of favour due to nephrotoxicity and neurotoxicity reported during their use in the 1960s.
Aim Epidemiological analysis of the use of colistin in the treatment of MDR infections in an ICU.
Patients and methods We prospectively recorded the clinical and microbiological efficacy, and safety profile of colistin (polymyxin E) in the treatment of MDR Gram-negative bacterial infections in an ICU, during a period of 18 months. Patients were treated with intravenous and/or aerosolized colistin.
Results Twenty-eight critically ill patients received a total of 33 courses of colistin administered in combination with another antimicrobial agent (mainly carbapenems or β-lactamase inhibitors). The patients' mean age was 66 years (range 29–84). Nineteen patients were male and nine female. Their mean APACHE II score was 18 (range 10–29). The infections treated were: 19 pneumonias (of which five had concurrent bacteremia), seven catheter-related bacteremias, three cases of peritonitis, one primary bacteremia, one infection of the catheter tip (without bacteremia) and one urinary tract infection. In one case the use of colistin was empirical. The responsible bacteria were *Acinetobacter baumanii* (47%), *Pseudomonas aeruginosa* (50%) and *Klebsiella pneumonia* (3%). The mean duration of colistin therapy was 14 days (range 2–36 days). The end of treatment mortality was 30%, and overall mortality at discharge was 48%. Nephrotoxicity was observed in two patients (7%) and neurotoxicity in one (3.5%). Both adverse events were reversible and had no serious outcomes.
Conclusion Colistin in combination with other antimicrobials can be considered a reasonable and safe treatment option for MDR Gram-negative respiratory tract infections in the setting of limited therapeutic options.

P101

Efficacy of an intravenous colistin regimen in ventilator-associated pneumonia and bacteraemia due to multiresistant Gram-negative bacteria: preliminary results

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Introduction Colistin has been recently reintroduced in clinical practice, because of the increasing prevalence of multiresistant Gram-negative strains in ICUs. There is controversy on the efficacy of the drug provided either as monotherapy or in combination with β-lactams in critically ill patients with ventilator-associated pneumonia (VAP). We compared prospectively the efficacy and safety of administration of colistin alone and in combination with β-lactams in patients with VAP and bacteremia caused by multiresistant Gram-negative bacteria.
Patients and methods Twelve patients (mean age: 57 ± 17 years) with VAP (quantitative cultures of tracheal aspirates of bronchoalveolar lavage [BAL]) and bacteraemia (at least one positive blood culture), caused by *Pseudomonas aeruginosa* (33%), *Acinetobacter baumanii* (58%) and/or *Klebsiella pneumonia* (25%), resistant to all antibiotics except colistin, were treated with intravenous colistin. Four of them (group A) received monotherapy with colistin (3×10^6 IU three times daily, adjusted for creatinine clearance) and eight of them received combination of colistin with cefepime, or piperacilline-tazobactam (group B). Follow-up cultures and clinical evaluation of all patients were performed 4 days after the initiation of therapy. Clinical success was defined by a lessening of the signs and symptoms of VAP, while microbiologic success was defined as eradication of the pathogen in blood culture.
Results Follow-up blood cultures revealed microbiologic success in one patient from group A (25%) and four patients from group B (50%), but the difference was not statistically significant ($P = 0.4$). Eradication of the pathogen from tracheal aspirates or BAL was confirmed in the same patients. Clinical success followed microbiologic success in one patient from group A (25%) and five patients from group B (62.5%), difference not statistically significant ($P = 0.3$). One patient from group B developed acute renal failure and was treated with continuous venovenous hemofiltration (8%). No differences concerning mortality were observed between the two groups (group A: 100%, group B: 62.5%, $P = 0.5$).
Conclusion Preliminary results demonstrate that combination therapy (colistin plus β-lactam) acts more effectively than monotherapy in VAP and bacteraemia from multiresistant Gram-negative strains. Colistin therapy in both groups was safe.

P102

Colistin monotherapy versus combination of colistin with a β-lactam or rifampicin for the treatment of serious infections in the ICU due to multidrug-resistant Gram-negative bacteria

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Introduction The resistance of Gram-negative strains in the ICU is a growing problem. Recent studies suggest *in-vitro* synergy of colistin with β-lactams and colistin with rifampicin against these strains. However, there is controversy on the efficacy of the drug provided either as monotherapy or in combination with these drugs in critically ill patients.
Aim To determine the clinical and microbiological efficacy of intravenous colistin as monotherapy or in combination with β-lactams or rifampicin.
Methods Sixteen patients admitted to a medical ICU between March 2005 and December 2005 who grew multiple-resistant strains of *Pseudomonas aeruginosa* (three patients), *Acinetobacter baumanii* (eight patients), *Klebsiella pneumoniae* (one patient) or mixed organisms (four patients) were included in the study. Fourteen patients had ventilator-associated pneumonia, one abdominal sepsis and one catheter-related sepsis. These patients

were allocated to treatment: with colistin monotherapy in a dose of 3 million units three times daily adjusted for creatinine clearance (group 1: six patients), with colistin in the same dose and β-lactams (group 2: eight patients), and with the combination of rifampicin (600 mg/day) with colistin (group 3: two patients). Follow-up cultures and clinical evaluation were performed 5 days after the initiation of treatment. Clinical success was defined as a lessening of the signs and symptoms of infection, while microbiologic success was defined as eradication of the pathogen in follow-up qualitive cultures or as a 2-log decrease in bacterial load in quantitive cultures (BAL). The outcome of patients (discharged from the ITU or died) was also determined.

Results In group 1, three patients (50%) showed clinical improvement and three did not improve (50%). In group 2, four patients improved (50%) and four did not (50%). In group 3, one patient improved (50%) and one deteriorated (50%). Microbiological improvement occurred in two out of six (33.3%) in group 1, five out of seven (71.4%) in group 2 and one out of two (50%) in group 3. Favorable outcome (discharged to the ward) occurred in one patient out of six (16.6%) in group 1, two out of seven (28.5%) in group 2 and one out of two (50%) in group 3. There is no statistically significant difference in clinical, microbiological or final outcome between the groups ($P > 0.05$). Three patients (18.75%) had significant side-effects (two renal impairment and one thrombocytopenia).

Conclusions Patients that received the combination of colistin with β-lactams and colistin with rifampicin had higher rates of microbiological response and better outcome than patients in the colistin monotherapy group. The difference is not statistically significant, which is probably due to the small number of patients, especially in the rifampicin group, and the study is continuing with the recruitment of more patients.

P103

Susceptibility to carbapenems of *Pseudomonas* spp. isolated from patients with ventilator-associated pneumonia

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Introduction Ventilator-associated pneumonia (VAP) is associated with the greatest mortality among nosocomial infections. Death rates associated with *Pseudomonas* spp. or with late-onset VAP seem higher. Antibacterial therapy is often complicated by resistance of nosocomial pathogens. This problem has been increasing in recent years.

Objective The goal of the study was to assess susceptibility of *Pseudomonas* spp. to meropenem and imipenem in patients with VAP. In a 12-bed surgical ICU, at a 400-bed surgical complex of a district hospital, we studied prospectively all patients with VAP, clinical and bacteriological (quantitive endotracheal aspirate culture, Protected Specimen Brush), diagnosed from January 2002 to January 2004. We looked for the demography, APACHE II score, mortality, attributable VAP mortality, days on mechanical ventilation, and length of stay in the ICU. One hundred and forty strains of *Pseudomonas* spp. from patients with VAP were isolated. In 102 isolated strains, the gel diffusion technique was used to investigate susceptibility to meropenem and imipenem.

Results Susceptibility to meropenem and imipenem was registered in 55/102 (53.9%), while 35/102 (34.3%) showed susceptibility to meropenem and resistance to imipenem. Another 12/102 (11.8%) isolated strains were resistant to both carbapenems. Eighty-five of 140 strains were *Pseudomonas aeruginosa*. Susceptibility to carbapenems was tested in 64 strains: 36/64 (56.25%) were susceptible to both antibiotics; 16/64 (25%) were sensitive to meropenem and resistant or intermediary resistant to imipenem. Ten out of 85 (11.8%) were resistant to both antibiotics. Fifty-five out of 140 (39.3%) were *Pseudomonas* species, and in 37 susceptibility to meropenem and imipenem was investigated: 16/37 (43.24%) were sensitive to both antibiotics; 16/37 (43.24%) were susceptible to meropenem and resistant to imipenem; 5/37 (13.5%) isolated strains showed resistance to both investigated antibiotics.

Conclusion Strains of *Pseudomonas* isolated from patients with VAP demonstrate a high level of resistance to imipenem. In the investigation period, *Pseudomonas* strains resistant to meropenem were isolated for the first time. Considering that carbapenems are drugs of choice for the treatment patients with VAP due to multiresistant strains, appearance of high resistance points to the necessity of their rational use.

P104

Cerebrospinal fluid penetration of linezolid in neurosurgical patients

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Introduction Linezolid is a new antimicrobial agent effective against drug-resistant Gram-positive pathogens commonly responsible for central nervous system (CNS) infections in neurosurgical patients hospitalized in ICUs.

Materials and methods We studied the penetration of linezolid into the cerebrospinal fluid (CSF) in 14 neurosurgical patients. Drug disposition in serum and CSF was studied by administering linezolid 600 mg twice daily (1 hour i.v. infusion) for the treatment of Gram-positive CNS infections or as chemoprohylaxis. Serum and CSF linezolid steady-state concentrations were analyzed by HPLC and the concentration–time profiles obtained were analyzed to estimate pharmacokinetic parameters.

Results Mean ± SD linezolid peak and trough concentrations were 19.7 ± 9.9 μg/ml and 5.8 ± 5.2 μg/ml in serum and 9.8 ± 5.6 μg/ml and 5.8 ± 4.2 μg/ml in CSF, respectively. The mean ± SD areas under the concentration–time curves during the 12-hour dosing interval (AUC0-Ts) were 195.6 ± 159.6 hour*μg/ml for serum and 88 ± 55 hour*μg/ml for CSF, with a mean penetration ratio AUC0-T CSF:AUC0-T serum of 0.50. The mean elimination half-life of linezolid in CSF was longer than that in serum (18.3 ± 19.2 compared with 5.9 ± 3.3 hours). Serum and CSF linezolid concentrations exceeded the breakpoint of 4 μg/ml for susceptible target pathogens for the entire dosing interval in the majority of patients. Two patients with documented *Staphylococcus aureus* CNS infection and one with primary MRSE bacteremia were successfully treated.

Conclusions These findings suggest that linezolid may achieve adequate CSF concentrations in patients requiring antibiotics for the management/prophylaxis of Gram-positive CNS infections. More studies are needed regarding clinical efficacy of linezolid regarding the management of CNS infections.

P105

An outbreak of *Acinetobacter baumanii* in an ICU: effectiveness of an extensive infection control program

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Introduction *Acinetobacter baumanii* (AB) has been increasingly reported in outbreaks affecting patients from ICUs and other hospital departments. The prevention of the spread of the infection needs exceptional measures in order to prevent transmission to other inpatients through health care workers (HCW). In this study we describe the effectiveness of an extensive infection control program introduced after the onset of an AB outbreak in an ICU.
Methods The AB outbreak occurred from January 2004 to April 2004 in an eight-bed ICU in a university-affiliated 1800-bed hospital. An infection control policy was instituted to contain the outspread of the infection from mid January (Table 1). In order to analyse the effectiveness of this intervention we have evaluated three periods: the period of AB outbreak (period AB from 1 January to 31 March 2004), the period after AB outbreak (period post-AB from 1 April 2004 to 31 March 2005) and the period before the AB outbreak (period pre-AB from 1 January to 31 December 2003). Statistical analysis was performed with Student's *t* test, the Mann–Whitney U test and the chi-square test.

Table 1 (abstract P105)

	Pre-AB	Post-AB
Surveillance cultures	No	Yes
Antibiotic prophylaxis	Yes	No
Antibiotic therapy	Empirical	Microbiological data
Length antibiotic therapy	NA	Time/clinical stop
Antibiotic formulary	Not limited	Restricted
Oropharyngeal decontamination	No	Yes
HCW barrier	Gloves	Total
Subglottic suction	No	Yes
Semirecumbent position	Recommended	Always
Microbiologist cons.	Standard	Implemented
Epidemiology report	Yearly	Quarterly
Hand washing	Yes	Implemented
Skin disinfection	Iodine-povidone	Clrexidine
Invasive procedures	Sterile technique	Implemented

Results A total of 855 patients (pre-AB 400, AB 101, post-AB 354) were involved in this study. ICU LOS was higher in period AB (9.99 days in comparison with 7.27 and 7.37 days in period pre-AB and post-AB, respectively) and the mean SAPS II was statistically higher in period AB (43.4) and post-AB (39.2) rather than pre-AB (33.9). The AB outbreak was contained and the pathogen was successfully eradicated from ICU in the remaining time period. No difference in mortality was reported.
Conclusions The full knowledge of an infection control policy, and its aggressive application, has successfully contained the AB outbreak in a short period of time. It has also prevented the re-occurrence of the pathogen that was completely eradicated from the ICU environment in the following year. The main features of this policy are surveillance cultures, microbiologist consultation and up-to-date antibiotic prescription schemes.

P106

Rate of microbiologically proven infections among patients with severe sepsis/septic shock: results from the German prevalence study

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Objectives To examine the percentage of microbiologically proven infections (MPI) among patients with severe sepsis/septic shock with clinically suspected infection (CSI) in a large and representative sample of German ICUs.
Background In a European ICU survey, 55% of community-acquired and 71% of nosocomial infections were reported to be microbiologically proven [1].
Design and setting A prospective observational cross-sectional 1-day-prevalence study from 15 January 2003 to 14 January 2004. A representative random sample of 310 hospitals with 454 ICUs out of a total of 1380 German hospitals with 2075 ICUs was obtained, forming five strata according to hospital size: strata 1–4 comprised all nonuniversity hospitals with <200, 201–400, 401–600, and >600 beds, respectively, and stratum 5 comprised all university hospitals. Visits by experienced ICU physicians from SepNet's 17 regional study centers were randomly selected over a 1-year period to allow for seasonal variations.
Patients A total of 3877 patients were screened according to the ACCP/SCCM Consensus Conference criteria. Patients with CSI needed to have evidence of an infection such as white blood cells in a normally sterile body fluid, perforated viscus, chest X-ray consistent with pneumonia and associated with purulent tracheal production, or a clinical syndrome associated with a high probability of infection (e.g. ascending cholangitis).
Results In total 1348 patients (34.7%) were infected, 736 (54.6%) of whom had CSI and 612 (45.4%) MPI. MPI was more frequent in larger hospitals, CSI more frequent in smaller hospitals ($P < 0.0001$). Among infected patients, the rate of MPI was highest in university hospitals (59.0%) and lowest in hospitals with < 200 beds (33.5%), reflecting the availability of microbiological laboratories (laboratory present in 16.3% in hospitals with 400 beds and in 70.0% in hospitals with 600 beds). Among the 1348 patients with infections, 415 (30.8%) had severe sepsis or septic shock. Patients with severe sepis/septic shock more often had MPI than patients without (57.3% vs 40.1%, $P < 0.0001$).
Conclusions This epidemiological study shows a low overall rate of MPI in German ICUs. This is partly due to the lack of microbiological laboratories in small and middle-sized hospitals. It underlines the need for better culture-independent laboratory methods with a faster turnaround.
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P107

Intrusion of antibacterial therapy protocol decreased mortality associated with VAP in severe trauma patients

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Objective To evaluate the efficiency of antibacterial protocol in severe trauma patients on the incidence and mortality of VAP.
Methods This study was approved by the local ethics committee. A comparable analysis of incidence, attributive mortality (chi-square test) and pathogens of VAP in severe trauma patients was performed during two periods: 2001 (before introduction of protocol) and 2004 (after introduction of protocol) years. The developed protocol included:

1. Abandoning of antibiotic prophylaxis of VAP.
2. Intrusion criteria of early diagnostics of VAP.
3. Exclusion of all cefalosporine I–III generation, aminoglycosides and fluoroquinolones as empiric therapy of VAP.
4. Cefepime or cefoperazone/sulbactam (APACHE II score < 20) and carbapenems (APACHE II score > 20) were used as empiric therapy of VAP.
5. Efficacy of antibiotic treatment was evaluated after 48 hours.
6. Carbapenems and/or vancomycin was added if empiric therapy was inefficient. In the case of suspected diagnosis of VAP, microbiological analysis of broncoalveolar lavage fluid (BAL) was performed.

Results In this study were included 499 patients with severe trauma and respiratory support for longer than 48 hours (2001, 220 patients and 2004, 279 patients). There was no difference in ISS and APACHE II score between the groups. The incidence of VAP was 10% in 2001 (22/220) and 9% in 2003 (25/279), difference not significant. The attributive mortality due to VAP in 2001 was 63% (14/22) and in 2004 was 24% (6/25) ($P < 0.01$).
A widespread using of broad-spectrum antibiotics shifted the structure of nosocomial pathogens. We observed a decrease in the rate of MRSA and a significant increase in the rate of *Klebsiella pneumoniae* (from 0.6 to 18.1%, most strains were resistant to cefalosporine III) and *Acinetobacter baumanii* (from 1.2 to 12.3%, most strains were resistant to ceftazidime).
Conclusions Intrusion of antibacterial protocol in patients with multiple trauma and VAP results in a decrease of attributive mortality ($P < 0.01$) without a change in incidence of VAP.

P108

Antimicrobial use and antimicrobial resistance in an intensive care burn department

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The increasing consumption of antibiotics in hospitals and the economic implications of this increase led us to survey this consumption in the various hospital units. Our study proposes to measure the annual antibiotic use and antimicrobial resistance in an intensive care burn department in order to direct the control measures.
During a 5-year period from 1 January 2000 to 31 December 2004 we studied the consumption of the following antibiotics: oxacillin, imipenem, ceftazidime, ofloxacin, ciprofloxacin, vacomycin. We measured antibiotic consumption with the antimicrobial density (AD), which takes into account the quantity of antibiotics in grams converted to the defined daily dose (DDD) and the number of days of hospitalization. The DDD was proposed by the World Health Organisation. The calculation of the AD for each molecule was carried out according to the following formula: AD = (quantity consumed [g] for the particular antimicrobial × 1000) / (DDD for that antimicrobial × number of days hospitalized).
The study of the total consumption of antibiotics showed a peak in 2002. The distribution by families of antibiotics shows variations according to various molecules. Among oxacillin, a significant decrease in the consumption of this molecule was observed in 2004 (AD = 44 in 2004 vs AD = 128.2 in 2002). At the same time, a significant increase in the consumption of vancomycin (AD = 28.15 in 2002 vs 73.9 into 2004) was also observed. This intensive use of vancomycin was explained by the high incidence of the methicillin-resistant *Staphylococcus aureus* in our burn department (MRSA = 64% in 2004). As elsewhere, no vancomycin intermediate *S. aureus* was detected during the period of study, in spite of the significant use of this antibiotic. There were statistically significant relationships between increasing use of ceftazidime and ceftazidime-resistant *Klebsiella pneumoniae* ($rs = 0.93$, $P = 0.02$). Concerning the fluoroquinolones, there were statistically significant relationships between increasing use of ciprofloxacin and incidence of resistant *P. aeruginosa* to this antibiotic ($rs = 0.89$, $P = 0.043$). In addition to the resistance to the drug itself, the consumption of ciprofloxacin was significantly associated with resistance to the imipeneme in *P. aeruginosa* ($rs = 0.87$ $P = 0.05$). A restriction of the use of ciprofloxacin was taken during 2003 and 2004; this was followed by a significant decrease of resistance in *P. aeruginosa*. The use of fluoroquinolones was not significantly associated with MRSA ($rs = 0.70$, $P = 0.1$).
The monitoring of both antibiotic consumption and antibiotic resistance makes it possible to set up targeted policies and to control their effectiveness. Nevertheless this monitoring must be integrated into a policy of good use and control of antibiotic use.

P109

Relationships between antimicrobial use and antimicrobial resistance in *P. aeruginosa* in an intensive care burn department

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Increasing resistance in *P. aeruginosa* to multiple antibiotics has been observed and is posing therapeutic dilemmas. Antibiotic utilization is one factor that has been associated with the emergence of antimicrobial resistance.
We examined the relationships between annual antibiotic use and the incidence of resistance of *P. aeruginosa* isolates within the burned patients admitted to our intensive care department in order to direct measurements of control.
During a 5-year period (1 January 2000–31 December 2004), 203 nonrepetitive strains of *P. aeruginosa* were isolated from different specimens. Antimicrobial susceptibility testing has been carried out by the disk diffusion method according to the French Society of Microbiology. We studied the consumption of the following antibiotics: imipenem, ceftazidime, ciprofloxacin and amikacin. We measured antibiotic consumption with the antimicrobial density (AD), which takes into account the quantity of antibiotics in grams

converted to daily doses dispensed and the number of patient-days in hospital. The defined daily dose was defined according to the World Health Organisation. Statistical analysis was conducted to explore the relationships between antibiotic use and the susceptibility patterns of *P. aeruginosa*. SPSS software was used to calculate the Spearman rank correlation coefficient. Statistical significance was defined as $P < 0.05$ for the corresponding correlation coefficients.

The consumption of ceftazidime showed no association with resistance to this drug. There were statistically significant relationships between increasing use of ciprofloxacin and incidence of resistant *P. aeruginosa* to this antibiotic ($rs = 0.89$, $P = 0.05$). In addition to the association between ciprofloxacin use and resistance to the drug itself, our study revealed a significant correlation between ciprofloxacin consumption and resistance to imipeneme ($rs = 0.89$, $P = 0.043$). A restriction of the use of ciprofloxacin was taken during 2003 and 2004; this was followed by a significant decrease of incidence of resistance in *P. aeruginosa*. The consumption of amikacin had no apparent association with resistance in *P. aeruginosa* to this drug.

Our data support a major role for ciprofloxacin in the emergence of multiresistance in *P. aeruginosa*. The use and/or duration of treatment with this antibiotic should be restricted as part of efforts to control the emergence of multidrug-resistant *P. aeruginosa*.

P110

Introduction of an integrated infection control program in an ICU: effects on epidemiology and antimicrobial resistance of *Staphylococcus aureus*

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Background Extensive use of antibiotics is responsible for the emergence of multiresistant strains, in the clinical setting. In our institution a profound remodelling of antibiotic prescription policy and implemented procedures to control cross-patient transmission were introduced in the first quarter of 2004, in response to an outbreak of *Acinetobacter baumanii* (AB). In this study we reported the effects induced by this new infection control program on the frequency of isolation of *Staphylococcus aureus* (SA) and its antibiotic resistance profile.

Methods From January 2004 to April 2004 a new infection control program was instituted to contain an outbreak of AB. The key features of this approach consisted of the introduction of surveillance cultures, in an extensive use of microbiological sampling to guide therapy, a restricted antibiotic prescription policy (limited prophylaxis, selection of drugs on the basis of microbiological assays, early discontinuation of antimicrobials at clinical resolution, de-escalation therapy, restricted formulary), and VAP containing measures/devices (extended use of individual protection garments, controlled hand-washing procedures). The infection control program has remained operative after the resolution of the outbreak. The impact of the program on the frequency and sensibility of SA was evaluated for a 12-month period (period A from May 2004 to April 2005). The 12 months preceding the introduction of the program were considered a historical control period (period B from January 2003 to December 2003). The incidence of methicillin-sensitive SA (MSSA) and of methicillin-resistant SA (MRSA), the consumption of vancomycin and oxacillin, demographic data of admitted patients and outcome measures (ICU LOS and ICU mortality) were evaluated in the two periods. Statistical analysis: Student's *t* test, Mann–Whitney U test and chi-squared test.

Results In period A more trauma patients and less surgical patients were admitted to the ICU. The SAPS II was significantly higher in period A. No difference in outcome measures was reported. In period A, a significant increase of MSSA ($P = 0.009$) and a significant decrease of MRSA ($P = 0.03$) were reported. Due to this epidemiological modification the consumption of oxacillin has noticeably increased, in association with a significant reduction of vancomycin consumption ($P = 0.04$).

Conclusions The integrated infection control program introduced for the containment of an AB outbreak has resulted in profoundly affecting the microbiological environment of the ICU. In particular, it has significantly reduced the occurrence of MRSA. The increase in methicillin sensitivity of SA improved the use of oxacillin in place of vancomycin, with potentially favourable effects on costs. The finding that a different prevalence of trauma and surgical patients has occurred in the two study periods is a potentially confounding variable. Nevertheless, the higher severity of patients admitted in period A not being associated with an increase in mortality and LOS seems to confirm the positive effects of the renewal introduced.

P111

An epidemiological study of sepsis in ICUs: Sepsis Brazil Study

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Introduction Sepsis represents the major cause of death in the ICUs all over the world and is a major challenge in these units. Many studies had been shown an increasing incidence over time and only a slight reduction in mortality. Many new treatment strategies are arising and we should know our incidence of sepsis and features.

Methods A prospective cohort study was conducted in 65 hospitals of all regions of Brazil. The patients who were admitted or who developed sepsis during the month of September 2003 were enrolled. They were followed until the 28th day or less according to their discharge. The diagnoses were made in accordance with the criteria proposed by ACCP/SCCM. The final classification was made considering the worse stage in the first 4 days after the diagnosis of sepsis. Parameters evaluated were demographic features, APACHE II score, SOFA (Sepsis-related Organ Failure Assessment) score, mortality, sources of infections, microbiology and interventions. Also recorded was underlying diseases and length of stay (LOS).

Results A total of 3128 patients were identified and 526 (17%) filled the criteria of sepsis, severe sepsis or septic shock. Two hundred and sixty-six (50.6%) patients had septic shock, 157 (30%) severe sepsis, and 102 (19.4%) had sepsis. The average age was 61.7 years (SD ±18.9), 293 (55%) were males, and the overall 28-day mortality rate was 46.2%. The average APACHE II score was 20(SD ±7.8) and the SOFA score on the first day was 7 (SD ±3.8). The SOFA score on the mortality group was higher on day 1 (8), and had increased on day 3. The mortality rate for sepsis, severe sepsis and septic shock was 15.7%, 33.8% and 65%, respectively. The average LOS was 16 days. The two main sources of infection were the respiratory tract (50.2%) and the

abdomen (16.3%). Gram-negative bacilli were more prevalent (55.6%). Gram-positive cocci accounted for 32% and fungi infections for 5%. Chronic obstructive pulmonary disease was the most frequent underlying disease seen.

Conclusion A high incidence and mortality of sepsis was observed in ICUs in our country. The high frequency of septic shock and severe sepsis demonstrated a group at high risk of death.

P112

Management of sepsis and septic shock in critically ill patients transferred by a dedicated transport team in the West of Scotland

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Over 500 critically ill patients are transferred by the dedicated transport team known as the 'Shock Team' each year in the West of Scotland. With the advent of international guidelines for the management of severe sepsis and septic shock, there are now criteria by which the management of these conditions can be assessed [1]. We undertook a prospective audit over a 3-month period to determine what proportion of the patients transferred have these conditions and to determine how management conforms to the guidelines.

Patients were deemed to have sepsis if they had suspicion of infection and two or more of the following: T >38°C or < 36°C; WCC < 4 or >12 × 10^3/mm^3; HR >90/min; RR >20/min; SBP <90 mmHg or MAP <65 mmHg or needing a vasopressor. We adapted sepsis resuscitation bundles derived from the guidelines [2] and devised a data collection form with relation to the following: serum lactate measurement; blood cultures prior to antibiotics; antibiotics given within 3 hours; MAP <65 mmHg and management with a minimum 20 ml/kg fluid challenge, vasopressors, and CVP monitoring; achievement of MAP ≥65 mmHg; measurement of central venous oxygen saturation ($ScvO_2$). Data were collected for every patient transferred during June, July, and August 2005.

Data were collected for 82 patients. Forty-five patients (55%, 95% CI 44–66%) met criteria for sepsis. Of these, eight patients had blood cultures prior to antibiotics (18%, 95% CI 8–32%), and in 23 (51%, 95% CI 35–66%) this information was not available or unclear. Similarly, 24 patients (53%, 95% CI 28–68%) had antibiotics within the time window, and in 17 (38%, 95% CI 24–54%) this was unclear. Twenty-eight (62%, 95% CI 47–76%) patients had circulatory failure with 19 of these (68%, 95% CI 48–84%) requiring more than a fluid challenge alone. MAP ≥65 mmHg was achieved in 43 patients (96%, 95% CI 85–100%). Two patients with sepsis had serum lactate measured (4%, 95% CI 0.5–15%). One patient of the 19 who had not responded to a fluid challenge had $ScvO_2$ measurement (5%, 95% CI 0–26%).

A significant number of critically ill patients with sepsis and septic shock are transferred each year. Many have circulatory failure and this is managed consistently with fluids, vasopressor and CVP targeting. Documentation and communication of blood culture withdrawal and antibiotic therapy may be poor. Serum lactate and $ScvO_2$ measurement may not yet be part of routine management of patients with sepsis transported in the West of Scotland.

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P113

Surveillance of ICU-associated infections

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Introduction Healthcare-associated infections (HAI) affect around 9% of all patients in hospital [1]. It is generally accepted that the infection rate in the ICU is higher than elsewhere in the hospital and these patients are subject to many invasive procedures that increase their risk of acquiring an HAI. Our aim was to conduct a prospective pilot audit of HAI in ICUs in Scotland using the Hospitals in Europe Link for Infection Control through Surveillance (HELICS) protocol for surveillance of nosocomial infections in ICUs using the current Scottish audit database (Ward Watcher software; Critical Care Audit Ltd, Yorkshire, UK).

Methods Between 1 May 2005 and 31 August 2005, five of the 25 adult, general ICUs in Scotland participated for 3 months each in a prospective pilot audit of HAI in ICUs. Daily data were recorded on enabling identification of the first episode of infection: HELICS Level 2 surveillance of blood stream infections (BSI), catheter-related infections and ventilator-associated pneumonia surveillance.

Results In this 3-month pilot study a total of 386 patients were admitted to the five pilot sites, 52% (199) of whom stayed in the ICU for at least 2 days. For these five ICUs the average occupancy was 78.3%, the first 24-hour APACHE II score 19.8 and the average length of ICU stay 5.7 days. In 32 patients (16%) there were 44 episodes of infection diagnosed using the criteria: BSI = 11.4%, PN = 68.2% and CVC = 20.5%. The overall infection rate was 30.5 infections (95% CI 22.2–40.9) per 1000 patient-days. Twenty-three (72%) patients developed one episode of infection, five (16%) had two episodes, three (9%) developed three episodes and one (3%) patient had four episodes. The majority of pneumonias (60%) were PN4 because quantitative microbiological analysis (PN1 and PN2) is not available routinely.

Conclusion Of all patients admitted to ICU during the pilot study 16% developed an ICU-associated infection. As expected, the majority of infections diagnosed were pneumonias (68%). This is consistent with the findings of the European Prevalence of Infection in Intensive Care (EPIC) study [2].

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P114

Feasibility of surveillance of ICU-associated infections in Scotland

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Introduction Healthcare-associated infections (HAI) affect around 9% of all patients in hospital [1]. It is generally accepted that the infection rate in the ICU is higher than elsewhere in the hospital

and these patients are subject to many invasive procedures that increase their risk of acquiring an HAI. Our aim was to study the feasibility of utilising the current Scottish audit database (Ward Watcher; Critical Care Audit Ltd, Yorkshire, UK) to collect surveillance data electronically, and the application of the Hospitals in Europe Link for Infection Control through Surveillance (HELICS) definitions for ICU-associated infection in Scotland.

Methods Between 1 May 2005 and 31 August 2005, five of the 25 adult, general ICUs in Scotland participated for 3 months each in a prospective pilot audit of HAI in ICUs. Daily data were recorded on software modified to enable identification of the first episode of infection: HELICS Level 2 surveillance of blood stream infections (BSI), catheter-related infections and ventilator-associated pneumonia surveillance.

Results The results of the pilot audit indicate that surveillance of infections acquired in ICUs in Scotland using Ward Watcher for data collection and the HELICS definitions for infection is a feasible process. The HELICS definitions for ICU-associated infection are applicable in Scotland; definitions for pneumonia, bloodstream infections and CVC-related blood stream infections could be applied in all hospitals. Feedback for Ward Watcher as a tool to collect data for surveillance purposes was positive; all participants found that the system was easy to use. The major criticism of the system was that data from patients admitted for less than 2 days were required as some of these data would not be analysed. The initial decision to include these patients was taken as an attempt to simplify data collection. It is probable that further development of Ward Watcher could facilitate the requirement to collect data only for those patients who have a stay of more than 2 days.

Conclusion The pilot was successful. Surveillance activity throughout Scotland would be dependent on several factors including some refinements to Ward Watcher to improve the efficiency, accuracy and ease of data collection.

Acknowledgements SICSAG is funded by NHS Boards in Scotland and this study was supported by the Scottish Executive Health Department.

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P115

Evaluation of the viability of a hemodynamic optimization protocol to high-risk surgical patients using less invasive monitoring tools

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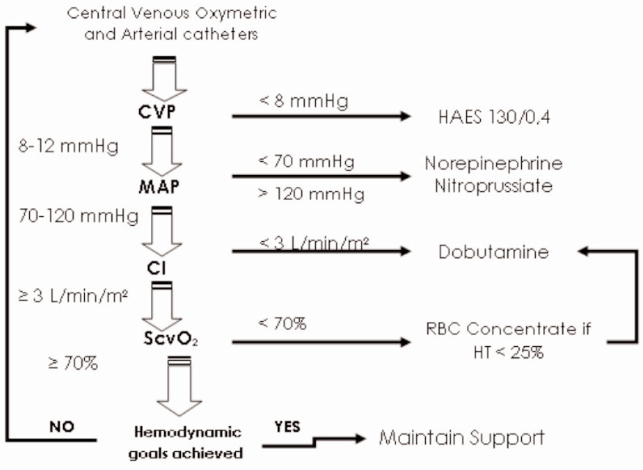
Introduction Clinical, hemodynamics and perfusion variables are important tools to identify instable patients and guide therapy. There is a strong suggestion that shock-induced organ failure is attributable to peripheral tissue hypoperfusion and/or cellular hypoxia. The aim of this study was to evaluate the efficacy of a hemodynamic optimization protocol to correct tissue hypoxia during the initial postoperative period.

Patients and methods Fifteen high-risk surgical patients according to Shoemaker's criteria were prospectively included when hyperlactatemia (arterial lactate ≥3 mmol/l) was present at ICU admission. Patients were monitored with Vigileo™ (Edwards Lifescience, Irvine, CA, USA) and resuscitated during the first 12 postoperative hours using the protocol shown in Fig. 1. The patients were considered as responders if at the end of resuscitation $SvcO_2$ ≥70% and arterial lactate ≤2 mmol/l.

Figure 1 (abstract P115)



Results The mean age was 66 ± 13 years and 66% were male. The median APACHE II and MODS scores were 20.1 ± 6.4 and 5.6 ± 3.1, respectively. The main surgical procedure performed was resection of abdominal neoplasia (10/15). The mean amount of colloids administered during resuscitation period was 1715 ± 760 ml. Five out of 15 and 4/15 patients have used dobutamine and norepinephrine, respectively. Only two patients were transfused. Twelve patients were considered responders with 8.3% of the hospital mortality rate. Two of three nonresponders patients died before hospital discharge.

Conclusion This hemodynamic optimization protocol based in less invasive technologies was efficient to correct tissue hypoxia in this sample of patients. These results warrant validation in a control trial.

P116

Antimicrobial treatment in patients with severe sepsis and septic shock: results from the German Prevalence Study

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Critical Care 2006, **10(Suppl 1):**P116 (doi:10.1186/cc4463)

Objective To determine the usage of antibiotic therapy for severe sepsis and septic shock in German ICUs.

Background Appropriate antimicrobial therapy is one of the cornerstones in the treatment of severe sepsis and septic shock. Broad-spectrum antibiotics, as ureidopenicillins, fourth-class cephalosporins, carbapenems or fluorchinolons, are recommended agents for empirical antibiotic therapy. To date, nothing is known about how patients with severe sepsis and septic shock are actually treated in Germany.

Design and setting A prospective observational cross-sectional 1-day-prevalence study from 15 January 2003 to 14 January 2004. A representative random sample of 310 hospitals with 454 ICUs out of a total of 1380 German hospitals with 2075 ICUs was obtained, forming five strata according to hospital size. Hospitals were visited by experienced ICU physicians from SepNet's 17 regional study centers.

Patients From 3877 patients screened, 415 (11%) patients – representing a total of 1545 (95% CI, 1305–1786) daily patients

in German ICUs – fulfilled the ACCP/SCCM criteria for severe sepsis or septic shock and were included in the analysis.

Results The predominating origin of infection was respiratory tract infections (64%), followed by intra-abdominal infections (25.7%). Microbiological documentation was found in 57.3% of patients, 57.6% of whom had Gram-positive, 55.5% Gram-negative and 25.6% fungal infections; 9.6% of positive cultures were blood cultures. Less than 2% of patients had MRSA infections. Seven hundred and fifty-seven different antimicrobial agents were administered alone or in combination in the 415 patients with severe sepsis/septic shock on the study day: ureidopenicillins (12.0%), cephalosporins (12.6%), fluorchinolones (11.8%), carbapenems (10.4%), aminoglycosides (8.1%), glycopeptides (7.9%), metronidazole (8.2%), macrolides (4.5%), and antimycotics (9.8%). Of the antimicrobial prescriptions, 64.9% were administered empirically and 31.8% were microbiologically guided. Seventy-one (17.1.0%) patients received antimycotic treatment, but in only 11.6% were fungal isolates considered the likely cause of sepsis.

Conclusions The usage of broad-spectrum antibiotics among patients with severe sepsis/septic shock is high in German ICUs, indicating that most patients probably receive appropriate antibiotic therapy. Aminoglycosides, which according to a recent meta-analysis [1] have been shown not to have additional benefit as an adjunct to broad spectrum-antibiotics, but rather renal side effects, have a rather low prescription rate. There may be an overuse of antimycotics, underlining the need for better diagnostic tools in patients colonized by fungi.

Acknowledgments Supported by BMBF grant number 01 KI 0106 and Lilly Deutschland GmbH.

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P117

Prevalence of infection in German ICUs: results from the German Prevalence Study

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Critical Care 2006, **10(Suppl 1):**P117 (doi:10.1186/cc4464)

Objective To compare prior findings from the German subgroup of the EPIC study with recent data from the German Prevalence study.

Background In a European 1-day-prevalence study in 1992 (EPIC), 10,038 patients in 1417 ICUs throughout Europe with 2010 patients on 268 ICUs in Germany were studied [1]. The overall infection rate was 44.8%; community-acquired infections (CAI) were present in 13.7%, hospital-acquired infections (HAI) in 9.7%, and ICU-acquired infections (IAI) in 20.6%. A strong correlation between IAI and mortality was found, but rates of IAI varied between countries.

Design and setting A prospective observational cross-sectional 1-day-prevalence study from 15 January 2003 to 14 January 2004. A representative random sample of 310 hospitals with 454 ICUs out of a total of 1380 German hospitals with 2075 ICUs was obtained, forming five strata according to hospital size. Hospitals were visited by experienced ICU physicians from SepNet's 17 regional study centers. Visits were randomly selected over a 1-year period to allow for seasonal variations. A total of 3877 patients were screened according to the ACCP/SCCM Consensus Conference criteria.

Patients In total 1348 patients (34.7%) were infected, comparable with the prevalence of infection in German ICUs in the EPIC study (36.6%). Prevalence of CAI was 13.6% (EPIC: 11.2%), HAI 4.8% (EPIC: 8.1%) and IAI 11.4% (EPIC: 17.3%). In our study, among the 1348 patients with infections, 415 (30.8%) had severe sepsis (sevSep) or septic shock (SS). The prevalence of CAI in patients with sevSep/SS was 35.4%, HAI 19.8% and IAI 36.6%, respectively. Comparing infected patients with and without sevSep/SS, HAI and IAI were more frequent than CAI in patients with sevSep/SS ($P = 0.0002$). However, there was no difference in ICU mortality between sevSep/SS patients with CAI (51%), HAI (60%) and IAI (54%), respectively. In the EPIC study, the mortality of patients in German ICUs was 14.9%. However, the prevalence of sevSep/SS was not assessed.

Conclusions Our findings show a lower prevalence of IAI, a higher prevalence of HAI/CAI and a substantially higher mortality rate, independent of the origin of infection, as compared with data from the German subgroup in the EPIC study. This difference may be due to different hospital sizes, as university hospitals were more frequent in the EPIC sample (35%) and ICUs participated by invitation, in contrast to our representative sample with random selection of ICUs. In order to reduce preventable infections, implementation of infection control policies should not be restricted to patients with IAI, but should include patients with CAI and HAI as well.

Acknowledgements This study was supported by the Federal Ministry of Education and Research (BMBF) grant number 01 KI 0106 and Lilly Deutschland GmbH.

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P118

Bloodstream infections in the ICU: incidence and outcome

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Critical Care 2006, **10(Suppl 1):**P118 (doi:10.1186/cc4465)

Objective To evaluate the risk factors for the incidence and the outcome of patients with bloodstream infections (BSIs) in a multidisciplinary ICU.

Methods During a 1-year period (August 2004–July 2005), all ICU patients with more than 48 hours ICU stay were studied. All episodes of BSIs were recorded with the exception of those due to coagulase-negative staphylococci because of difficulties in the clinical interpretation. The prognostic value of clinical and laboratory variables were determined.

Results Of the 693 patients admitted to the ICU during the study period, 572 patients had a stay longer than 48 hours. Among them a total of 125 patients developed one or more episodes of BSI. There was a significant difference between patients with and without BSIs in the length of ICU stay (6 vs 26 days, median, respectively), and in days of mechanical ventilation (7 vs 26 days, median, respectively). The median time between ICU admission and the first BSI was 10 days. The most common isolated pathogen was *Acinetobacter baumannii* (32.5%), followed by *Klebsiella pneumoniae* (21.3%), *Pseudomonas aeruginosa* (13.8%), *Enterobacter aerogenes* (6.9%), *Staphylococcus aureus* (5.8%) and *Enterococcus faecalis* (5.3%). The APACHE II score on admission was significantly higher in patients with BSI (19 ± 6.3 vs 16 ± 7, $P < 0.001$). The best independent prognostic factors of the development of BSI were APACHE II score on admission (OR, 1.05; 95% CI 1.02–1.086, $P < 0.001$), the presence of ARDS (OR, 2.63; 95% CI 1.42–4.87, $P = 0.002$) and a history of diabetes (OR, 2.26; 95% CI 1.3–3.93, $P = 0.004$). The ICU mortality rate was 46.4% and 22% for patients with and without BSIs, respectively ($P < 0.001$). Independent predictors of mortality were admission APACHE II score (OR, 1.13; 95% CI 1.1–1.2, $P < 0.001$), and the presence of BSI (OR, 2.5; 95% CI 1.6–3.9, $P < 0.001$).

Conclusion In our ICU patients the illness severity on admission, the history of diabetes and the presence of ARDS are risk factors for the incidence of BSI. The severity of illness and the presence of BSI are factors independently associated with the outcome.

P119

Nosocomial infection in patients with brain trauma

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Critical Care 2006, **10(Suppl 1):**P119 (doi:10.1186/cc4466)

Objective To determine the incidence of nosocomial infection in critically ill patients with brain trauma.
Methods A prospective study was performed during 12 months of patients with brain trauma admitted to a 24-bed medical–surgical ICU of a 650-bed university hospital. Infections were diagnosed according to CDC criteria. Infections were classified based on the onset moment as early onset and late onset: early onset (EO) were those developed during the first 4 days of the ICU stay; and late onset (LO) were those developed 5 days after ICU admission. The statistical analysis was performed using the SPSS 11.0 program. Continuous variables are reported as means and standard deviation, and categoric variables as percentages.
Results We included 67 patients, 57 males. The mean age was 38.02 ± 17.49 years. The mean APACHE II score was 18.32 ± 12.21. A total of 27 patients (40.29%) developed 38 nosocomial infections (18 EO and 20 LO): 27 pneumonias (15 EO and 12 LO; seven MSSA, one MRSA, six *Pseudomonas aeruginosa*, four *Hemophillus influenzae*), six urinary tract infections (one EO and five LO; three CNS), two primary bacteremias (one EO and one LO; one CNS and one Acinetobacter), one catheter-related bacteremia (one LO; one Enterobacter), one ventriculitis (one EO; one CNS) and one wound surgical infection (one LO; one *Pseudomonas aeruginosa*). The microorganisms responsible for nosocomial infections were the following: eight MSSA, one MRSA, seven *P. aeruginosa*, five CNS, five *H. influenzae* and 12 others. Death occurred in 14 patients (20.89%).
Conclusions In our series, 40% of patients developed some infection. Two-thirds of nosocomial infections had a respiratory origin. The most frequent microorganisms were MSSA and *P. aeruginosa*. One-quarter of patients died.

P120

Representative survey of criteria used for the diagnosis of severe sepsis/septic shock among German ICU physicians: results from the German Prevalence Study

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Critical Care 2006, **10(Suppl 1):**P120 (doi:10.1186/cc4467)

Objective To assess the use of sepsis criteria in daily clinical practice in German ICUs.
Background Different definitions for sepsis are used by clinicians, epidemiologists and microbiologists. In 1992, a set of definitions was agreed upon by an ACCP/SCCM panel of experts. However, a recent poll of the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM) showed that 87% of the responding intensivists doubt the validity of these criteria for sepsis at the bedside.
Design and setting A prospective observational cross-sectional 1-day-prevalence study from 15 January 2003 to 14 January 2004. A representative random sample of 310 hospitals with 454 ICUs out of a total of 1380 German hospitals with 2075 ICUs was obtained, forming five strata according to hospital size: strata 1–4 comprised all non-university hospitals with <200, 201–400, 401–600, and >600 beds, respectively, and stratum 5 comprised all university hospitals. Visits by experienced ICU physicians from SepNet's 17 regional study centers were randomly distributed over a 1-year period to allow for seasonal variations. ICU directors were asked whether they used the sepsis criteria or not and marked either 'always', 'frequently', 'sometimes', 'rarely' or 'never' for their use of sepsis markers.
Results Essential for diagnosis were: clinical criteria according to individual experience (96.5%), positive blood culture (81.5%), ACCP/SCCM Consensus Conference Criteria (56.6%). In total 37.9% stated never using Gram-stains of respiratory specimens, and in 13.2% of these ICUs the laboratory turn around for first blood culture results was >24 hours. Of ICU directors, 90.5% stated using laboratory markers for sepsis diagnosis. The absolute leucocyte count was used in 92.7% ('always'); the differential leucocyte count, however, was used only in 47.8% ('always'). C-reactive protein was the most preferred biochemical marker ('always': 90.1%), compared with procalcitonin ('always': 13.9, 'frequently': 9.5, 'sometimes': 15.2%), IL-6 (3.7, 4.2, 5.9%) and lipopolysaccharide-binding protein levels (2.4, 2.0, 3.7%).
Conclusions The acceptance of the ACCP/SCCM criteria is low in Germany, similar to results from US and European surveys. For the diagnosis of sepsis, ICU physicians seem to rely more on their personal experience rather than on expert recommendations of standardized criteria. Procalcitonin levels are used by one-third of ICU physicians in addition to conventional laboratory markers and clinical signs of sepsis.
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P121

Changing patterns of microbial resistance in an Indian cancer hospital ICU

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Aim To analyse the pattern of microbial isolates and antibiotic sensitivity with time, changing antibiotic prescription and improved infection control.
Methods A 550-bed tertiary referral cancer center with 11 ICU and 10 HDU beds. In 2004–05, the ICU had 640 admissions, with a mean APACHE II score of 15. Prospectively collected microbial culture and sensitivity data sent from the ICU over 34 months (between September 2002 and June 2005) was retrospectively analysed with respect to microbial isolates and antibiotic sensitivity. Data between September 2002 and December 2003 (P1) was compared with that from January 2004 and June 2005 (P2). Between the two periods, empirical use of third-generation cephalosporins was curtailed, with an increase in use of piperacillin-tazobactam and carbapenems, and emphasis was laid on handwashing and other infection control measures.
Results In P1, 622 (43.1%) of 1443 culture samples in 330 patients were positive and grew 750 organisms. In P2, 1807 culture samples were sent in 445 patients, of which 577 (32%) were positive and grew 664 organisms. There were fewer polymicrobial isolates in P2 (12% vs 16%, $P = 0.01$). There was no difference in the number of Gram-negative bacteria (GNB) (77% vs 80%), but there were fewer Gram-positive bacteria (GPB) (14% vs 19%, $P = 0.01$) and more fungi (5.7% vs 3.5%,

$P = 0.04$). The major GNB grown were similar between the two periods with the largest being *Pseudomonas aeruginosa* (PA) followed by *Klebsiella pneumoniae* (KP) and *Escherichia coli* (EC). There was a reduction in the proportion of MRSA in P2 (12% vs 8%, $P = 0.01$) and a trend towards an increase in Acinetobacter (12% vs 9%) and candida spp. (5.4% vs 3.4%, both $P > 0.05$). There was a significant decrease in MRSA from thoracic isolates in P2 (36% vs 3% $P = 0.0004$). In P2, resistance of PA to ciprofloxacin reduced from 61% to 37%, and to ceftazidime from 81% to 65% ($P < 0.001$ for both). However, resistance to imipenem and meropenem increased from 49% to 61%, and from 32% to 56%, respectively ($P < 0.01$). Seventy-one percent of KP and 68% of the EC strains were resistant to ceftazidime in P2 (vs 53% [$P = 0.030$] and 60% [$P > 0.05$], respectively, in P1), probably reflecting an increase in ESBLs. Sixteen percent of KP and 14% EC strains were resistant to meropenem, versus 6.3% ($P = 0.003$) and 6% ($P > 0.05$), respectively, in P1. VRE (four cases) was observed in the ICU for the first time ever in P2. Overall, most GNB in P2 were sensitive to ciprofloxacin (65%), followed by the carbapenems (62%) and piperacillin-tazobactam (50%).

Conclusion There is high incidence of resistant organisms in our ICU. Reduced use of cephalosporins has resulted in a significantly increased sensitivity of GNB to ciprofloxacin; however, resistance to the carbapenems has increased. Infection control measures may have helped reduce GPB infections. Monitoring changing trends in bacterial resistance can help rationalize empirical antibiotic therapy in the ICU.

P122

Severe sepsis and septic shock in Croatian ICUs

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Introduction Diagnosis of sepsis is one of the most frequent in ICUs. Severe sepsis and septic shock, major complications of infection with mortality rates of 20–60%, are among the gravest problems for ICU physicians. The Surviving Sepsis Campaign with its guidelines aims to reduce mortality of severe sepsis by 25%, but no data concerning the incidence and mortality of sepsis in Croatia existed until now. The purpose of our study was to determine basic epidemiological facts about sepsis in Croatia.

Methods Twenty-four ICUs from five clinical hospitals and four general hospitals participated in the project named croicu-net. Participating units cover the population of about 1 million (roughly one-quarter of the Croatian population). All patients admitted to the participating ICUs were reported to the web database in which patients with sepsis were given special attention. Data were analyzed after the period of 1 year. National incidence was estimated based on the portion of Croatian population covered by the participating ICUs.

Results The participating ICUs reported a total of 5293 admissions. Sepsis at admission or during the ICU stay was reported for 587 patients (11.1%), of which 180 (3.4%) met criteria for severe sepsis and 129 (2.4%) for septic shock. ICU mortality for patients with sepsis, severe sepsis and septic shock was 29.1%, 35% and 34.1%, respectively. The duration of ICU stay for septic patients was 9.4 ± 1.1 days. Most of the patients with sepsis (75%) were septic on admission. The most prevalent source of the infection was the urinary tract (30.4%) followed by the respiratory tract (21.1%). The most common failing organ system was the respiratory system (73%). The most prevalent microorganisms isolated from the blood cultures were *E. coli* (11.6%), *P. aeruginosa* (9.9%) and MRSA (9.3%), and blood cultures were negative in 24% patients. There were no differences in incidence, mortality or LOS between surgical and medical ICUs. There were significant differences in mortality and ICU stay between the ICUs in clinical hospitals (28.7%; 8.3 ± 0.9 days) compared with the ICUs in small towns (55.5%; 9.1 ± 1.3 days) and large towns (31.8%; 8.6 ± 1.1 days), which did not match the differences in severity of disease measured by APACHE II and SOFA scores.

Conclusion Sepsis is one of the most prevalent reasons for admission to ICUs in Croatia. The estimated annual incidence of sepsis in Croatia is 0.06% of population. Differences in mortalities and LOS could be reduced by equaling the quality of care, which could be accomplished by following the Surviving Sepsis Campaign guidelines. Planned data collection in the future will show how much improvement will be accomplished.

P123

Portuguese network data: compliance with the Surviving Sepsis Campaign bundles

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Introduction In the context of the worldwide ongoing Surviving Sepsis Campaign (SSC) we decided to characterize community-acquired sepsis (CAS) of our country, using a Portuguese ICU network. We intend to show compliance with the SSC bundles.

Methods A prospective multicentre nationwide study on community-acquired sepsis in Portuguese ICUs was created in 2004. Seventeen units came together in this project, which lasted from 1 December 2004 until 30 November 2005. During this period data collection included epidemiological characteristics and comorbidities, the community-acquired sepsis episode (locale of infection, responsible organism, first intention antibiotherapy and associated organ dysfunction) and the compliance with the SSC bundles and recommendations.

Results During this period 2643 patients were included and 606 had CAS (23%). Five hundred and twenty patients (20%) had severe sepsis/septic shock:

- 59% had serum lactate measured (median time from hospital admission and serum lactate measurement was 6.58 hours) and 65% had fluids administered to get a mean arterial pressure of 65 mmHg in the first 6 hours of hospital admission;
- 92% had blood cultures done (median time from hospital admission and blood cultures done was 8.6 hours) and 49% had antibiotics administered in the first hour after sepsis diagnosis (median time from hospital admission and antibiotherapy administration was 5.08 hours);
- 80% had started glucose control measures, 91% had ventilation programmed to achieved a plateau pressure <30 cmH_2O and 6% had drotrectogina administered in the first 24 hours of hospital admission.

Two hundred and eighty patients had septic shock:

- 49% had CVP measured, 14% had $SvcO_2$ measured, 81% had vasopressors administered and 56% had inotropes in the first 6 hours of hospital admission;
- 53% had low-dose corticoids administered in the first 24 hours of hospital admission.

Discussion We have a heterogeneous reality on CAS cases admitted to the ICU. We planned courses on sepsis and severe infection centred on SSC recommendations pretending to improve

clinical practice. Organizational rearrangements on Emergency Departments are needed to improve SSC recommendation compliance.

P124

Comparison of Belgian and US validation studies of ICU-acquired infection surveillance

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Introduction Many validation studies measured the effectiveness of infection surveillance in ICUs. Few, such as Belgium and USA, did so nationwide. The American National Nosocomial Infection Surveillance System (NNIS, CDC) is a worldwide benchmark, although its pilot study showed low sensitivity (SS) on detecting ICU-acquired pneumonia infections (PN). This paper compares the American and Belgian validation studies regarding methodology and likely impact of design differences on PN surveillance assessment.
Methods The methodology and capacity to estimate PN surveillance's performance of the Belgian and American validation studies are assessed on epidemiological criteria.
Results The NNIS system set up an accuracy pilot study in 1993, published in 1998. The sample included nine hospitals. All reported nosocomial infections (NI) and a selection of high-risk and low-risk PN-negative patients were examined. In a first phase, 32 external data collectors found over 2.5 times more PN than reported. The PN SS was 39% although hospitals with six consecutive month's surveillance participation and high NI incidence were chosen. In a second phase, two CDC epidemiologists re-examined a nonrepresentative sample of discrepant charts achieving 68% PN SS. Confidence intervals were not reported.
The Belgian validation study used a blind retrospective chart review as the NNIS. Investigators were members of the national surveillance program (NSIH). A two-step (patient and ICU) sampling was used. A sample for single proportion determined the number of PN patients to be reviewed. To get the requested PN cases, 45 ICUs were selected by systematic random sampling from all ICU participation-quarters. The required negative charts were a 20% random sample of all negative charts in these ICUs. The PN SS was 56.31% (95% CI = 47.92–65.21).
Discussion The NSIH study re-examined a representative sample of 45 out of all participating ICUs (30%), while the NNIS did so in nine of them. At the patient level, the Belgian sample was representative of the ICU case mix since all reported NI infections and a random sample of reported negative charts were reviewed. This methodology allowed CI determination.
The investigators' experience is known to influence the accuracy of identifying NI. Regular NSIH employees collected data in Belgium while such personal was involved in the second phase of the NNIS study only.
Conclusion The NSIH validation study tackles difficulties with statistical inference found in the NNIS 'accuracy of reporting pilot study'. Given the differences in validation methodology, the surveillance SS in both countries (NNIS: 39–68% in phase 2 vs NSIH: 56%) should be compared cautiously.
Being part of a nationwide surveillance routinely performed on continuous basis, the Belgian validation study design offers an alternative to validate national surveillance systems.

P125

Portuguese network data: epidemiology of community-acquired sepsis

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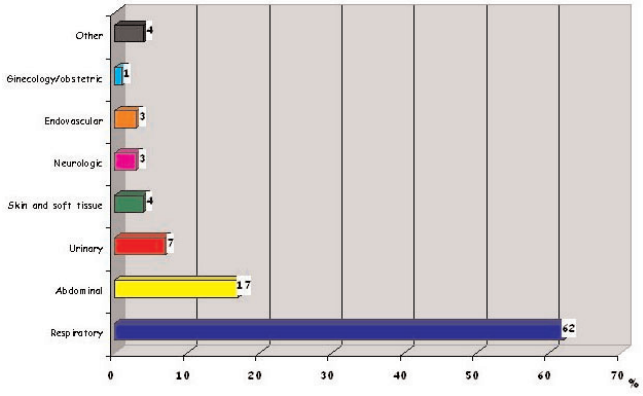
Introduction A prospective multicentre nationwide study on community-acquired sepsis (CAS) in Portuguese ICUs was created in 2004 with two main objectives: to know the epidemiology and to promote good practice. In this poster we intend to show data collected in the first 10 months.
Methods Seventeen units came together in this project. It lasted from 1 December 2004 until 30 November 2005. Data collection included epidemiological characteristics and comorbidities, the CAS episode (locale of infection, responsible organism, first intention antibiotherapy and associated organ dysfunction) and the compliance with the SSC recommendations. For statistics, the chi-square and Mann–Whitney tests were used. $P < 0.05$ was considered significant.
Results During this period 2643 patients were included in the study and 606 had CAS (23%) – of these, 240 (41%) had severe sepsis and 280 (48%) septic shock. Men had more sepsis (33% of all men) than women (25%, $P = 0.004$). No significant association was seen between age and sepsis, severity of sepsis or mortality. Twenty-three percent (137 patients) of the septic patients had an infection associated with health care. Forty percent had a microbiologically documented infection, 22% had positive blood cultures. Patients with sepsis had a longer ICU stay (median = 8 days) than those without (median = 5 days). This difference is significant for those who survive (median = 9 vs 5 days, $P < 0.01$) and for those who died (median = 6 vs 5 days, $P = 0.049$). Patients with sepsis had higher ICU mortality rate than those without (31% vs 22%, $P < 0.01$).
Discussion Comparing with previous similar studies we had: more patients admitted with CAS; more severe sepsis and septic shock; similar distribution by focus of infection; and a low number of microbiological documented infections. New analyses are being done regarding the focus of infection and severity of sepsis, responsible agent, first intention antibiotherapy and mortality.

Figure 1 (abstract P125)



Focus of infection.

P126

Sepsis: a study of physician's knowledge about the Surviving Sepsis Campaign in Puerto Rico

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Background In recent years, an increase incidence of sepsis has been reported. The literature suggests that over 650,000 cases of sepsis are diagnosed annually in the United States, leading to more than 100,000 deaths.
Despite medical and technological advances in treatment, the overall mortality rate in most institutions has remained between 40 and 45%. In 2003, a group of international critical care and infectious diseases physicians gathered to develop guidelines to improve the outcome of patients with sepsis. At the end of that year the Surviving Sepsis Campaign (SSC) Guidelines were published for sepsis management.
Objective To measure the degree of physician's knowledge of the SSC management guidelines in Puerto Rico.
Methods A validated questionnaire was given personally to 160 physicians. It included therapeutic interventions and important elements of the above guidelines. It was administered to a broad base of physicians including internal medicine and general surgery along with subspecialties from public and private hospitals around the entire island.
The questionnaire included a total of 13 questions. Questions 1–4 address general knowledge regarding the SSC and its goals. Question 5 measures knowledge of the diagnostic criteria for SIRS. Question 6 addresses outcome of severe sepsis. Questions 7–13 look at the specific guidelines.
Results Although 90% of all responders knew of the published guidelines, 60.1% and 36.8% had heard of the SSC or the sepsis bundles, respectively. Only 31.4% correctly identified SIRS criteria. Of the questions concerning bundle components, the worst scores were on those focused on use of steroids (32.5%), glucose control (40.9%) and ventilation (46%). Regarding our institution, which is a teaching hospital, there was no statistically significant difference in the percentage of correct answers between postgraduate year PGY-1 and PGY-2 residents ($P = 0.51$) or PGY-3 residents ($P = 0.61$). No significant differences were found between attending physicians and PGY-3 residents ($P = 0.80$).
Conclusions Recognizing septic patients remains a clinical challenge. Our results revealed no difference in knowledge between in-training doctors and private physicians. This is quite unexpected, as one would anticipate improved knowledge through years of training. These results prove that future strategies to correct these deficiencies are needed.

P127

A way to audit compliance with the Surviving Sepsis Campaign bundles

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Introduction A prospective multicentre nationwide study on community-acquired sepsis (CAS) in Portuguese ICUs was carried out with two main objectives: to promote good practice through implementation of the Surviving Sepsis Campaign (SSC) recommendation and to know the epidemiology, which is essential in the treatment of sepsis. In this presentation we intend to show how clinical practice changed over time.
Methods Seventeen units came together in this project. It lasted from 1 December 2004 until 30 November 2005. Data collection included epidemiological characteristics and comorbidities, the CAS episode (locale of infection, responsible organism, first intention antibiotherapy and associated organ dysfunction) and the compliance with the SSC bundles and recommendations – following a detailed protocol that contained a summarized description of all SSC guidelines. We consider for this poster the first 10 months of the study and compare the compliance of the SSC bundles in the first month with the last 2 months of this period (December 2004/January 2005 vs August/September 2005). The 95% confidence interval (95% CI) for the difference of proportions and Fisher's exact test were used to analyse categorical data; $P < 0.05$ was considered statistically significant.
Results During this period, 2643 patients were included in the study and 606 had CAS (23%) – of those, 520 (20%) had severe sepsis/septic shock. Over time more patients with septic shock received inotropes (45% vs 88%, 95% CI 0.149–0.701, P 49), had $SvcO_2$ measured (8% vs 32%, 95% CI 0.073–0.412, $P < 0.01$) and low-dose corticoids administered (38% vs 70%, 95% CI 0.123–0.510, $P < 0.01$). No significant difference was seen for CVP measurement (57% vs 47%, 95% CI −0.299 to −0.105, $P = 0.408$) or administration of vasopressors (78% vs 95%, 95% CI 0.035–0.307, $P = 0.102$).
In the last 2 months more patients had specimens collected for microbiological studies before antibiotic administration (72% vs 85%, 95% CI 0.010–0.250, $P = 0.067$) and more blood cultures done (89% vs 97%, 95% CI 0.010–0.142, $P = 0.1$). No significant differences were found in the first 6 hours of hospital admission for: measurement of serum lactate (61% vs 64%, 95% CI −0.121 to 0.186, $P = 0.74$), administration of fluids (67% vs 67%, 95% CI −0.145 to 0.158, $P = 1.0$) and antimicrobial administration (47% vs 49%, 95% CI −0.140 to 0.188, $P = 0.867$). No significant difference was seen in mortality in both periods.
Discussion During the study period our performance improved in the compliance of the majority of the bundles. We need to feedback to the participating ICUs the weak points of their practice on the SSC recommendations implementation as part of the audit process.

P128

The 2004 tsunami disaster: injury pattern and microbiological aspects

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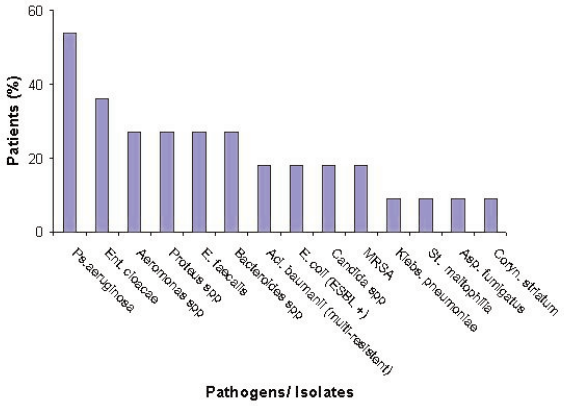
Introduction On 26 December 2004, a giant earthquake shocked south-east Asia triggering deadly flood waves (tsunami) across the Indian Ocean. More than 300,000 people have been reported dead and millions left destitute. Shortly thereafter, the German government organized airborne home transfer of the most severely injured tourists using 'MedEvac' aircraft (Medical Evacuation). Upon arrival, patients were distributed to various medical centers. One cohort was admitted to the Cologne-Merheim Medical Center (Germany) for further surgical and ICU treatment.
Objective To describe the unique pattern of injuries and microbiological findings associated with the 2004 Tsunami disaster.

Figure 1 (abstract P128)



Methods Seventeen severely injured tsunami victims were screened upon arrival for characteristic injury patterns. In parallel, multilocal microbiological assessment was performed to identify pathogens responsible for high-level wound contamination.

Results The predominant pattern of injury comprised multiple large-scale soft-tissue wounds (range: 2 × 3–60 × 60 cm^2) located at lower (88%) and upper extremities (29%), but also the head (18%). Additional injuries included thoracic trauma with hemopneumothorax and serial rib fractures (41%) and peripheral bone fractures (47%). A major problem associated with wound management was significant contamination. Microbiological assessment identified a variety of common (Pseudomonas 54%, Enterobacteriae 36%, *Aeromonas hydrophilia*/veronii 27%) but also uncommon isolates with high resistances (multiresistant Acinetobacter and ESBL-positive *E. coli* 18% each). Upper respiratory tract specimens contained an unusual high rate of multiresistant Acinetobacter species, but also MRSA, *A. hydrophilia*, Pseudomonas and *Candida albicans*.

Conclusion Individuals who survived their initial injuries and who were evacuated to Europe had traumatic injuries to the head, chest, and limbs that were often contaminated with highly resistant bacteria. Transferred patients from disaster areas should be placed into isolation until their microbial flora is identified as they may introduce new pathogens into an ICU.

P129

Relationship between polymorphonuclear leucocytes and the outcome of patients with severe trauma

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Introduction Major trauma is accompanied by a marked inflammatory reaction that involves infiltration of blood polymorphonuclear leucocytes (PMNs) into the injured area. This process is dynamic and evolves rapidly over the first 24–72 hours after injury. Activated PMNs can contribute to tissue damage by release of oxygen radicals, proteolytic enzymes and proinflammatory cytokines. The acute respiratory distress syndrome (ARDS) that occurs early after major trauma is characterized by a neutrophil infiltrate within the lungs. Also the inflammation, in response to brain injury, involves infiltration of neutrophils into the injured brain parenchyma.

Purpose The aim of the study was to test the hypothesis that the outcome of severe traumatized patients would be influenced by the PMN count.

Methods From December 2004 to November 2005, 40 multiple injured patients (28 male, 12 female, mean age 39 ± 18 years old) admitted to our ICU were retrospectively studied. The study protocol was approved by the local ethics committee. Ten of them had severe brain injury (GCS < 8) and 30 were admitted after major multiple trauma (ISS > 20). From the hematologic tests of the first 2 days post injury drawn from their records, the total peripheral leukocyte count, absolute neutrophil count and absolute lymphocyte count were recorded. The average values of the first 2 days for total leucocytes, absolute neutrophils and absolute lymphocytes were calculated for each patient. The overall outcome of the patients in the hospital was also recorded. The Student *t* test and the chi-square test were used for statistical analysis.

Results Patients were divided into two groups according to their outcome. The absolute neutrophil count in survivors was significantly lower than those in nonsurvivors ($P = 0.01$). No significant difference was found in total leukocyte count and absolute lymphocyte count between the groups. The mortality rate was significantly higher in patients with absolute neutrophils >8000 than in those with absolute neutrophils <8000 ($P = 0.03$). See Table 1.

Table 1 (abstract P129)

Outcome	Total leukocyte	Absolute neutrophils	Absolute lymphocytes
Survivors	14,429 ± 5438	10,318 ± 4018	2163 ± 1860
Nonsurvivors	16,362 ± 5176	13,283 ± 4725*	1948 ± 1161
P value	NS	$P = 0.01$	NS

*Statistically significant.

Conclusion A high absolute neutrophil count detected at the first and second day after severe injury is associated with an increased mortality. This finding must be verified in a prospective study with a large number of traumatized patients.

P130

Interhospital transport of the critical patients with polytrauma

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The aim of our study was the organization and tactics optimization of the interhospital transport of critical patients with polytrauma.

During the past 5 years the proper transport service of the Federal State Medical Prophylactic Institution Scientific Clinical Center of Miners' Health Protection (Leninsk-Kuznetsky) delivered 1023 patients from Kuzbass territory and other nearby regions, 390 of them were in a critical state. During the transportation 121 patients were conducted on MLV, 48 of them used PEEP. The antishock cloth 'Chestnut' was used in the transportation of 358 patients. Motor-car transportation was carried out for a 400 km distance; a helicopter was used for a long distance in individual cases. The maximum transportation time was 4 hours. During the transportation we determined the central hemodynamics and oxygen-transport function parameters.

The state of 110 of 390 transported critical patients with polytrauma was appreciated as decompensated. According to the ISS, the severity value = 24 ± 4 marks. The prognosis of the

probable lethal outcome during the nearest day was 100%. Transportation realized by the specialized team did not deteriorate the patients' state thanks to the conducted complex intensive therapy and prophylactic measures, in 19% cases a tendency to improvement of the state was observed. Lethal outcome during transportation was not registered.
The solution of the problem of safe interhospital transport of critical patients with polytrauma depends on the exact coordination of all interested services. Apart from the main quality criteria the essential point is competent guidance of the whole system that is connected with the clinics and transport service in this case.
All these components secure the high quality of the transportation of critical patients.

P131

Added medical value of a helicopter-transported medical team on emergency prehospital pediatric care in The Netherlands

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Introduction The aim of this study was to evaluate the effect of a helicopter-transported medical team (HMT) on the prehospital treatment of vitally compromised children. The study was performed in a Dutch HMT that provides advanced medical care in the eastern part of The Netherlands. The HMT consists of a specially trained physician and paramedic transported to the incident location by helicopter in the day-time. The Dutch HMT is activated together with the emergency medical service (EMS) by the dispatch centre or by the EMS paramedics at the incident location. Activation is according to a structured list of incident situations and/or the medical condition of the patient.
Design Retrospective analysis of 297 HMT calls for prehospital vitally comprised children (<16 years) from 2001 to 2005 by the HMT-Netherlands-East. Registered data included age, sex, physiological parameters and medical treatment. Specified was whether the medical procedures performed outside the hospital were provided by the EMS paramedic or the HMT physician; in all cases, EMS paramedics arrived at the incident location first. Medical procedures in children were classified into three groups: restricted to physician by Dutch law, physician more experienced than EMS paramedic, physician and EMS paramedic as experienced as each other. SPSS was used for descriptive analysis.
Results The EMS on scene canceled the pediatric HMT calls before the landing of the helicopter in 36% ($n = 107$) – reasons: no serious injury 82% ($n = 88$), deceased 10% ($n = 11$), other 8% ($n = 8$).
The HMT examined and treated 190 children on scene, with a total of 1461 medical procedures provided by the HMT physician (mean 7.7, SD 3.9). Medical procedures restricted to HMT physicians were given to 71% ($n = 135$) of the children (e.g. general anesthesia, thoracosynthesis, central venous cannulation). Medical procedures when classified as the HMT physician more experienced than the EMS paramedic were given to 76% ($n = 144$) of the children (e.g. endotracheal intubation, intra-osseous infusion, pain management). The combination of these two groups constituted 84% ($n = 158$) of all children examined by the HMT.
Conclusion The Dutch-HMT provides crucial additional medical expertise not provided by the EMS paramedics. Eighty-four percent of the vitally compromised children received a prehospital medical procedure restricted to a physician or for which a physician was more experienced.

P132

Assessment of a medical regulation concept for MEDEVAC during military operations

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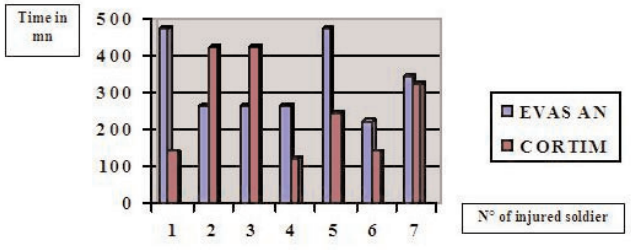
Critical Care 2006, **10(Suppl 1):**P132 (doi:10.1186/cc4479)

Objectives In order to reduce the waiting period before surgical treatment, the CORTIM project aims to develop a management system with the use of the NTIC system and operational radio network. To assess the benefits of a medical operational information system, we compared the current procedure (EVASAN) and the procedure of the CORTIM concept.
In EVASAN, evacuation of the injured soldiers is performed through mandatory stages of treatment or dispatching. Emergency categorization is made at surgical clearing center after first-level evacuation from the battalion first-aid post. Medical reports are written on the Field Medical Card (NATO format).
In CORTIM, the front unit medical officer collects medical data through a computer software application and transmits reports to the brigade surgeon who organizes MEDEVACs and can dispatch casualties directly to the specified field hospitals that are able to treat respective injuries.
Methods During the large-scale manoeuvre of an armoured brigade, MEDEVACs of seven casualties were performed with EVASAN and CORTIM procedures. Each procedure had at its disposal three places in helicopters, and four places in ambulances. The medical chain included one Front Unit Medical Team, one Forward Surgical Team with one operating room, and one Field Hospital with three operating rooms.
The data collected were quality of information written on the Field Medical Card and waiting periods before surgical treatment (in minutes).
Results On the Field Medical Card, only 54.5% of administrative and medical information is written, 70% of which with errors. With the medical electronic device, all the information required is available.
The compared waiting periods before surgical treatment are shown in Fig. 1. For 5/7 casualties, the CORTIM procedure and medical regulation reduced the waiting period before surgery. For three of them, the period was reduced from 220 min to less than 150 min.
Conclusion In our experiment, using a medical electronic device improved the quality of medical information and the CORTIM procedure reduced the time period before surgery.

Figure 1 (abstract P132)



Waiting period before surgical treatment.

P133

Short-term outcome in major trauma: land versus air emergency medical rescue in Tuscany

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Critical Care 2006, **10(Suppl 1):**P133 (doi:10.1186/cc4480)

Introduction Trauma is the major cause of death for people younger than 40 years in developed counties. In Italy an incidence of 120 deaths per 100,000 inhabitants for trauma is reported. An efficient emergency medical response system (EMRS) must therefore be assured in order to provide adequate treatment on the scene and allow a quick rescue to a referral hospital centre.
Methods The area of Florence in Tuscany consists of a population of 1.5 million inhabitants. In this area the EMRS is provided by a network of land ambulances staffed with an emergency physician and a helicopter with an intensivist on board.
In this study we considered all 291 trauma patients initially admitted to the Emergency Department (ED) and subsequently admitted to the eight-bed ICU of Careggi Hospital in Florence in the period from January 2003 to June 2005. Two groups of patients were considered: 144 patients rescued by the helicopter (group A) and 147 patients rescued by land (group B). The two groups were confronted for the category of trauma, GCS, SpO_2, fluid resuscitation volume, mean artery pressure (MAP), on-scene intubation, intubation within 5 min of arrival at the ED, scene time, lactates at ED admission, ICU LOS, and ICU mortality.
Results The groups' results were comparable for sex, age, trauma severity scoring, GCS and mean ICU LOS (group B 11.3 ± 10.5 days; group A 9.1 ± 7.9 days). Statistically significant differences* in the two groups were reported concerning the following variables: SpO_2 (group A 95.85% ± 5.21; group B 93.53% ± 8.06*); time on scene (group B 30.3 min; group A 36.52 min*); fluid resuscitation volume and MAP (group B 916.5 ml ± 513.16 and 89.9 mmHg ± 14.5; group A 1122.7 ml ± 564.37 and 92.7 mmHg ± 20.3); out-of-hospital intubation (group B 29%; group A 56.25%*); intubation in the ED (group B 40.8%; group A 11.1%*); lactates at ED admission (group B 3.06; group A 2.0*); and ICU mortality (group B 19.2%*; group A 13.2%).
Conclusions In our model, air rescue with a helicopter with an intensivist on board assures a higher standard of care, in comparison with land rescue. These achievements positively affect the outcome, with a decrease in ICU LOS and mortality.

P134

Elastic fixation of the diaphyseal fractures of the femoral bone in children

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The standard treatment of most fractures of the femoral bone in children was conservative. There are a variety of circumstances (polytrauma, head injury, open fracture, vascular injuries, impossibility of the satisfactory reposition by traction) that require surgical operation.
The aim of this study is the appreciation of the diaphyseal fractures' fixation using the elastic pins.
We propose the experience of the use of the elastic pins in nine patients (seven boys, two girls) aged from 7 to 12 years, with closed fractures of the femoral bones' diaphysis, who were treated by close reposition method with following elastic pins' fixation. The causes of the trauma were the results of traffic incidents: six cases (66%), street incidents: three cases (34%), fall from a height. Six patients had a polytrauma and three had the isolated trauma. All fractures were closed, transverse or oblique-transverse. The time of stay in the hospital from admission to surgery was 1.5–15 hours.
During the first week the patients were in a bed regimen, beginning from the second week their ambulation was exercised with crutches. Hospital stays lasted from 12 to 29 days (average 15.7 bed-days). The complete load was allowable in 8 weeks after surgery. One case demonstrated a reverse prolapse of the pins in 4 months, which were removed because of the fracture's fusion. There were no other complications. All fractures knitted well during 8–10 weeks. The observation time was from 8 to 26 months.
We used the ESIP principle in the treatment of femoral fractures by two elastic pins in children aged from 7 to 12 years. This method allows one to combine stable and elastic immobilization. The stability is achieved not only by pins, but by the surrounding soft tissue. The bone forms the axial stability in the cortical contact when the pins are fixed in the metaphysis. Rotation stability is created using the incurvated pins that compose the three-point fixation. Elastic mobility allows one to have the determined motion amplitude at the fracture's site, stimulating callus formation.

P135

Treatment of pelvic fractures of patients with polytrauma

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We treated 310 patients with pelvic fractures. According to the classification of M.Tile, the fractures were allocated in the following manner: A, 43%; B, 29%; C, 28%. Forty-four percent of these patients were admitted with different rates of severity of shock state. Osteosynthesis was carried out in 44% cases: 23%, external fixation only; 9%, internal constructions only; and 12%, combined synthesis. The treatment of pelvic fractures must correspond to the requirements of anti-shock measures and to the treatment of intra-articular lesions. The most informative method of the radial diagnosis is CT examination with three-dimensional pelvic reconstruction. We oriented toward the severity of pelvic lesion (A, B, C) for the determination of the terms, the volume and the order of surgical interventions. We carried out the total volume of surgical interventions in the consideration of the severity of pelvic lesions in the shock of I and II rates. We used internal or combined osteosynthesis in the partial or total loss of pelvic stability (B and C types). Internal osteosynthesis of the pelvis is biomechanically substantiated, because it regains the circular form and, consequently, also the pelvic stability, it decreases hemorrhage from the fracture regions, and it removes the pain more rapidly. Hemorrhage compensation was realized by intraoperative autohemotransfusion. In case of another dominant lesion, we operated by means of two brigades. In the shock of III and IV rates we carried out the pelvic stabilization only by the external fixation apparatus for the improvement of the common state of the patient. Closed reposition and osteosynthesis by external fixation apparatus with an anterior frame does not ensure complete success in the fractures of type C, but it is the most rapid method to obtain and to maintain reposition in the future.
Functional results were appreciated at the moment of discharge and after 12 months according to the Majeed S.A. scale (1989) and according to the data of computerized optic topography to appreciate the postural balance. Good and excellent results

(70–100 points for the workers and 55–80 points for nonworkers) were in 48% patients at the moment of discharge and in 78% patients after 12 months. The lethality value was 5.5%. The invalidism value was 7%. The mean time of hospital stay was 34 days and the mean time of resuscitation department stay was 1.5 days.
The treatment of the patients with severe injuries of the pelvis in polytrauma must be realized in special clinics, with necessary equipment and specially prepared nursing. Treatment tactics depend on the severity of the common state and on the severity of pelvic injuries.

P136

New shape of battle casualty with effects of body armor

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Background Common use of body armor (BA) and kevlar helmets by soldiers has lead to a change in war penetrating injuries.
Methods From 2002 to 2005, the anaesthesiologist and surgical staff of the Military Hospital Laveran, Marseille, France, participated in the combat support hospital for an international task force during peacekeeping operations in Kosovo, Afghanistan and Ivory Coast. Prospective data were collected on all combat casualties affecting wounded soldiers equipped with BA.
Results One hundred and sixteen wounded soldier cases wearing BA were included. The incidence of bullet wounds was 2%, of shell/rockets was 47%, of fragments of grenade was 16%, of mines was 6% and of bombing explosions was 29%. Injuries topographically affected the head, groin and neck (23%), thorax (10%), abdomen (3%) and extremities (96%).
Twelve percent died on the battlefield. Eighty-two percent of wounded soldiers reached the medical facility before 25 ± 15 min and were evacuated with a medical team to the combat support hospital in 127 ± 65 min between attack and admission; vital emergencies accounted for 17%, including 83% of hemorrhagic shock, 28% of respiratory distress and 11% of coma. After surgical care, the wounded soldiers had strategic medical evacuation to a military hospital in France in 37 ± 15 hours.
Discussion In the urban battlefield since Sarajevo (1992–1996) and Mogadishu (1993), bullet wounds of soldiers equipped with BA were higher (60%) than in our study (2%), whereas fragment injuries were fewer (30% vs 98%) [1,2]. Without BA, injuries affected the head and face (11%), chest (19.5%), abdomen (25.8%) and limbs (68.9%). In our study, penetrating injuries affected essentially the limbs (100%) and head (23%), but the thorax (10%) and abdomen (3%) were protected. The incidence of fatal wounds was similar in spite of modern BA (11–12%) but vital emergencies decreased in our study (17%) compared with injuries in the urban battlefield (44%). In the battlefield, delayed evacuations were typical because of unsafe air space, but wounded soldiers could receive fast medical facility and evacuation to intensive care and surgical support.
Conclusion Modern BA has reduced the number of fatal penetrating chest and abdominal injuries, and vital emergencies have decreased, but not the death rate, despite the efficiency of the combat medical support chain, because of specific employing of weapons (lethal injuries due to sniping, in the urban battlefield, aerial attacks, mine or bombing explosions).
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P137

Improving the outcome of trauma patients: is it possible in the absence of a trauma system?

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Background It is widely accepted that planning a trauma system, which allows the centralization of major trauma to the trauma centers with a high volume of activity, is able to reduce the mortality of trauma [1]. Nevertheless, the reorganization of the inhospital trauma care could improve the outcome of major trauma even in absence of a well-designed trauma system.
Methods Retrospective evaluation of the impact on outcome of a standardized approach to the trauma patients admitted to a general ICU in an 450-bed hospital not designated as a trauma center. The interventions adopted were the following:
- Specific training of all the physicians and the nurses involved in the trauma care in the Emergency Department and the ICU.
- Formal adoption of the team approach for trauma patients and of specific guidelines for the diagnostic and therapeutic pathway in the Emergency Department.
- Agreement between the prehospital and inhospital trauma teams on the clinical and dynamic criteria used to alert the trauma team in the field.
- Formal adoption of specific therapeutic protocols for the trauma patient in the ICU.
- The data of 1 year of activity, before, during and after the interventions, were collected and analyzed with the chi-square test.

Results There was an increase of the number of patients from 44 to 69 and 66 per year without differences in the mean age (38.8 ± 21.6, 38.2 ± 18.8 and 42.2 ± 22.6 years) and severity scores (SAPS II: 30.2 ± 14.2, 31.4 ± 14.3, 31.4 ± 12.8; ISS: 29.2 ± 12.1, 28.2 ± 12.0, 29.6 ± 11.9), respectively, in 2003, 2004, and 2005. There was a progressive increase of the use of some therapeutic techniques, such as FAST and the CT study of the C-spine in the Emergency Department and non-invasive ventilation and ultrafiltration in ICU. The mortality showed a reduction from 36.3% in 2003 to 24.6% in 2004 and 17.2% in 2005, with a statistically significant difference between 2003 and 2005 ($P = 0.034$).
Conclusion A reorganization of the response of the hospital to the trauma could improve the outcome even in the absence of a trauma system and a high volume of activity.
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P138

Empyema in the critical care patient

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Introduction The purpose of this study is to determine the incidence, mechanisms, causing pathogens and treatment of empyema in ICU patients.
Methods Over a 6-year period, 22 ICU patients developed empyema (1.5% of total admissions). Mean age: 41.1 ± 16.2 years. Mean stay: 21.4 ± 8.7 days. Initial APACHE II score: 17.1 ±

3.1. All patients underwent mechanical ventilation. Empyema was diagnosed at admission in four patients (18.2%) or during the ICU stay in 18 patients (81.8%). In all patients pus or bacteria was present in the pleural cavity. Besides the daily chest X-ray, a CT scan was performed at least twice during their stay.
Results Causes of empyema: pneumonia 10, mediastinitis 4, subphrenic abscess 3, hematogenous spread 3, soft tissue infection 2. Underlying diseases: chest injury in multiple trauma patients 15, chest surgery 5, other 2. Radiographic pattern: free pleural effusion: 18 patients (81.8%), loculated four patients (18.2%). In cultures of pleural fluid and blood were isolated: *P. aeruginosa* 38%, *A. baumannii* 26%, *S. aureus* 18%, *S. epidermidis* 7%, *K. pneumoniae* 7%, *E. coli* 4% (in eight patients polymicrobial, while two patients had frank pus but no bacteria were isolated). Pericardial effusion was present in five patients (22.7%). Twelve patients (54.5%) were treated with chest drainage alone (single or multiple), while in 10 patients (45.5%) several thoraco-surgical procedures were required (four patients were operated twice and one patient three times). Antibiotics were administered according to sensitivity tests. Mortality rates: 3/22 = 13.6%.
Conclusions Empyema is rare in the ICU, but it presents severe clinical features and increases the length of stay. Pneumonia is the commonest cause of empyema, followed by mediastinal and abdominal surgical infections. In more than 80% the chest X-ray revealed free pleural effusion. In more than 45% tube chest drainage alone was not effective to treat empyema. Causative pathogens of empyema did not differ from common ICU isolates.

P139

Combination antifungal treatment in critically ill patients failing first-line therapy for invasive fungal infections

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Introduction Combination antifungal therapy (CAT) appears an appealing option in critically ill patients with invasive fungal infections (IFI), especially in those experiencing failure to primary therapy.
Methods From November 2003 to April 2005, 18 patients affected by IFI (eight with candidemia due to *C. albicans*, three due to *C. glabrata*, two due to *C. krusei*, and five with pulmonary aspergillosis), who had failed primary antifungal therapy, were treated with caspofungin (CAS) 70 mg on the first day, and 50 mg thereafter, plus low-dose (LD) amphotericin B deoxycholate (dAmB) 0.5 mg/kg/day. All patients had high-risk underlying conditions (five acute myelogenous leukemias, six solid tumors, five prolonged ICU stays, and two major abdominal surgical interventions). Failure to prior therapy was determined by: fever and worsening of clinical conditions, and persistent candidemia, or worsening of the lung CT scan together with increase of Aspergillus galactomannan antigenemia (AGA), after 96 hours from the start of antifungal therapy.
Results All 18 patients were clinically unstable and critically ill, and 13 out of 18 had been admitted to the ICU at the time of switching therapy; five patients never required admission to ICU. All patients survived. Within 72–96 hours from the beginning of CAT, indeed, the clinical stability and fever clearance, together with a negative blood culture, or negative AGA were observed, and confirmed thereafter. LD dAmB did not require any premedication, but none of the patients suffered from side effects, and nor was treatment discontinuation needed. The mean CAT duration was 26 days, but the mean ICU stay was 9 days, before patient transfer to either medical or surgical wards. None of the patients relapsed within a follow up period of at least 60 days from the end of treatment.
Conclusions CAT including new drugs, such as CAS, is an appealing option supported by promising data. In our experience, CAT with CAS and LD dAmB appears effective in critically ill patients with IFI failing primary treatment. The experimentally demonstrated synergistic activity of dAmB, even at LD, plus CAS seems to be clinically relevant; due to the safety demonstrated, LD dAmB also allows remarkable cost sparing in comparison with lipid formulations. Moreover, compared with the available clinical data in similar situations, both the time to clinical stability and time to discharge from the ICU appear shortened in patients under CAT. Wider clinical studies in these selected settings are needed to clarify the impact on survival of this salvage treatment schedule.

P140

Increasing fungal infections in cardiovascular ICUs

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Introduction In past years there has been an increase in the occurrence of systemic fungal infections in ICUs. Although Candida species are the leading cause of hospital fungal infections, severely ill patients can develop invasive infection by emerging fungus or by innocuous inhabitants of the environment.
Objective To describe the occurrence of bloodstream and urinary tract infections in ICUs of a cardiology hospital.
Methods We analyzed all cases of bloodstream and urinary tract fungal infections that occurred in two clinical ICUs at the Heart Institute of São Paulo University School of Medicine from January 2000 to November 2005.
Results Among 376 bloodstream infections, 26 (6.9%) were caused by Candida species and one by Trichosporon spp. Seventy-three percent of candidaemia occurred in the last 2 years of study. The mean age was 61.6 years and the mean ICU length of stay before the diagnosis was 35 days. The following Candida species were identified: *C. albicans* = 42%, *C. parapsilosis* = 23%, *C. tropicalis* = 19%, *C. glabrata* = 11% and *C. guillermondi* = 4%. Among 585 urinary tract infections episodes, 253 (43%) were caused by fungi: 47% by *C. albicans*, 34% by non-albicans Candida species and 18% by Trichosporon spp.
Conclusions We observed an increasing incidence of bloodstream fungal infections caused by non-albicans Candida species, predominantly in the last 2 years in severely ill long-staying inhospital cardiac patients. Trichosporon spp. is a fungus once thought to cause only superficial infections, but has been increasingly identified as an opportunistic systemic pathogen in severely immunodepressed patients. The occurrence of bloodstream infection and the high incidence of urinary tract infection caused by Trichosporon spp. in this study led us to begin a prospective study to identify risk factors and treatment strategies.

P141

Effects of candiduria–candidemia infections on mortality and morbidity in the ICU and the risk factors of these infections

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Objective Yeast infections have increasing importance among ICU infections. Candida species have been raised to the fourth most

frequently seen ICU infections. Among Candida species, *Candida albicans* is the most frequently seen yeast infection. We aimed to investigate the candidemia–candiduria ratio, their risk factors, and their mortality and morbidity in ICU patients.

Methods Intensive care medical records of 935 patients who attended an ICU between 2002 and 2005 were analyzed retrospectively. The risk factors, mortality and morbidity of candiduria–candidemia infections were assessed.

Results Candida infections developed in 28 of all patients (Table 1). The ratio of candidemia/yeast infection was 32%. Risk factors of Candida infections are presented in Table 2. Even though the mortality ratio of ICU was 39.4%, it was found to be 57.9% in candiduria and 66.7% in candidemia.

Table 1 (abstract P141)

Yeast infection	Number of patients	Ratio (%)
Candida infection	28	3
Candiduria	19	2
Candidemia	3	0.32
Candidemia + candiduria	6	0.64

Table 2 (abstract P141)

Risk factor	Candidemia	Candiduria
TPN application (%)	44.4	12
Time of mechanical ventilation (days)	29	29
Time of ICU stay (days)	37	37
APACHE II score	25	20
Age (years)	48.56	48.56
Use numbers of antibiotics	2.6	2.6
Time of antibiotics (days)	14	8.8
Days of invasive catheter	21.4	21.4
SOFA score	9.56	8.47

Conclusions We found high mortality and morbidity in Candida infections, and there was a relationship between high APACHE II scores, long ICU stay, long mechanical ventilator time, numbers of antibiotics, TPN application, and days of invasive catheter use.

P142

Tetanus in the ICU: increasing incidence in the past 5 years

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Background Since 1973 the total number of cases of tetanus in our ICU is 30, almost all before 1990 (22 cases). Since 2000, six cases have taken place. The aim of the present study was to describe the characteristics of infection by *Clostridium tetani* in this period.

Methods We retrospectively analysed the data of tetanus from 2000 to 2005. Clinical features, treatment and comorbidities were recorded.

Results Six cases of tetanus were described in this period: two cases of cephalic tetanus and four of generalized tetanus. Study patients had a mean age of 64 years (three were male), and period of the year was one case in spring, three in summer, two in autumn. The mean incubation period (from inoculation to first symptom) was 7 days in cephalic tetanus and 15 days in generalized tetanus, and the mean period of onset (from first symptom to first spasm) 10.5 days in cephalic tetanus and 14.5 days in generalized tetanus. The mean ICU length of stay was 28.2 ± 13 days, and the mean hospital length of stay was 43 ± 21 days. Mean days under mechanical ventilation were 21 ± 10 days. Clinical manifestations included trismus and generalized spasm in all cases, facial nerve paralysis in both cases of cephalic tetanus and abdominal pain in one case of generalized tetanus. All patients were treated with metronidazol, antitetanus immunoglobulin and toxin. Sedatives (midazolam and propofol) and neuromuscular blocking agents (cisatracurio and vecuronium) were used. Tracheostomy was performed in all cases as soon as possible. Complications included ventilator-associated pneumonia in four cases, infection of the urinary tract in two cases, asystole in one case, acute renal failure in one case, and seizures in one case. All patients were discharged from the ICU. One of them died in the hospital.

Conclusions Tetanus is a rare disease in the ICU, but with low mortality. Strategies to fight tetanus include the training of the intensivist in earlier diagnosis and adequate interventions (attention to the airway and to ventilation is paramount at the time of presentation). Tetanus is entirely preventable worldwide. Revaccinating the population with antitetanus toxin might be considered in our setting.

P143

Analytical survey of human rabies prevalence in the province of Kerman, Iran

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In order to determine the frequency rates of domestic and wild animal bites as well as the evaluation of the prevalence rates of rabies disease in human population in the province of Kerman, a retrospective study was designed to analyze statistically the collected recorded data related to this project. The required data such as the numbers of persons who were bitten by animals, the distribution of the studied variables such as geographical locations, age groups of people, jobs and professional relationships, pre-exposure prophylaxis treatment for rabies, and topographical conditions of the injured organs of bodies due to the animal bites, as well as the mortality rates of individuals resulting from rabies, were collected during one decade starting from 21 March 1994 to 21 March 2003 in all 10 cities including the rural areas of the province of Kerman. All data were finally analyzed by SPSS software (Version 11.5).

On the basis of recorded statistical analysis, the mortality cases of human rabies in the province of Kerman during one decade was 10 persons (eight males and two females). One-half of them (50%) were bitten by dogs and the others (50%) by foxes. The mean of age of the people who were bitten by dogs was 24.80 years (SD = ±14.6), while the mean age of the people who were bitten by foxes was 57.25 years (SD = ±1.50). There was a significant difference between the mean age of these two groups of the people ($P < 0.05$). The most frequent rate of injured people was reported in the age group of 10–19 years old and the frequency rate of males (76.00%) was more than females (24.00%). There was therefore statistically a significant difference between males and females in this study ($P < 0.01$).

Among the people who were bitten and injured by animals during one decade in the province of Kerman, 85.70% of them have not been treated by a rabies prophylaxis treatment regimen. Among all of them who were bitten by animals, 50% were injured through the hands and feet, 40% of them through heads and faces, and 10% of them through trunks, cervical regions and other organs of the bodies. In the persons who were bitten by animals in the head region, the mean time of the latency period for rabies was 33 days (SD = ±12.2 days), while the mean time of the latency period in

the persons who were bitten through the hands and feet was 77 days (SD = ±45.8 days). $P < 0.1$. The results of this study showed that there is a significant reciprocal correlation between the annual raining level and the frequency rate of animal bites in the province of Kerman ($r = 0.5$, $P < 0.01$).
According to this study, the role of foxes in the epidemiological cycle of human rabies in the province of Kerman, located in the south-east of Iran, seems very important.

P144

Effects of antibiotics on intestinal microcirculation, cytokine release and *in-vitro* vascular reactivity in septic rats

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Background Antibiotic treatment represents a key component of therapy for severe sepsis. Apart from the sensibility of the causing microorganisms, when choosing antimicrobial agents in septic conditions possible effects of antibiotics on the microcirculation, inflammatory mediators and vascular (hypo)reactivity should be taken into account.
Objectives The aim of this study was to evaluate the effects of metronidazole (MET), imipenem (IMI), tobramycin (TOB) and vancomycin (VAN) on the intestinal microcirculation in septic rats using intravital microscopy (IVM), on the release of the cytokines TNF-α, IL-1β, IL-6 and IL-10, and on the *in-vitro* reactivity of the rat aorta.
Methods We induced sepsis in the animals (Lewis rats) using the Colon Ascendens Stent Peritonitis (CASP) model. MET (10 mg/kg), IMI (20 mg/kg), TOB (25 mg/kg) and VAN (70 mg/KG) were given intravenously 16 hours following sepsis induction. Intravital microscopic examination was performed 2 hours later. Cytokine release was estimated at the end of the experiments. Direct effects of the antibiotics on vascular tonus were studied in normal rat aortal rings *in-vitro* precontracted either with phenylephrine (PE) (5×10^{-8} M) or 20/40 mM KCl.
Results In the CASP model we observed a reduced functional capillary density in the muscular and mucosal layers of the intestine and an increased number of temporary and firmly adhering leukocytes in submucosal venules. Acute treatment with MET attenuated this response. TNF-α release in untreated CASP animals was twice as high as compared with MET-treated animals. *In vitro*, higher concentrations (up to 10^{-4} M) of some antibiotics produced moderate relaxation: TOB 47% (PE), VAN 44% (PE), MET 48% (20 mM KCl).
Conclusion Antibiotics may exert, in addition to their antimicrobial action, effects on the microcirculation, and potentially could influence vascular (hypo)reactivity in septic conditions.

P145

Genetic variation of TNF is associated with sepsis syndrome and death in severely injured patients

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Objectives Patients encountering severe trauma are at high risk of developing MOF, which is often associated with an unregulated production of mediators of the systemic inflammatory response syndrome [1]. Previous studies suggested an association of TNF and LTA SNPs and the incidence of sepsis among ICU patients [2-4]. By examining several candidate genes (TNF, PAI-1, IL-1, IL-6), previously reported to be associated with sepsis outcome in our cohort [5,6], we now report that genetic variation in TNF and/or LTA is predictive for the development of sepsis in multiple trauma patients with a low prevalence of other clinically confounding factors.
Patients and methods One hundred and fifty-nine multiple trauma patients were included prospectively following admission to the ICU with an ISS of 12 points or more after complete assessment of injuries. We genotyped all known SNPs including those in the 5′ region of the TNF gene, including LTA, with a reported allele frequency of the rare allele of greater than 5% in Caucasians ($n = 9$ SNPs). Univariate analysis and multivariate logistic regression analysis were performed.
Results Seventy-two patients (45.3%) fulfilled the criteria for sepsis after severe trauma and 32 (38.9%) patients died from a sepsis leading to MOF. Allele distributions were according to the HW equilibrium. A significant association for the incidence of sepsis after multiple trauma was observed for the TNF –308A allele (OR 7.14; 95% CI, 3.1–16.45; $P < 0.0001$), and the completely linked LTA +252G allele (OR 1.96; 95% CI, 1.02–3.78; $P < 0.042$). Additionally, both alleles showed significant association with death after severe trauma (TNF –308A: OR 7.65; 95% CI, 13.27–17.93; $P < 0.0001$; LTA +252G: OR 5.58; 95% CI, 2.02–15.44; $P < 0.0002$).
Conclusion The presence of one or two copies of the TNF –308A, LTA +252G haplotype is strongly predictive for the incidence of sepsis and death in multiple trauma patients.
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P146

Whole genome expression profiling in multiple trauma patients

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Introduction Severe trauma may be followed by an uncontrolled inflammatory response that is associated with high mortality and morbidity and the patient is at high risk of developing MOF [1]. Serial gene expression analysis of peripheral blood obtained from patients with polytrauma should provide a molecular portrait of mechanisms leading to sepsis. Genome-wide transcriptional profiling will permit identification of novel predictive biomarkers for earlier diagnosis of sepsis and MOF than current strategies using serum markers and clinical scores.
Methods Whole blood Paxgene samples were collected at the initial time point (TP 0) and then every 24 hours until day 28 post hospital admission from 21 patients with multiple trauma. Ten patients developed sepsis during the stay in the ICU while 11 remained nonseptic. Total RNA was isolated from peripheral blood

of each patient at TP 0 and subjected to microarray analysis using the CodeLink UniSet Human I Bioarray (Amersham Bioscience) containing 9877 human genes. Data analysis was carried out using ImaGene5 (Amersham Bioscience), dChip (www.dchip.org) and SAM (www-stat.stanford.edu).

Results Multiple testing with a FDR of 1.1 [2] revealed in total 692 significantly regulated genes in septic patients at TP 0, of which 480 genes had significantly higher and 212 genes significantly lower expression levels compared with nonseptic patients at TP 0. The highly expressed genes were mainly involved in inflammatory and stress responses, apoptosis and development, while the lower expressed genes could be assigned to defense responses, protein biosynthesis and lipid binding. Hierarchical clustering of the samples clearly differentiated between the time point of admission and sepsis.

Conclusion Statistical analysis of expression data enabled clear differentiation between nonseptic and septic traumatic patients at admission to the ICU (TP 0). Septic patients showed significant overexpression of genes involved in immune responses and antiapoptosis, indicating a strong inflammatory interaction at time of admission as compared with nonseptic patients. The early vigorous inflammatory response appears to activate a program, subsequently leading to SIRS and, finally, MOF.

Acknowledgement This work was supported by grants from the Ministry of Science and Education, Germany (NGFN 01GS0401).

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P147

Prothrombin gene and factor V Leiden gene polymorphism in patients with deep vein thrombosis: prevalence, diagnostic and therapeutic implications

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Risk profiling in deep vein thrombosis (DVT) has been classically concerned with traditional factors of obesity, postoperative status, prolonged recumbency, longstanding varicosity, etc., with subsequent stagnation of blood and damage to vascular endothelium. Only recently, there has been increasing concern with procoagulant factors as protein C, protein S, antithrombin III deficiencies as well as elevated factor VIII, hyperhomocysteinemia, dysfibrinogenemia, etc., all of heredofamilial nature.

The present study is intended to assess the prevalence of two genetic disorders promoting coagulation; namely, the mutant form of factor V (Leiden) and the prothrombin gene in Egyptian patients with acute DVT.

We studied 30 patients admitted with acute DVT (16 male, 14 female, mean age 44 ± 14 years), and 30 control subjects (19 males, 11 females, mean age 37 ± 10 years). Excluded from the study were patients known to have bleeding diathesis, those with acute or chronic liver disease, and those on oral or parenteral anticoagulation.

Following clinical evaluation including 12-lead ECG and routine laboratory tests, all patients were subjected to venous duplex and gene identification. The latter comprised DNA extraction, PCR amplification, and gene mutation detection using the THROMBOTYPE reagent kit.

Compared with control subjects, patients with acute DVT had significantly higher prevalence of factor V Leiden Gene mutation (66.7% vs 23.3%, $P = 0.003$). Compared with noncarriers of this mutant form, carriers exhibited significantly more frequent familial incidence (55% vs 15%, $P = 0.035$), younger age of presentation (40 years vs 51 years, $P = 0.048$) and more frequent complications (55% vs 10%, $P = 0.049$). Prothrombin gene mutation was exhibited by three out of 30 patients with acute DVT (10%) and was associated with factor V Leiden in two of them. None of the control subjects exhibited this mutant form of the prothrombin gene.

In conclusion, acute DVT among young patients and particularly those with recurrent DVT should urge the cardiologist to search for factors promoting coagulation. Our data show abnormally high prevalence of the mutant form of factor V Leiden (associated with prothrombin gene mutation in a minority). Besides the diagnostic value, gene mutation detection has therapeutic and prognostic implications through the need to adjust the dose and the duration of oral anticoagulation.

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Inhibition of inducible nitric oxide synthase prevents the attenuated response to noradrenaline during human endotoxemia

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Vasodilatory shock is the main cause of mortality during sepsis. Animal experiments suggest that the decreased vasopressor sensitivity present in vasodilatory shock is caused by increased levels of nitric oxide (NO). Human data on this subject are sparse. The administration of *Escherichia coli* endotoxin (LPS) to human volunteers induces an inflammatory response and, as clinically observed in sepsis, an attenuated vasoconstrictive response to noradrenaline. The present study investigated the effects of NO inhibitors L-NMMA and aminoguanidine on the attenuated vasoconstrictive response to noradrenaline during human endotoxemia.

Thirteen human volunteers received 2 ng/kg *E. coli* LPS intravenously. The brachial artery was cannulated for infusion of noradrenaline and L-NMMA. The response to noradrenaline was determined by intra-arterial infusion (1–3–10–30 ng/min/dl) and determination of forearm blood flow (FBF) using venous occlusion plethysmography. The noradrenaline dose–response was determined before and 4 hours after LPS administration.

Group A ($n = 6$): to determine the local effect of NO inhibitor L-NMMA on noradrenaline dose–response, a dose of 0.2 mg/min/dl L-NMMA was infused intra-arterially at $t = 5$ hours after LPS administration. During the infusion of L-NMMA the noradrenaline dose–response was determined again.

Group B ($n = 7$): to assess the effect of systemic NO inhibition the selective inducible NO synthase (iNOS) inhibitor aminoguanidine was administrated i.v. at $t = 1$ hour post-LPS administration and continued until $t = 5$ hours (370 mg loading dose and 60 mg/hour continuously). Data are expressed as the mean ± SEM. FBF is expressed as the ratio of the flow in the infused/non-infused arm and is presented in percentages compared with the baseline. Differences were tested by repeated-measures ANOVA. $P < 0.05$ was considered to indicate significance.

LPS administration induced the expected flu-like symptoms, fever (38.3 ± 0.1°C), and a decrease in mean arterial pressure and increase in heart rate in both groups. The intrabrachial infusion of L-NMMA increased noradrenaline sensitivity after endotoxin administration (LPS alone 92 ± 5, 85 ± 4, 68 ± 11, 44 ± 13; LPS + L-NMMA 71 ± 8, 66 ± 7, 48 ± 11, 21 ± 3%, $P = 0.009$). The systemic inhibition of iNOS completely prevented the attenuated response to noradrenaline at $t = 4$ hours (before LPS 83 ± 5, 76 ± 7, 58 ± 9, 31 ± 2; after LPS + aminoguanidine 89 ± 3, 82 ± 4, 57 ± 5, 34 ± 5%, P = NS).

The local administration of nonselective NO-inhibitor L-NMMA restores the attenuated noradrenaline sensitivity during human endotoxemia. Moreover, systemic iNOS inhibition by aminoguanidine completely prevents an attenuated vasoconstrictor response. The present study indicates that noradrenaline insensitivity during human endotoxemia is mediated by induction of inducible NO synthase.

P149

Plasma obtained during human endotoxemia increases endothelial permeability *in vitro*

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Objective In order to gain insight into the pathogenesis of increased vascular permeability during sepsis, we studied the effect of plasma obtained during human experimental endotoxemia on the permeability of cultured endothelial monolayers *in vitro*.
Methods Eight healthy subjects received an i.v. dose of 2 ng/kg *Escherichia coli* O:113 lipopolysaccharide (LPS). The concentration of various plasma mediators that supposedly induce vascular permeability was measured over time. Plasmas that were obtained prior to and 2 and 4 hours after the administration of LPS were added to human umbilical venular endothelial cells (HUVEC) that were cultured on semipermeable membranes.
The permeability of the endothelial monolayers to FITC-labeled bovine serum albumin was determined and expressed as the relative concentration of FITC-BSA when compared with that measured across empty Transwell-COL membranes (i.e. without endothelial monolayers). The permeability levels were correlated with the plasma concentrations of various mediators.
Results Experimental endotoxemia resulted in elevated levels of TNF-α, IL-1β, IL-6, IL-8, IL-10 and VEGF, and a moderate increase of IL-12 and IFN-γ (all $P < 0.01$). Incubation of HUVEC with plasma obtained 2 and 4 hours after the administration of LPS increased the relative permeability from a baseline level of (median [range]) 17% [14–31%] to 23% ([12–39%], P = NS) and 28% ([11–40%], $P < 0.05$), respectively. Plasma levels of VEGF and IL-10, but not TNF-α, or any of the other mediators, significantly correlated with the increase in endothelial permeability ($r = 0.47$, $P = 0.038$ and $r = 0.43$, $P = 0.038$, respectively).
Conclusion The data presented here demonstrate that plasmas obtained from experimental human endotoxemia increase endothelial permeability *in vitro*. This response was independent of the incubation time (45 min–6 hours) of endotoxic plasma on the endothelial monolayers. The increase in endothelial permeability was moderately correlated with VEGF and IL-10 levels in plasma. Our observations may facilitate future experiments that try to elucidate the pathophysiology of increased vascular permeability during systemic inflammation.

P150

Endothelial and coagulation dysfunction during porcine bacteremia: effects of combining iNOS inhibitor and radical scavenger

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Introduction We showed recently that both selective iNOS inhibition and the radical scavenger Tempol prevented live bacteria from causing key features of hemodynamic, microcirculatory and metabolic derangements in porcine sepsis [1,2]. Here we investigated the effects of combined selective iNOS inhibition (L-NIL) with a free radical scavenger (Tempol) on *P. aeruginosa*-induced endothelial and hemostatic stress.
Methods Twelve hours after induction of sepsis with continuous i.v. *P. aeruginosa*, 16 pigs received either no drug (CONT, $n = 8$) or a combination of L-NIL + Tempol (COMB, $n = 8$). Before and 12, 18 and 24 hours after the start of *P. aeruginosa*, plasma levels of markers related to endothelial function (von Willebrand factor [vWf]), hypercoagulability (thrombin–antithrombin complexes [TAT]), oxidative stress (8-isoprostane) and inflammation (TNF-α) were assessed.
Results See Table 1. Combined treatment prevented a sepsis-induced increase in plasma 8-isoprostane and substantially attenuated the gradual increase in TNF-α.

Table 1 (abstract P150)

		Baseline	12 hours	18 hours	24 hours
vWf (mU/g protein)	CONT	8 (7; 31)	15 (13; 48)‡	22 (14; 57)‡	25 (15; 99)‡
	COMB	7 (7; 18)	11 (9; 14)‡	13 (12; 14)‡§	14 (10; 17)‡§
TAT (μg/g protein)	CONT	1 (1; 3)	3 (1; 5)	6 (3; 13)‡	6 (5; 14)‡
	COMB	2 (1; 3)	2 (1; 3)	2 (1; 5)§	3 (2; 5)§

Data presented as the median (interquartile range), $P < 0.05$. ‡ vs baseline; § COMB vs CONT.

Conclusion Live bacteria-induced sepsis resulted in endothelial activation/dysfunction associated with activated coagulation, which were markedly attenuated by the combined iNOS blockade and radical scavenging. Suppression of oxidative stress and excessive inflammation might contribute to these results.
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P151

Effect of intravenous immunoglobulin in critically ill adult patients with sepsis: a meta-analysis

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Context Intravenous immunoglobulin therapy has been proposed as an adjuvant treatment for sepsis. Yet the benefit of the therapy remains unclear. Furthermore, its use is not currently recommended.
Objective To evaluate the effect of polyclonal intravenous immunoglobulin therapy on mortality in critically ill adult patients with sepsis.
Data sources Medline (1966–September 2005) and the Cochrane Register of Controlled Trials (September 2005).
Study selection All randomized controlled trials of polyclonal intravenous immunoglobulin therapy with a placebo comparison or no intervention during the course of sepsis, severe sepsis or septic shock in critically ill adult patients. No restriction was made for language or type of publication.

Data extraction Data were independently extracted by two investigators using a standardized form.
Data synthesis The literature search identified 4462 articles, of which 32 were deemed potentially eligible. Nineteen trials ($n = 2415$) met eligibility criteria and were included in the analysis. Polyclonal intravenous immunoglobulin therapy was associated with an overall survival benefit (risk ratio [RR] = 0.72, 95% confidence interval [CI], 0.59–0.88) compared with placebo or no intervention. The number needed to treat was 10 [95% CI: 4–16]. In sensitivity analyses, we documented improved survival when the analysis was limited to published and peer-reviewed trials (RR = 0.69, 95% CI, 0.55–0.87) (16 trials, $n = 1659$) and blinded trials (RR = 0.61, 95% CI, 0.40–0.93) (seven trials, $n = 896$). A dosage regimen higher than 1 g/kg and a duration of therapy longer than 2 days were strongly associated with this survival benefit.
Conclusions We observed a survival benefit with the use of polyclonal intravenous immunoglobulin therapy in sepsis compared with placebo or no intervention. The magnitude of the benefit is advantageously comparable with activated protein C. Because of methodological limitations of the current literature, a large randomized controlled trial of this therapy is recommended.

P152

VX-166, a novel potent small molecule caspase inhibitor, as a promising new treatment for sepsis

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Introduction Lymphocyte apoptosis has been identified as an important factor contributing to both the onset of sepsis and to the progression into septic shock and multiple organ failure. Anti-apoptotic therapy through caspase inhibition therefore offers a novel and promising approach to the treatment or prevention of sepsis. Significantly, administration of caspase inhibitors has already been shown to be beneficial in animal models of the disease. We have designed VX-166, a novel broad caspase inhibitor that has an advantageous pharmacokinetic and toxicity profile and should be suitable for use in man. The present study was performed to evaluate VX-166 as a therapeutic agent for the treatment of sepsis.
Methods and results VX-166 demonstrated extremely potent anti-apoptotic activity in a variety of cell assays using a number of different apoptotic stimuli. *In vivo*, VX-166 was tested in a murine model of endotoxic shock and a rat caecal ligation and puncture model (CLP) of peritoneal sepsis. In the first model, male CD-1 mice ($n = 28$ per group) were administered lipopolysaccharide (LPS) (20 mg/kg i.v.) and their survival monitored for 96 hours. VX-166 administered by repeat i.v. bolus (0, 4, 8 and 12 hours post-LPS) dramatically improved survival in a dose-dependent fashion ($P < 0.0001$). This result was confirmed in a second study where the optimal dose (30 mg/kg) of VX-166 substantially improved survival from 0% in the vehicle group to 75% in the VX-166 group ($P < 0.0001$). In the second model, adult male Sprague–Dawley rats ($n = 12$ per group) underwent CLP. Their necrotic caecum was excised 20 hours later and survival was monitored over 10 days. Continuous administration of VX-166 by mini-osmotic pump immediately following surgery improved survival ($P < 0.01$) from 38% in the control group to 88% in the compound-treated group. Mode of action studies in this model confirmed that VX-166 reduced thymic atrophy and lymphocyte apoptosis ($P < 0.01$). This is good evidence of the anti-apoptotic activity of the compound *in vivo*. In addition, plasma endotoxin levels were reduced ($P < 0.05$), strongly suggesting that VX-166 can improve clearance of bacteria from the bloodstream in sepsis. Most importantly, we demonstrated that VX-166 fully retained its efficacy when dosed 3 hours after insult ($P < 0.01$), by improving survival from 42% in the control group to 92% in the dosed group.
Conclusion These results show that VX-166 substantially improves survival in experimental sepsis. As VX-166 also has an excellent toxicity profile and pharmacokinetic properties that make it suitable for use in man, we believe that VX-166 represents an exciting opportunity as an anti-apoptotic therapy for the prevention and treatment of sepsis.

P153

TAK-242, a novel Toll-like receptor 4 signal transduction inhibitor, protects mice in *Escherichia coli*-induced and lipoteichoic acid-induced lethality models

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Objectives Toll-like receptor 4 (TLR4) is a pattern recognition receptor of various host and bacterial ligands. TLR4 ligands such as lipopolysaccharide activate immune cells and induce production of many cytokines, which are involved in the onset of sepsis. TAK-242 is a novel small molecule that selectively inhibits TLR4-induced production of multiple cytokines by monocytes and macrophages. The *in-vivo* potential of TAK-242 was examined in models of *Escherichia coli* (Gram-negative)-induced and lipoteichoic acid (LTA) (Gram-positive)-induced lethality in mice.
Methods *E. coli* was inoculated intraperitoneally in *Bacillus calmette guerin*-primed mice. One hour after bacterial inoculation, TAK-242 was intravenously administered with antibiotics. LTA-induced lethality was induced by the intraperitoneal administration of LTA and D-galactosamine. Cytokine levels in sera were determined by specific ELISAs and survival through 7 days was recorded.
Results TAK-242 coadministered with ceftazidime (CAZ) dose-dependently protected mice from *E. coli*-induced lethality; CAZ alone was ineffectual. Statistically significant protection was observed at 0.3 mg/kg or more of TAK-242 ($n = 10$, $P \leq 0.05$) and 3 mg/kg prevented lethality in all mice. The increases in serum levels of not only proinflammatory cytokines such as TNF-α and IL-1β, but also an anti-inflammatory cytokine, IL-10, were significantly and dose-dependently suppressed by TAK-242. Increase cytokine levels were quickly and markedly suppressed by the treatment with TAK-242 even when cytokine levels had already increased significantly. The doses that prevented lethality and inhibited cytokine production were similar, suggesting that TAK-242 rescued mice by suppressing excessive cytokine production and inflammation. TAK-242 did not increase bacterial counts in blood, although it suppressed cytokine production. TAK-242 showed similar protective effects when the antibiotics imipenem or gentamicin were used in place of CAZ, suggesting TAK-242 would work in combination with various types of antibiotics. In addition, TAK-242 dose-dependently suppressed the LTA-induced increase in serum IL-6 levels in mice and rescued mice from death. Statistically significant protection was observed at 0.3 mg/kg or more of TAK-242 ($n = 10$, $P \leq 0.05$) and 3 mg/kg rescued all mice. The efficacy in the LTA model was, therefore, comparable with that in the *E. coli* model.
Conclusion TAK-242 showed marked and similar protective effects in Gram-negative and Gram-positive murine models of

sepsis. These data suggest that TAK-242 may be a novel therapeutic treatment for sepsis. A pivotal clinical trial of TAK-242 to test this hypothesis is ongoing.

P154

Selective inhibition of Toll-like receptor 4 signaling by the small molecule TAK-242

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Objectives Sepsis is a clinical syndrome whose pathophysiology reflects the activation of an innate host response to infection. Toll-like receptors (TLRs) recognize structural components of various microbes and activate inflammatory signaling. TLR4 detects Gram-negative bacteria through recognition of the lipid A moiety of lipopolysaccharide (LPS). The cyclohexene derivative TAK-242 inhibits multiple inflammatory mediators produced by LPS-stimulated murine RAW264.7 macrophages. We determined the selectivity of TAK-242 against the TLR family and its efficacy *in vitro* and *in vivo*.
Methods The selectivity of TAK-242 against the TLR family was examined in a NF-κB reporter gene assay using 293 cells transfected with human TLR expression vectors. The amount of nitric oxide (NO) in the medium was determined by measuring the fluorescence of 2,3-diaminonaphthalene; cytokine levels in the medium and activation of the signal pathway of TLR4 were examined by BioPlex cytokine and phosphoprotein panel assay systems. To evaluate the efficacy and selectivity of TAK-242 *in vivo*, cytokine levels in sera of mice injected intraperitoneally with LPS, lipoteichoic acid (LTA), or peptidoglycan (PGN) (10 mg/kg each) were measured by ELISA. TAK-242 was administered intravenously 1 hour before the challenge.
Results TAK-242 almost completely inhibited production of NO and cytokines (e.g. TNF-α, IL-1α, and IL-6) in LPS-stimulated RAW264.7 cells; the IC_{50} for LPS-induced NO production was 7.0 nmol/l. The LPS-induced activation of IkB kinase (IKK), p38, extracellular signal-regulated kinase (ERK), and c-Jun N-terminal kinase (JNK) pathways were also markedly inhibited by TAK-242, but it showed little effect on NO production induced by Pam3CSK4 (TLR1/2), PGN (TLR6/2), double-strand RNA (TLR3), or CpG oligonucleotide (TLR9). The NF-κB reporter gene assay showed that LPS-induced TLR4 activation was inhibited by TAK-242 in 293 cells transiently expressing TLR4 and the TLR4 co-receptors MD2 and CD14. TAK-242 also inhibited LPS-independent NF-κB activation resulting from overexpression of TLR4, but showed little effect on NF-κB activation by other TLRs (TLR1/2, TLR6/2, TLR3, TLR5, TLR7 and TLR9). TLR4 selectivity was also observed *in vivo*. Intravenous administration of TAK-242 to mice at a dose of 1 mg/kg inhibited the increase in serum IL-6 levels induced by TLR4 ligands LPS or LTA, but not by the TLR6/2 ligand PGN even at a dose of 10 mg/kg.
Conclusion TAK-242 is a potent and selective inhibitor of TLR4 signaling *in vitro* and *in vivo*, and therefore represents a novel therapeutic approach to the treatment of sepsis.

P155

Tifacogin increases bacterial clearance from blood

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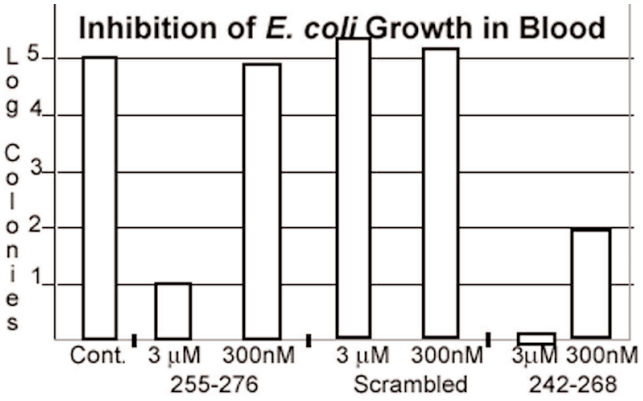
Multiple animal studies show that tifacogin (rTFPI; Chiron Corp.) improves survival when administered after lethal challenge with bacteria. Since some anticoagulant agents fail to rescue challenged animals, this effect of tifacogin may be due to mechanisms beyond anticoagulant activity. Other data relevant to tifacogin action include: IL-6 levels decrease in tifacogin-treated animals, infused tifacogin circulates as fragments, domains essential for anticoagulation are confined to TFPI's N-terminus, the C-terminus of tifacogin binds to LPS and, in a preliminary experiment, we found that a tifacogin peptide (amino acids 255–276) inhibited LPS-induced IL-6 and TNF-α production. We hypothesize that tifacogin's C-terminus acts on the innate immune system to promote bacterial clearance. To test this we mixed C-terminal tifacogin peptides with whole blood inoculated with opsonization-resistant bacteria (*Escherichia coli* 018:K1:H7 or a clinical isolate of coagulase-negative Staphylococci ATCC 700583), and then assessed bacteria growth. Controls were: a scrambled peptide from tifacogin's C-terminus or cultures without fragments. Both controls supported vigorous bacterial growth. Peptide 255-276 almost eradicated *E. coli* at 3 μM but not at 300 nM. Peptide 242–268 eliminated most bacteria at 3 μM and 300 nM, and in separate experiments inhibited growth by 90% at 10–30 nM. This region of tifacogin is also associated with heparin binding. Not surprisingly, 3 U/ml heparin completely antagonized peptide 242–268's activity. Unlike the bactericidal peptide LL37, peptide 242–268 was unable to clear bacteria in the absence of whole blood. This suggests that tifacogin interacts with a blood component, such as cellular mediators of immunity. Similar results were obtained with Staphylococci. The finding that tifacogin has bacterial clearance activity in addition to its anticoagulant activity is additional support for the rationale underlying Chiron's ongoing phase III study of tifacogin in patients with severe community-acquired pneumonia.

Figure 1 (abstract P155)



P156

Desialylated endothelial cells membrane enhance its fibrinolytic potential

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Background Endothelial cell dysfunction may be implicated in the development of multiple organ failure (MOF) by a number of mechanisms. Among these, altered plasma fibrinolysis promotes fibrin deposition, which may create microvascular alterations.

Previously, we observed that critically ill patients were characterized by a more marked red blood cell membrane and transferrin desialylation (sialic acid removed) [1,2] in septic patients. Sialic acid (SA), due to its negative charge, is involved in diverse cell–cell, cell–molecule and molecule–molecule interactions. We aimed to test the effect of endothelial cell membrane desialylation on the complete fibrinolysis process (coagulation and fibrinolysis) at the surface of endothelial cells *in vitro*.

Methods The endothelial cell line Ea.hy926 was used. The cells were inoculated on polyethylene terephtalate (PET) microporous membrane, in glass circular microcuvettes (51 mm^2) and grown for 6 days until confluence in DMEM with 10% FBS. The cell were incubated for 20 min in medium containing 0.5 U, 1 U and 2 U neuraminidase. To study the fibrinolysis process, a euglobulin fraction (a plasma fraction) was placed on the cell surface, and the clotting was induced by thrombin addition. The lysis time was measured in a newly designed apparatus and expressed in minutes [3].

Results The results are expressed as the ratio of the lysis time of treated cells to control cells. Neuraminidase treatment (1 U and 2 U) induced a 0.79-fold and 0.83-fold decrease in lysis time (ANOVA; $n = 6$: $P < 0.001$). This indicates an increase of fibrinolytic activity.

Conclusions In this work, we show the importance of SA in fibrinolytic activity of endothelial cell membranes. This mechanism could protect the endothelium from the fibrin deposition. The fact that desialylation occurs in the bloodstream from septic patients could also impair the endothelium function. Studies are needed to determine the possible desialylation of endothelial cells in sepsis and the implications of this mechanism in the physiopathology of sepsis.

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P157

Altered coagulation in systemic inflammatory response syndrome: role of protein C in diagnosis and prognosis

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Background Evidence has accumulated to suggest that more complex mechanisms might be involved in the relationship between inflammation and coagulation.

Objective In this study we aimed to use some coagulation markers, especially activated protein C (APC), in the diagnosis and prognosis of patients with systemic inflammatory response syndrome (SIRs), whether infectious or non-infectious.

Methods We enrolled 20 patients who had been hospitalized for SIRs as well as 20 age-matched and sex-matched subjects who served as the control group. All patients and control groups were subjected to full clinical evaluation with application of APACHE II scoring, routine laboratory investigations as well as specific investigations, namely; plasma levels of protein C, D-dimer (DD), antithrombin III (ATIII), and thrombin–antithrombin complex (TAT) upon admission, 48 and 96 hours later and on discharge in survivors.

Results The study showed that APC levels were significantly lower in patients with SIRS compared with control subjects (38.6 ± 23% vs 87.8 ± 6.1% $P < 0.0001$) respectively. When we compared levels in survivors and nonsurvivors, the former showed a persistent rise of the level to normal values in contrast to the latter, in which the levels were persistently low (34.8 ± 26% vs 40.6 ± 22% on admission and 82 ± 13% vs 41 ± 21%, $P < 0.01$ after 144 hours), respectively. Patients with septic shock also showed significantly lower levels of APC compared with those without shock (28.8 ± 12% vs 56.8 ± 28% $P < 0.007$ on admission and 41.7 ± 21.8% vs 82 ± 13% after 144 hours, $P < 0.001$), respectively. APC levels also were lower in patients with multiorgan failure syndrome (MODS) as compared with those without MODS (40.8 ± 27.8% vs 116 ± 29%, $P < 0.01$), respectively, with a statistically insignificant lower level in patients with APACHE score >20 as compared with those with APACHE score <20 (35.2 ± 22% vs 45 ± 24%, P = NS). The other coagulopathy markers of sepsis, DD, ATIII, TAT complex, did not show any significant difference between survivors and nonsurvivors (2 ± 3.6 ng/ml vs 4.9 ± 8 ng/ml for DD, 40.75 ± 17.6% vs 40 ± 15.7% for AT III and 24.7 ± 25 μg/ml vs 22 ± 19 μg/ml for TAT, P = NS), respectively.

Conclusion The protein C level is a useful biological marker in patients with SIRS for both diagnostic and prognostic aspects regarding MODS, septic shock and mortality, and also it is superior to other coagulopathy markers for determining the ultimate clinical outcome. In the view of our study results, we recommend monitoring APC levels in patients with SIRS as early as possible to screen those with sepsis syndrome to target aggressive therapy for them

P158

Frequency of early coagulopathy in multiple injury: an analysis of 8724 patients from the German Trauma Registry

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Introduction There is increasing evidence for acute traumatic coagulopathy occurring prior to emergency room (ER) admission but detailed information is still insufficient.

Objective To evaluate the frequency of traumatic coagulopathy on ER admission in patients with multiple injury.

Methods Retrospective analysis using the German Trauma Registry database including 17,200 multiple injured patients to determine to what extent clinically relevant coagulopathy has already been established upon ER admission, and whether its presence was associated with impaired outcome and mortality.

Results A total of 8724 patients with complete data sets were screened. Coagulopathy upon ER admission was present in 2989 (34.2%) of all patients. Males were more affected than females (72.5% vs 27.5%) and in 96% the trauma mechanism was blunt. The mean ISS score in the coagulopathy group was 30 ± 15, while trauma patients without coagulopathy upon ER admission generally presented with lower ISS scores (mean ISS 21 ± 12; $P < 0.001$). Twenty-nine percent of patients with coagulopathy developed multiorgan failure ($P < 0.001$). Early inhospital mortality (<24 hours) was 13% in patients with coagulopathy ($P < 0.001$) and overall inhospital mortality totalled 28% ($P < 0.001$).

Conclusion There is a high frequency of established coagulopathy in multiply injury upon ER admission. The presence of early traumatic coagulopathy was associated with injury severity and impaired outcome.

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P159

Antithrombin reduces ischemia/reperfusion-induced liver injury in mice by enhancing the activation of sensory neurons through protein kinase A activation

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We recently demonstrated that antithrombin (AT) reduces ischemia/reperfusion (I/R)-induced liver injury in rats by increasing hepatic tissue levels of calcitonin gene-related peptide (CGRP), a neuropeptide released from the sensory nerve endings. In the present study, we examined the effect of AT on I/R-induced liver injury in wildtype mice ($CGRP^{+/+}$) and congenital α CGRP-deficient mice ($CGRP^{-/-}$). We further investigated whether AT affects CGRP release from dorsal root ganglion neurons (DRG) isolated from $CGRP^{+/+}$. Based on results obtained in the present study, we attempted to determine whether the anti-inflammatory activity of AT *in vivo* is dependent mainly on sensory neuron activation. AT enhanced I/R-induced increases in hepatic tissue levels of CGRP and 6-keto-$PGF_{1\alpha}$, a stable metabolite of PGI_2, in $CGRP^{+/+}$, while it did not enhance these increases in $CGRP^{-/-}$. AT inhibited reperfusion-induced increases in serum alanine aminotransferase levels by increasing hepatic tissue blood flow and by attenuating increases in hepatic levels of tumor necrosis factor and myeloperoxidase in $CGRP^{+/+}$, while it showed neither of these therapeutic effects in $CGRP^{-/-}$. AT increased CGRP release from cultured DRGs only in the presence of anandamide, and the AT-induced increase in CGRP release was not observed in the presence of KT5720, an inhibitor of protein kinase A (PKA). AT markedly increased intracellular levels of cAMP in the presence of anandamide. In conclusion, these results strongly suggest that AT might reduce I/R-induced liver injury by enhancing activation of the sensory neurons through activation of PKA in sensory neurons.

P160

Comparison of the effects of tranexamic acid, aprotinin and placebo on blood conservation, fibrinolysis and platelet function with extensive heart surgery

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Introduction CPB results in fibrinolysis as reflected by increased plasmin concentrations and fibrin degradation products, both of which have deleterious effects on platelet function. We designed a study to compare the effects of a high dose of aprotinin (A), tranexamic acid (TA) and no treatment (P) on blood loss, transfusion of blood products, fibrinolysis and platelet function during and after heart surgery.
Methods After IRB approval, 60 consecutive consenting patients undergoing combined aortic valve replacement surgery with CABG were studied. They were randomized to either: high-dose A (280 mg loading dose, 70 mg/hour infusion rate and 280 mg in the prime) ($n = 20$), TA (100 mg/kg loading dose, 1 mg/kg/hour infusion rate) ($n = 20$), or saline ($n = 20$). The effect of A and TA on some markers for the activation of thrombin formation and fibrinolysis was studied (D-dimer, plasminogen, α_2-anti-plasmin, antithrombin and glycocalicin, a fragment of the platelet-membrane GPIb). Sampling was at induction (t1), at the start and end of CPB (t2, t3), and at 1, 4 and 24 hours after CPB (t4, t5,t 6). ANOVA for repeated measurements was applied for statistical comparisons between groups. $P < 0.05$ was considered significant. Data are expressed as mean values ± SEM.
Results Study groups did not differ with regard to demographic data and type of operation. Blood loss and chest tube drainage was significantly less in the A and TA groups as compared with the P group at all time points and was accompanied with the use of less blood products, volume replacement and higher hemoglobin levels. The duration of the surgical post-CPB period was significantly shorter in the A and TA groups (55 ± 18, 71 ± 19 and 84 ± 26 min, respectively). There was no difference in platelet count between groups. There were no re-explorations for postoperative bleeding. Inhibition of fibrinolysis was significant with both antifibrinolytic drugs (D-dimers 578 ± 81, 550 ± 105 and 3603 ± 440 μg/ml at t4). During and after the operation, the D-dimers were much higher in the placebo group. α_2-antiplasmin levels were higher in the A group compared with the TA and P groups. This effect was present until 24 hours after CPB. TA had no effect on this parameter. Plasminogen levels were lower in the TA group at t4, t5 and t6. TA patients more often received additional boluses of heparin to maintain ACT >480 s during bypass (15/20 patients versus 9/20 and 8/20 patients in the A and P groups, respectively). aPTT values were significantly prolonged at the end of CPB in the A group. Antithrombin values were significantly higher in the A group at t3, t4 and t5. Glycocalicin values were slightly higher in the TA group during bypass.
Discussion TA can inhibit fibrinolytic activity by blocking plasmin(ogen) activity measured as the D-dimer level, but seems to have no influence on neutralization of plasmin by α_2-antiplasmin. Both A and TA effectively suppress the appearance of markers of fibrinolysis as compared with placebo. The results also suggest that the antifibrinolytic effects of TA and A can reduce blood loss in patients undergoing extensive CPB surgery.
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P161

Use of anti-Xa factor titration as efficacy marker of enoxaparin in critically ill patients

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Introduction Low molecular weight heparins (LMWH) are frequently used for thrombosis prophylaxis or anticoagulation treatment in critically ill patients without efficacy control in specific patient groups.
Objective To evaluate the efficacy of sodium enoxaparin in critically ill patients and the acute decompensation of baseline conditions.
Method We evaluated critically ill patients admitted to a cardiology critical care unit with indications of anticoagulation, either prophylactic or therapeutic. Patients with body weight >110 kg or serum creatinine ≥2.5mg/dl were excluded. Anthropometrics, clinical data and the prognostic index were recorded. Anti-Xa factor was titrated in three different moments: baseline (before enoxaparin administration), and T1 (first or second day) and T2

(fifth to seventh day) after use of enoxaparin, 40 mg/day for prophylaxis and 1 mg/kg every 12 hours for anticoagulation therapy. Lower limb sonography was performed to scan for deep vein thrombosis (DVT) in the prophylactic group of patients.

Results Thirty-two patients were included (16 patients in the prophylactic group and 16 patients in the therapeutic group). Mean age was 62 ± 16 years (from 20 to 92 years). The main diagnosis included cardiogenic shock (10 patients), decompensated cardiac failure (five patients), arrhythmia (six patients), pulmonary embolism (two patients), lung infection (three infections), prosthetic valve dysfunction (one patient) and others (five patients). The mean APACHE II score was 10.9 ± 5. The T1 mean anti-Xa factor titration for the prophylactic group was 0.35 ± 0.10 IU/ml and for the therapeutic group was 0.57 ± 0.10 IU/ml (Mann–Whitney test, $P < 0.001$). The T2 mean anti-Xa factor titration for the prophylactic group was 0.46 ± 0.11 IU/ml and for the therapeutic group was 0.69 ± 0.08 IU/ml (Mann–Whitney test, $P < 0.001$). One patient presented with DVT in spite of proper anti-Xa factor levels for prophylaxis.

Conclusions Sodium enoxaparin in the used schedules was effective. Anti-Xa factor titration is useful in monitoring critically ill patients, especially those with low cardiac output.

P162

Continuous administration of LMWH in critical patients: a contribution to the monitoring of hemocoagulation

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Objective To monitor hemocoagulation in patients with systemic inflammation while continually i.v. administering LMWH, plus dosage adjustment, while trying to reflect on coagulation changes, mainly regarding the values of anti-Xa and Ddim.

Background LMWH is used in the prophylaxis of as well as therapy of DVT, in the prevention of thrombus formation in extracorporal circulation through CRRT, in the therapy of unstable angina pectoris and non-Q myocardial infarction, and in the therapy of stroke. We have asked ourselves the question of whether the same administration routine could be applied in critically ill patients where we assume a pronounced prothrombotic state. Critically ill patients commonly demonstrate hyperfibrinogenemy, reactive thromobocytosis, and changes of the plasmatic coagulation system. Due to the favourable therapeutic potential of LMWH, we decided on a continual i.v. administration of enoxaparin as well as hemocoagulation monitoring.

Materials and methods The study included patients with an expected length of stay >48 hours and with no contraindication to anticoagulation therapy. We monitored the coagulation parameters INR, aPTT, TT, FBG, AT, Ddim, PLT count, leukocyte count, anti-Xa, vWfF level, PLT activation, and the dosage of LMWH within the past 24 hours. The patients were divided into two groups: with SOFA <5 and with SOFA≥5. The initial daily dose of LMWH was administered based on the patient's weight. Dose modifications were carried out so that the anti-Xa level would be between 0.2 and 0.5 IU/ml and/or the Ddim count would demonstrate a steady (in the standard levels) or falling (in elevated levels) tendency. Flow cytometry was used for quantification of blood cells carrying the CD61 antigen (i.e. platelet identification), out of which those that carried CD62 antigen on the surface were selected (i.e. activated platelets).

Results Preliminary evaluation includes 10 patients, 109 sets of measuring. The average dose of LMWH was 490 IU anti-Xa/24 hours (8.05 IU anti-Xa/kg/24 hours, respectively). The average value of anti-Xa was 0.21 IU/ml. The average value of activated PLT was 53.16%, within the 16–97% range. The increased activity of the coagulation system as well as the endothelium (the level of vWF reached 482% on average, within the 185–825% range) correlated ($P = 0.001$) with the intensity of systemic inflammation (CRP, leucocytes), especially in patients with SOFA score ≥5.

Conclusion Monitoring vWF levels and the number of activated platelets indicates a prothrombotic potential of the hemocoagulation system in critically ill patients. The established methods of administering LMWH quite probably do not correspond with the prothrombotic activation of the coagulation system in these patients. As it turns out, it will be necessary to carry out much more research.

P163

Solvent-detergent plasma: use in neonatal patients, in adult and paediatric patients with liver disease and in obstetric and gynaecological emergencies

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We assessed the efficacy and tolerance of solvent-detergent (SD) plasma in neonates, in obstetric and gynaecological patients, and in patients with liver disease in three large hospitals in Dublin over an 18-month period.

Forty-one neonates received 67 transfusions of SD plasma at a mean dose ± standard deviation of 18.4 ± 3.2 ml/kg. Thirty-eight obstetric and gynaecological patients received 57 SD plasma transfusions at a mean dose of 15.3 ± 7.7 ml/kg. Thirty-six women (94.7%) had haemorrhage with mean blood loss per patient of 3345.8 ± 2738.1 ml. Fifteen children with liver disease received 33 SD plasma transfusions at a mean volume of 38.0 ± 41.5 ml/kg body weight. Seventeen adult patients with severe end-stage liver disease were transfused with SD plasma either following liver transplantation or prior to other invasive procedures, at a mean dose of 10.2 ± 3.4 ml/kg.

There were statistically significant decreases in APTT and PT in neonates, in obstetric and gynaecological patients, and in patients with liver disease. Pre-transfusion and post-transfusion APTT was measured in 40/67 neonatal transfusion episodes, PT in 43/67, fibrinogen in 39/67, and platelets in 49/67. After plasma infusion the mean APTT improved from 68.9 ± 37.4 s to 44.0 ± 15.6 s ($t = 4.79$; $P < 0.001$); PT from 28.7 ± 20.3 s to 20.7 ± 14.2 s ($t = 2.64$; $P < 0.02$); fibrinogen from 1.94 ± 1.1 g/l to 2.51 ± 1.14 g/l ($t = 3.41$; $P < 0.002$). Pre-transfusion and post-transfusion APTT was measured in 41/57 transfusions in the obstetric/gynaecology group; PT and fibrinogen in 42/57. The mean APTT improved from 50.1 ± 18.4 s to 32.7 ± 6.9 s ($t = 6.40$; $P < 0.001$); PT from 21.0 ± 5.2 s to 15.6 ± 1.9 s ($t = 7.71$; $P < 0.001$); fibrinogen from 1.55 ± 0.75 g/l to 2.74 ± 0.86 g/l ($t = 9.15$; $P < 0.001$). Pre-transfusion and post-transfusion APTT, PT and platelets were measured in 22/33 transfusion episodes in the group of children with liver disease, and fibrinogen in 13/33. The APTT decreased from 61.5 ± 33.0 s to 47.8 ± 12.5 s ($t = 5.15$, $P < 0.001$) and the PT from 24.4 ± 10.0 s to 19.9 ± 4.2 s ($t = 5.05$, $P < 0.001$). Fibrinogen improved from 1.46 ± 0.75 g/l to 1.66 ± 0.59 g/l ($t = 1.25$; $P > 0.05$). In the group of adult patients with severe end-stage liver disease, precoagulation and postcoagulation test results were available for 14 of 17 transfusion episodes. There was a statistically significant improvement in the PT from 23.2 ± 4.9 s

to 18.6 ± 2.9 s (t = 4.46, P < 0.001) and in the APTT from 45.1 ± 8.9 s to 36.4 ± 7.1 s (t = 3.95, P < 0.002).
No adverse reactions were observed for SD plasma infusion.
Use of SD plasma in critically ill neonates, in women with obstetric and gynaecological emergencies, and in patients with liver disease appears safe, and improves laboratory indices of coagulopathy.

P164

Two years experience with low-dose recombined activated factor VII treatment of non-haemophilic patients

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Background Recombined activated factor VII (rFVIIa) (NovoSeven®; Novo Nordrisk) is a relatively new drug, which gives new opportunity in the treatment of patients with severe bleeding. The severe bleeding in haemophilic patients was the first indication for which rFVIIa was registered, but nowadays this drug is becoming more popular also in treatment of severe bleedings of other origins.
Objective The aim of this research was to evaluate the effectiveness of rFVIIa in treatment of severely bleeding patients in the ICU.
Methods Retrospective analysis of 24 patient who received rFVIIa in our ICU between January 2001 and October 2005. We used the questionnaires of Novo Nordrisk to assess the indications and effectiveness of treatment. We compared the amount of blood lost within 12 hours before and within 12 hours after giving rFVIIa, and the dynamics of bleeding (assessed in ml/hours) before and after treatment.
Results In the aforementioned period of time rFVIIa was used 28 times in our ICU in treatment of 24 patients (four patients received two doses) with severe bleeding, none of whom was suffering haemophilia. The average patient age was 49.5 years (range 24–77), and average body mass was 70.4 kg (range 55–120). The following diseases were diagnosed: cancer – six patients (liver cancer, two patients; ovarian cancer, two patients; prostate, one patient; kidney, one patient), post-abdominal surgery bleeding – four patients, ruptured abdominal aorta aneurysms – three patients, sepsis – three patients, acute pancreatitis – two patients, post-kidney transplant complications – two patients, postpartum bleeding – two patients, GI bleeding – two patients. One of the mentioned patients with sepsis was a lady treated with drotreocogin (Xigris, Lilly) infusion. The average dose of rFVIIa was 22.53 μg/kg (range 10–56). The average blood loss within 12 hours before treatment was 2728 ml and the average blood loss within 12 hours after treatment was 184 ml. The average dynamics of bleeding before treatment was 1163 ml/hours versus 184 ml/hours after treatment. The differences between the volume of blood lost and dynamics of bleeding after and before treatment were statistically significant.
Conclusion Our 4-year experience with rFVIIa makes us convinced that this drug is very useful in treatment of severely bleeding patients. It seems reasonable to start treatment with relatively low doses, which are very often efficient enough to stop bleeding, and the costs of such therapy are not so high as with higher doses.

P165

Efficacy of recombinant activated factor VII in the management of severe hemorrhage following cardiac surgery

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Introduction Severe bleeding after cardiac surgery is often difficult to manage. The efficacy of traditional drugs vary, which is why it is necessary to use newer agents for beneficial control and prevention of massive bleeding. The aim of this study is clinical evaluation of the efficacy of recombinant activated factor VII (rFVIIa) in the treatment of bleeding during and after cardiac surgery by stimulation of clot formation at the site of injury.
Patients and methods rFVIIa (NovoSeven®; Novo Nordisk, Bagsvaerd, Denmark) was used in 37 adult patients aged between 49 and 68 years who underwent open heart surgery (10 patients coronary surgery, five patients valvular surgery, six patients surgery of congenital heart defects, three patients surgery of dilated cardiomyopathy) or surgery for aortic aneurisms (13 patients) in 2002–2005. All patients had normal coagulation parameters before surgery. In these patients, bleeding (10–20 ml/min) has developed intraoperatively or postoperatively. In 21 patients the bleeding started after surgery intraoperatively, and in 16 patients severe hemorrhage developed in the postoperative period. Treatment of bleeding included infusions of fresh frozen plasma, platelet concentrate, aprotinin and μ-aminocaproic acid. Two patients underwent surgical re-exploration for bleeding. However pharmacological and surgical management failed to stop the hemorrhage. Prior to administration of rFVIIa, blood loss reached 2.5–3 l in some patients. rFVIIa was administered in doses of 60–90 μg/kg body weight. We used Student's t test for statistical analysis the laboratory data prior to and after rFVIIa.
Results After administration of the first median dose (75.3 ± 10.1 μg) rFVIIa bleeding stopped in 27 patients (74%), and markedly decreased in four patients during 1 hour. Six patients who did not benefit from initial rFVIIa administration received additional drug in doses of 70–90 μg/kg, with good results in four patients. (Five patients received one additional dose, one patient received four doses.)

Table 1 (abstract P165)

Variable	Before rFVIIa	30 min later	3 hours later
Prothrombin time (s)	38.4 ± 3.7	18.0 ± 1.8*	19.4 ± 1.7*
Thrombin time (s)	12.9 ± 1.3	14.4 ± 1.9	11.0 ± 0.5
APTT (s)	51.3 ± 2.9	44.9 ± 3.9	43.7 ± 3.1
ACT (s)	105.4 ± 4.2	95.9 ± 4.9	97.9 ± 5.8
Platelet count	126.9 ± 15.1	139.2 ± 19.1	142.4 ± 13.3
Platelet agg (%)	27.6 ± 5.4	38.8 ± 5.4	53.3 ± 6.5*
Clot time (min)	11.8 ± 0.9	9.3 ± 1.1	10.8 ± 1.6

*P < 0.05 vs before rFVIIa.

There was considerable reduction in the need for replacement therapy after rFVIIa administration. Analysis of laboratory data (Table 1) revealed a significant decrease of prothrombin time after 30 min and improvement of platelet function after 3 hours of rFVIIa administration. There were no significant differences in the dynamics of other parameters of hemostasis. Adverse events have not been seen after drug injection.

Conclusion These results suggest that rFVIIa has high efficacy in treatment of massive hemorrhage and reducing the need for hemotransfusions when other hemostatic therapy has failed.

P166

Experience of NovoSeven administration in management of coagulopathic bleedings after surgical interventions with extracorporeal circulation

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Objective To analyze the clinical experience of administration of recombinant activated factor VII (rFVIIa) (NovoSeven) in post-surgical bleedings refractory to the traditional haemostatic therapy in patients who underwent surgical interventions with extra-corporeal circulation (EC).

Materials and methods Assessment of 17 patients (age 31–53, 44.3 ± 2.9 years) who underwent surgical interventions on the heart with EC (prosthetic repair of one or two heart valves, coronary artery bypass graft, prosthetic repair of the ascending aorta with a valvular conduit, etc.) was performed. Duration of EC was 172 ± 34 min. The aorta was occluded for 107 ± 19 min. Indications for administration of the rFVIIa were considered when there was a postsurgical bleeding (exceeding 750 ml/hour) in the absence of surgical sources of the bleeding and lack of efficacy of the conventional hemostatic procedures: adequate neutralization of heparin with protamine sulfate, high doses of aprotinin, aminocaproic acid, fresh frozen plasma transfusion. NovoSeven was administered 44–158 (105 ± 24) min after neutralization of heparin with protamine sulfate. The dosage of the agent was 1.8 ± 0.3 mg, or 22 ± 3 μg/kg. The data were statistically processed, with evaluation of the significance of the differences using Student's *t* test.

Results For 2 hours immediately after the administration of rFVIIa, the rate of the bleeding decreased from 1270 ± 240 to 182 ± 26 ml/hour. During the following hours of observation it was no different from the values acceptable for cardiosurgical interventions (125 ± 17–35 ± 7 ml/hour) (Table 1).

Conclusion The depletion of factor VII plasma activity that occurs during cardiosurgical interventions may cause coagulopathic bleeding refractory to the standard therapy. There are several possible mechanisms for the impairment of the factor VII activity during the EC surgeries: hemodilution; hypothermia; contact activation of the components of the haemostasis system due to interaction of the blood with foreign surface of the EC-device contour; consumption of the factor and depletion of its plasma concentration due to ingress of the tissue factors into the systemic circulation after aspiration of the wound contents into the cardiotomic reservoir of the EC device. NovoSeven produces a potent haemostatic effect in bleeding events refractory to the conventional therapy complicating the cardiosurgical interventions and substantially decreases the demand for blood transfusion.

Table 1 (abstract P166)

	Before NovoSeven	24 hours after
Bloodloss rate (ml/hour)	1273 ± 246	175 ± 58*
RBC transfusion (ml)	564 ± 57	260 ± 12*
Plasma transfusion (ml)	1205 ± 199	626 ± 110*
Autotransfusion (ml)	740 ± 142	243 ± 67*

*Statistically significant.

P167

Activated recombinant factor VII in management of bleeding in patients with thrombocytopenia

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The presented study evaluates the feasibility of recombinant activated factor VII (rFVIIa) (NovoSeven) to control bleeding in 28 patients with thrombocytopenia of different etiology (idiopathic thrombocytopenic purpura – 4/28, acute myelocytic leukemia – 10/28, acute lymphoblastic leukemia – 2/28, non-Hodgkin's lymphoma – 8/28, aplastic anemia – 2/28, chronic hepatitis C – 2/28) complicated with hemorrhagic syndrome. The platelet count in the selected group of patients varied from 3×10^9/l to 80×10^9/l (mean 31×10^9/l). Some of the patients suffered from coagulopathy (associated with hepatitis – five cases, associated with sepsis – 10 cases, and associated with bleeding – six cases). All patients experienced severe bleeds: postoperative – eight cases, CNS – seven cases, epistaxis – four cases, gastrointestinal – three cases, pulmonary hemorrhage – one case, after central line placement or other invasive manipulation – five cases. The majority received supportive treatment with FFP and/or PLT and RBC transfusions, which was unsuccessful. A mean dose of 86 mg/kg rFVIIa (range 41–114 mg/kg) was administered as an intravenous bolus injection. Fifteen patients received the treatment once, 11 patients were given a second dose of rFVIIa, and two patients received three doses.

Laboratory haemostatic tests revealed a reduction of the PT of 1.5–2 times compared with the levels before administration of rFVIIa (Table 1). Thromboelastography (TEG) was performed in 18 patients. Before administration of rFVIIa the reaction time (R) was within the normal range, but the kinetic time (K) was prolonged and the maximum amplitude (MA) decreased, both results indicating a low platelet count. After administration of rFVIIa, eight patients appeared to have improved TEG parameters, in seven cases these parameters worsened, and in three cases the TEG parameters

Table 1 (abstract P167)

Normal	Before rFVIIa	15 min after rVIIa	*P* value
APTT (30 s)	33 ± 11.9	29 ± 6.99	0.057
PT (14 s)	18.9 ± 2.2	9.5 ± 1.6	0.000
TT (12 s)	16 ± 3.3	15 ± 3.2	0.047
Fibrinogen (2–4 g/l)	2.9 ± 1.6	3.0 ± 1.6	0.411

Table 2 (abstract P167)

Normal	Before rFVIIa	15 min after rVIIa	*P* value
R (9–27 min)	14.4 ± 11.3	13.5 ± 9.2	0.771
K (2–9 min)	16.2 ± 13.9	13.7 ± 12.9	0.491
MA (44–64 mm)	28.8 ± 13.3	29.0 ± 15.0	0.875

remained unchanged (Table 2). In 16 cases bleeding stopped 10–30 min following the injection, and decreased dramatically in six cases. Six patients did not achieve effective hemostasis after administration of rFVIIa. Bleeding reoccurred in seven cases after 6 hours and more following infusion of rFVIIa. In 25 cases no adverse events were reported; two patients developed high temperature (38.7°C and 39.0°C) within 15 min after the injection of rFVIIa. The described observations suggest efficiency of rFVIIa in controlling the postoperative and spontaneous bleeding in patients with various types of thrombocytopenia. Nevertheless, the laboratory tests do not always correlate with clinical efficiency of this treatment.

P168

Use of recombinant activated factor VII after paediatric cardiac surgery

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Objective To evaluate the opportunities of recombinant activated factor VII (rFVIIa) in pediatric patients with bleeding after cardiac surgery.
Methods Since January 2003, 90 pediatric patients received rFVIIa for bleeding after cardiac surgery. Indications for rFVIIa were the following: prevention of bleeding after major surgery in newborns (arterial switch operation, radical correction of truncus arteriosus, Norwood's procedure) or bleeding rate 5 ml/kg/hour and more in older children – 75 patients (group A); severe tracheal bleeding in sepsis and multiple organ failure – six patients (group B); uncontrolled bleeding during total cardiopulmonary bypass with ECMO – nine patients (group C). Children's age was 2 days–18 years, body weight was 1.7–89 kg.
In group A the mean cardiopulmonary bypass time was 223 ± 29 min (108–423 min). Before rFVIIa was used the thrombocyte quantity increased up to 60 × 10^9/l, the ACT time was less 180 s and the body temperature was more than 35°C. FVIIa (120 μg/kg) was used 10–45 min after bypass. If needed, a repeated dose of 120 μg/kg was given after 1–1.5 hours (36 patients).
In group B severe tracheal bleeding developed in ventilated patients despite thrombocyte transfusions and 5000 UE/kg/hour aprotinin. rFVIIa was used in all patients twice (120 μg/kg).
In group C severe bleeding (8–42 ml/kg/hour) occurred during cardiopulmonary bypass with ECMO. Before rFVIIa administration the ACT was maintained between 180 and 200 s, the PLT quantity was not below 50 × 10^9/l and the aprotinin infusion rate was 10,000 UE/kg/hour. In all cases rFVIIa was used twice with a dose of 120 μg/kg.
Results In group A bleeding stoppage (<1 ml/kg/hour) was reached in 49 patients (65.3%) 40–75 min after FVIIa administration; in 17 cases (22.7%) the bleeding rate decreased to 1–4 ml/kg/hour (incomplete effectiveness) and stopped after 3–6 hours. In nine patents (12%) resternotomy was fulfilled because of ineffectiveness of rFVIIa therapy (bleeding rate 5 ml/kg/hour and more). Effectiveness of rFVIIa was higher in early administration of the drug (10–15 min after bypass). Following the hematology test, changes occurred: the APTT, INR and the SFMC concentration were decreased and the plasma FVIIa concentration was increased.
In group B life-threatening tracheal bleeding in mechanically ventilated septic patients with MOF was stopped in four of six cases (66.6%) during 30–75 min after rFVIIa administration. Both nonresponding patients were in severe uncorrectable respiratory/metabolic acidosis before and during FVIIa infusion (pH 7.14/7.11, BE −12/−16 and pCO_2 76/69 mmHg accordingly).
In group C the bleeding rate was decreased from 29 ± 12 ml/kg/hour to 4 ± 2.9 ml/kg/hour 2–5 hours after the second FVIIa infusion in six patients (66%). No cases of extracorporeal circuit/oxygenator thrombosis were occurred.
No significant adverse effects occurred in all groups.
Conclusion rFVIIa effectively prevents and treats bleeding in pediatric cardiac surgery, including life-threatening tracheal bleeding in septic patients and large blood loss during prolonged cardiopulmonary bypass with ECMO. Further research is required to determine the indications and dose regimens in these groups of patients.

P169

Cost-effectiveness analysis of recombinant activated factor VII as adjunctive therapy for bleeding control in severely injured trauma patients in Germany

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Introduction Uncontrollable bleeding is a leading cause of death in trauma patients and a major cause of preventable morbidity and mortality. Recombinant activated factor VII (rFVIIa) has been shown to decrease the need for red blood cell transfusion among severely injured blunt trauma patients. A significant difference in the incidence of acute respiratory distress syndrome was also observed relative to standard care together with a nonsignificant difference in mortality. While safety and efficacy of rFVIIa in trauma patients has been demonstrated, little is known about its cost-effectiveness.
Method The cost-effectiveness of rFVIIa relative to standard care was measured using patient-level data on survival and treatment patterns collected prospectively in a multicenter, international, trial, and outcomes data in the German Trauma Registry on patients matching key inclusion/exclusion criteria in the trial. Differences in survival observed at the end of trial and differences in healthcare cost were projected to a lifetime for each patient to produce an estimate of costs per life-year gained with rFVIIa. Analyses were conducted from the German third-party payer perspective, limited to healthcare costs and using a discount rate of 5%. The assessment considered adults with severe blunt trauma injury who had received 8 U RBC prior to random assignment to either three intravenous injections of rFVIIa (200, 100, and 100 μg/kg) or three placebo injections.
Results Projected to a lifetime, the mean cost per treated patient was €86,085 for rFVIIa and €65,875 for placebo, while life-years gained (LYG) were 13.17 and 12.22, respectively. The incremental cost of €21,210 and effect of 0.944 resulted in incremental costs per LYG of €21,410 for rFVIIa. Adjusting for quality of life (QoL) in residual life-years produced incremental quality-adjusted survival of 0.763 years and incremental costs per QALY gained of €26,502. Using a conservative threshold of €30,000 for cost-effective healthcare technologies, results appeared most sensitive to assumptions about residual life expectancy and QoL.
Conclusion rFVIIa is a cost-effective adjunctive therapy for control of bleeding in patients with severe blunt trauma injuries when compared with standard care in Germany.

P170

Effectiveness and safety of recombinant activated factor

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Introduction Patients with severe and persistent bleeding have high mortality. rFVIIa has been approved for the prophylaxis and treatment of the following types of hemorrhages: in patients with inhibitors of the coagulation, with congenital deficiency of FVII and with Glanzmann thrombasthenia. The aim of the study was to evaluate the role of rFVIIa on blood transfusion requirements and its safety. Recently there have been reports of this use in refractory severe hemorrhage (liver transplantation, trauma patients, upper GI bleeding, intracerebral hemorrhage).
Materials and methods Retrospective analyses of all the patients admitted to our hospital who received rFVIIa as treatment for severe bleeding and failure to standard therapy for massive hemorrhage, between January 2000 and November 2005, were made in this study. We obtained for all our patients: demographic data, cause of admission, cause of the hemorrhagic episode and the total doses of rVIIa. We analyzed the total number of blood products administered before and after rVIIa, the coagulation parameters, the adverse effects of rFVIIa and the mortality. We performed statistical analysis using the Wilcoxon test and considered statistical significance for $P < 0.05$.
Results A total of 30 patients fulfilling the definition of massive hemorrhage were included. Their mean age was 54.4 years. In two of 30 patients rFVIIa was used as preoperative prophylaxis in high-risk surgeries. rFVIIa was administered using the standard dosage: as an initial bolus of 60–90 μg/kg, and with repeated doses as needed for clinical control of hemorrhage (between one and three doses with 2–6 hour intervals). We were able to control the hemorrhage in 68.4% of our patients. Also the total number of packed red blood cell units decreased from 11 to 3 U per patient ($P < 0.014$). Moreover the administration of fresh frozen plasma decreased from an average of 7 to 1 U ($P < 0.044$). The total number of platelets units decreased but was not statistically significant ($P = 0.07$). The transfusion of rFVIIa also caused an improvement of the coagulation parameters, especially the prothrombin time ($P < 0.004$). We observed adverse effects in three patients (one ischemic stroke and two cardiac tamponades), although a direct association to the use of rFVIIa could not be made. Mortality at 30 days was 58%.
Conclusion The administration of rFVIIa in our patients with massive hemorrhage appears to decrease the transfusional requirements, although this is only a retrospective descriptive analysis. In our experience rFVIIa seems to be a fairly safe drug, although this is not a safety study.

P171

Does recombinant factor VIIa change the inflammatory response to trauma? Preliminary results of inflammatory biomarkers in critically ill trauma patients

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Introduction Recent advances have demonstrated a close association between coagulation and inflammation. The systemic inflammatory response syndrome (SIRS) is a common host response following trauma. Recombinant activated factor VII (rFVIIa) has been used to treat post-traumatic coagulopathy, but its impact on inflammation is unclear. The purpose of this study was to determine whether rFVIIa influences post-traumatic host inflammation.
Hypothesis rFVIIa will increase the inflammatory response following trauma.
Methods As part of an ongoing study to characterize the inflammatory response among critically ill trauma patients with SIRS, we identified four patients who received rFVIIa for treatment of traumatic coagulopathy. These patients were matched (TRISS, mechanism of injury, and age) with four SIRS patients who did not receive rFVIIa. Whole blood from both groups was analyzed for 78 inflammatory biomarkers by immunoassay. The average time from rFVIIa dose to sample was 36 hours. Data are expressed as the mean ± SD. Student's *t* test was used to determine significance between means of each group.
Results Both groups were similarly matched for mechanism (blunt: 75% each group), TRISS (0.76 rFVIIa vs 0.74 control), and age (66 years rFVIIa vs 63 years control). rFVIIa patients had significantly lower levels of factor VII detected by immunoassay compared with control (127.8 ± 9 vs 283.5 ± 77.2 ng/ml, $P < 0.04$). The proinflammatory proteins that increased in the rFVIIa group are presented in Table 1. No other proinflammatory or any anti-inflammatory markers demonstrated significant differences between groups.

Table 1 (abstract P171)

Biomarker	Group 1 (rFVIIa)	Group 2 (control)	*P* value
TNF-α (pg/ml)	12 ± 4.2	5.6 ± 2.7	0.04
IL-8 (pg/ml)	48.63 ± 12.5	20.25 ± 6.99	0.01
MIP-1β (pg/ml)	149.5 ± 19.8	97.0 ± 33.0	0.03
MDC (pg/ml)	339 ± 78	221 ± 32	0.03
MMP-2 (ng/ml)	639 ± 181	328 ± 174	0.05
CA-125 (U/ml)	14.21 ± 6.68	2.65 ± 1.22	0.01

Conclusions Based on our preliminary results, rFVIIa induces a mild proinflammatory (TNF-α) state associated with neutrophil chemoattractants (IL-8, MIP-1β) and extracellular matrix breakdown (MMP-2, MDC). Lower factor VII levels in the treatment group may be secondary to clotting factor consumption following rFVIIa administration.

P172

Assessment of intravascular retention of hydroxyethyl starch in mild hemorrhagic shock

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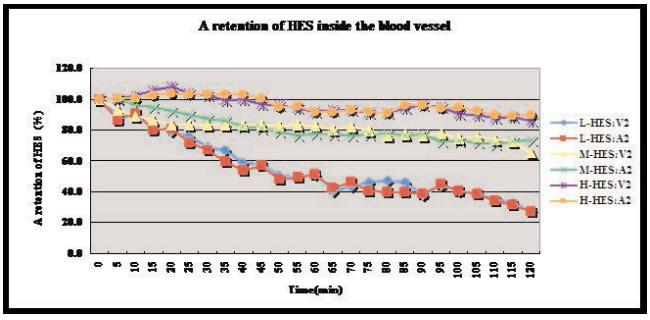
Objective To evaluate the retention of hydroxyethyl starch (HES) in the vessel at the microcirculation using intravital microscopy [1,2].
Methods Experiments were performed using a mild hemorrhagic (10% of total blood volume) shock model in rats. The blood vessels (A2 and V2) of the cremaster muscle were observed. One hour after hemorrhage was induced, FITC-labeled L-HES (MW 150,000–200,000) or M-HES (MW 175,000–225,000) or H-HES (MW 550,000–850,000) was administered within 15 min. The retention of HES was evaluated by the contrasting density of the brightness of fluorescence on the image stored on the PC.

Figure 1 (abstract P172)



Results A retention ratio of HES inside the blood vessel was different among groups. M-HES and H-HES retained in the vessels longer than L-HES, with no difference between M-HES and H-HES (Fig. 1).
Conclusion M-HES (MW 175,000–225,000) seems to have large molecules, which is enough to maintain the blood volume after hemorrhage.

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P173

Does volume substitution with HES 130/0.4 affect renal safety in abdominal aortic surgery?

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Abdominal aortic surgery patients are at risk for renal dysfunction, notably if preoperatively the renal function is impaired. This sensitive patient population was chosen to prove that the recent hydroxyethyl starch (HES) 130/0.4 has no adverse renal effects as asserted for less metabolisable HES preparations.
After IRB approval and signed informed consent, 65 adult patients scheduled for abdominal aortic surgery were randomly allocated to receive either 6% HES 1300.4 (Voluven, $n = 32$) or 3% gelatin solution (Plasmion, $n = 33$) for perioperative volume substitution. The daily dose limitation for HES was 50 ml/kg body weight Baseline renal function was impaired in all patients (creatinine clearance (CrCl) <80 ml/min). The primary renal safety parameter was the peak increase in serum creatinine through day 6 after surgery. Both groups were compared for non-inferiority of HES (predefined non-inferiority range HES < gelatin + 17.68 mol/l or 0.2 mg/dl). Other renal safety parameters were minimum postoperative CrCl, incidence of oliguria (urine output <500 ml/day), and adverse events (AEs) related to the renal system until hospital discharge.
Baseline characteristics, surgical procedures, and the mean total infused colloid volumes were similar between both groups. Postoperatively, the mean peak increase in creatinine was slightly higher in gelatin patients. Non-inferiority of HES was statistically proven by means of the appropriate nonparametric one-sided 95%

Table 1 (abstract P173)

	Peak increase in creatinine (µmol/l)	Range	Minimum postoperative CrCl (ml/min)	Range
HES	26.3 ± 55.3	−47.0 to 222.0	61.1 ± 34.2	6.5–153.9
Gelatin	36.5 ± 103.3	−22.0 to 561.0	53.5 ± 25.2	2.8–121.3

CI for the difference HES–gelatin (−∞, 11 µmol/l). The minimum postoperative CrCl was lower for gelatin (see Table 1, mean values ± SD). Oliguria occurred in a few patients only (three HES vs four gelatin patients). One patient of the gelatin group required dialysis treatment following a cascade of AEs related to surgical complications. Mortality in both groups was 6% (two deaths/group). No drug-related unfavourable effects on renal function were found for volume substitution with HES 130/0.4 compared with gelatin in patients with mild to severe renal insufficiency undergoing infrarenal abdominal aortic surgery.

P174

Impact of high-molecular hydroxyethyl starch solutions on plasma volume and haemodynamics in porcine faecal peritonitis

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Introduction Early fluid resuscitation is suggested to be beneficial sepsis therapy. Using a faecal peritonitis model we tested effects of two new synthetic high-molecular hydroxyethyl starches, 6%HES 700/0.42/2.5:1 (HES700/2.5:1) and 6%HES 700/0.42/6:1 (HES700/6:1), compared with 6%HES 130/0.42 (HES130) and ringer's solution (RS) on plasma volume (PV), heart rate (HR), mean arterial pressure (MAP) and mixed venous oxygen saturation (SvO_2).
Methods A prospective randomized, controlled animal laboratory study in a university animal laboratory. Twenty-five anaesthetized, ventilated pigs (28.4 ± 2.3 kg) received 1 g/kg/body weight faeces into the abdominal cavity to induce sepsis and were observed over 8 hours. Animals were randomized (five to each group) to volume replacement therapy with colloids or RS and were compared with a nonseptic control group receiving RS. The infusion rate was titrated to maintain a central venous pressure of 12 mmHg. PV was determined using chromium-51-tagged erythrocytes. Systemic haemodynamics and oxygenation were obtained before (Pre) and 8 hours after induction of sepsis. Statistics were performed with ANOVA.
Results The PV (ml/kg/body weight) was significantly higher at study end with every kind of colloid (HES700/2.5:1: 68.5 ± 11.7; HES700/6:1: 65.5 ± 14.3, HES130: 64.4 ± 4.6) compared with RS (40.6 ± 5.9; $P \leq 0.05$). The HR (1/min) rose in all peritonitis groups but not in the control group (NS). The MAP (mmHg) was significantly lower in the RS group (67 ± 11) compared with control (92 ± 4; $P \leq 0.05$), but not in colloid-treated groups (HES700/2.5:1: 87 ± 15; HES700/6:1: 88 ± 12, HES130: 86 ± 11). SvO_2 (%) remained stable in all HES-treated animals and the control group over 8 hours, with significantly higher SvO_2 in all groups (HES700/2.5:1: 69 ± 3; HES700/6:1: 67 ± 16, HES130: 69 ± 8; control 70 ± 5) compared with RS at the study end (44 ± 17; $P \leq 0.05$).
Conclusion In this model, new high-molecular artificial colloids and HES130 could maintain the PV and preserve SvO_2 and haemodynamics significantly better than RS.
Acknowledgement Supported by a grant from B. Braun Melsungen AG, Germany.

P175

Comparison effect of 6% hydroxyethyl starch with Ringer's solution on splanchnic perfusion in canine with septic shock

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Introduction 6% hydroxyethyl starch (HES) is an artificial colloid. HES and Ringer's solution (RS) are usually used to restore adequate volume in patients with septic shock, but their effects on splanchnic perfusion with septic shock were not clear. This prospective and randomized study was therefore to compare the effect of HES with that of RS on splanchnic perfusion in canine with septic shock.
Materials and methods Twenty-four mongrel dogs with septic shock induced by lipopolysaccharides (LPS) were randomized to be divided into two groups (HES group and RS group). Each group was to receive an intravenous infusion of HES or RS (1 ml/kg/min) for 60 min, followed by normal saline for 180 min at the same rate. Hemodynamic and oxygendynamic and splanchnic perfusion parameters were repeated at 0, 30, 60, 120, 180, 240 min after the basic measurement (pre-LPS).
Results After LPS infusion, the mean arterial pressure (MAP), cardiac output index (CI), and mesenteric blood flow decreased in all animals ($P < 0.05$). After fluid resuscitation, the MAP increased to pre-LPS value after 60 min in the HES group significantly, but after 120 min in the RS group. The CI increased significantly in both groups ($P < 0.05$).
After LPS infusion, the oxygen delivery (DO_2) and mesenteric blood flow decreased in all animals ($P < 0.05$). Compared with 0 min, DO_2 increased by fluid therapy in both groups. Mesenteric blood flow increased from 70 ± 35 to 100 ± 40 ml/min after 60 min in the HES group, and the intramucosal pH (pHi) also increased, and arterial lactate concentration and Pg-aCO_2 decreased significantly ($P < 0.05$), but there were no differences in RS group.
Discussion Our present study showed that both HES and RS could raise arterial pressure and oxygen delivery in canines with septic shock. HES and RS therefore had similar effects on systemic hemodynamics and oxygen delivery.
Pg-a CO_2 and pHi were important signals of intestinal perfusion – low pHi and high Pg-a CO_2 indicated inadequate intestinal perfusion and hypoxia. Therefore the gut has been regarded as the motor of MODS. Compared with baseline values, the mesenteric blood flow increased, and also the intramucosal pH (pHi) increased, and the arterial lactate concentration and Pg-aCO_2 decreased significantly in the HES group, but there were no differences in the RS group. Our results indicated that HES improve splanchnic perfusion.
Conclusion This work demonstrated both HES and RS could improve the hemodynamic state of canines with septic shock, but on splanchnic perfusion HES was better than RS.

P176

Comparison of 6% HES 130/0.4 in a balanced electrolyte solution versus 6% HES 130/0.4 in saline solution in cardiac surgery

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Background HES containing infusion solutions are used to effectively maintain circulating blood volume (normovolaemia) or to treat hypovolaemia in various medical fields. The exclusive use of normal saline-based fluids may be associated with the development of a hyperchloraemic metabolic acidosis. The goal of this study was to prove equivalence of 6% HES 130/0.4 in a balanced electrolyte solution (HES balanced) with 6% HES 130/0.4 in saline solution (HES saline) regarding colloid volume requirements in cardiac surgery. Effects on serum chloride, arterial pH, base excess (BE) and haemodynamic effects of HES balanced were investigated in comparison with HES saline. Superiority of HES balance regarding acid–base status parameters was to be proven.
Patients and methods A prospective, randomised, double-blind, parallel-group, multicentre, clinical phase III study. Up to 50 ml/kg study drug could be infused until 24 hours after cardiac surgery. Forty-three patients were treated with HES balanced, 38 patients were treated with HES saline. The volume of study drug needed for adequate volume therapy until 6 hours after the end of surgery, the chloride level and the arterial pH at the end of surgery were recorded. ANOVA/ANCOVA was performed as appropriate.
Results In the IIT analysis of the primary efficacy parameter, mean volumes of HES were 2391 ml in HES balanced or 2241 ml in HES saline, and equivalence (–500 ml; 500 ml) was proven (95% CI: –77 ml; 377 ml). Serum chloride levels were significantly lower after infusion of HES balanced. There were no differences in haemodynamic parameters between groups. The mean BE was at all times less negative in patients treated with HES balanced compared with HES saline. At the end of surgery the group difference of BE was 1.17 ± 0.42 mmol/l ($P = 0.0032$).

Table 1 (abstract P176)

	HES balanced	HES saline	*P* value
Cl^- (mmol/l)	110.0 ± 0.58	111.8 ± 0.61	0.0171
Arterial pH	7.378 ± 0.006	7.365 ± 0.007	0.0793

Conclusion The volume of HES needed was equivalent between treatment groups. Serum chloride levels were significantly lower after infusion of HES balanced, which reflects the lower chloride load of similar infusion volumes. Regarding the acid–base physiology, the HES balanced solution showed clear advantages. The significant lower serum chloride values were accompanied by less acidosis, as indicated by less negative BE values at all time points after baseline, and a trend towards a higher arterial pH.

P177

The Cost of Albumin Sepsis Treatment (COAST) study: efficacy analysis of albumin for severe sepsis. Modelling using the SAFE study and CUB-Rea data

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Introduction The use of albumin for the treatment of severe sepsis remains controversial. The SAFE study [1] reported a mortality rate of 35.2% in the group resuscitated with saline compared with 30.7% in the group that received albumin (relative risk 0.74, $P = 0.09$). This potential beneficial effect could be explained by several properties of albumin (correction of hypovolemia, of low oncotic pressure or of hypoalbuminemia, antioxidative and anti-inflammatory properties). Despite existing recommendations, albumin remains largely underused in this indication. Given its higher cost compared with other volume expansion products, modelling of its cost/efficacy ratio would be justified in light of the product's potential advantages.

Methods Everyday medical practice was compared with systematic use of albumin. The study population was defined as all adult patients having been treated for severe sepsis in one of the 35 units in the CUB-Rea database between 1 January 1998 and 31 December 2002, not including burn patients, patients with mediastinitis, organ transplant recipients and those having received extracorporeal circulation ($n = 11,137$). Only hospital stays longer than 24 hours and including at least circulatory, kidney or respiratory failure were considered. The costs of intensive care were calculated using the GHS cost (cost of stay) + the daily intensive care cost. Two indicators of efficacy were used: the number of lives saved and the number of years of life gained, using as the baseline case the 4.6% reduction in mortality in the albumin arm of the SAFE study. The cost of albumin was estimated based on the quantities administered in this same study (2.24 l). Life expectancy was determined using the DEALE method with the following factors: age, sex, IGS2 score and MacCabe score.

Results There were 5980 deaths in intensive care in the CUB-Rea database. The use of albumin induced a 4.6% reduction in the number of deaths (512 deaths avoided). Mean survival of the 5156 patients released alive from the hospital was estimated at 9.78 years (95% CI: 9.64–9.92). The average cost per patient of administration of albumin was evaluated at €78.10. The cost per life saved was €6073 and per year of life saved was €617.

Conclusion Application of the SAFE results to the CUB-Rea data showed a highly favourable cost/efficacy ratio for the use of albumin in severe sepsis.

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P178

Effect of bicarbonated Ringer's solution on $PaCO_2$ and tissue PO_2 in hemorrhagic shock rats

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Background and objectives Bicarbonated Ringer's solution (BRS) is considered to be an ideal extracellular fluid solution because it contains bicarbonate, which does not need metabolic processes to exert alkalinizing effect. But administration of a large amount of BRS arouses concern about negative effects of acute alkalinizing such as metabolic alkalosis and a leftward shift of Hb-O_2 saturation curves. In this study, we observed an impact of a large amount of BRS on $PaCO_2$ and tissue PO_2 during hemorrhagic shock.

Methods Fifty male SD rats were divided into five groups: a sham-operated group (Sham), hemorrhagic shock without infusion (HS group), hemorrhagic shock with infusion of normal saline (NS group) and bicarbonated and acetated Ringer's solutions (BRS and ARS groups). Thirty minutes after hemorrhage (2 ml/100 g), resuscitation fluids (three times as much as bleeding) were administered over 30 min. The tissue PO_2 and laser Doppler tissue blood flow was continuously observed, and blood gas analysis was performed.

Results HCO_3^- decreased in all the hemorrhagic groups. HCO_3^- increased in the BRS and ARS groups after resuscitation, while it kept decreasing in the NS group. PaO_2 and $PaCO_2$ recovered to their control values after infusion. PaO_2 kept increasing more, but $PaCO_2$ gradually decreased after resuscitation.

Conclusion Even if BRS was infused to large amounts for the hemorrhage shock, metabolic alkalosis did not occur. The difference was not seen on the tissue PO_2 among the resuscitation groups. The repression of breathing was not suggested from this result.

Figure 1 (abstract P178)

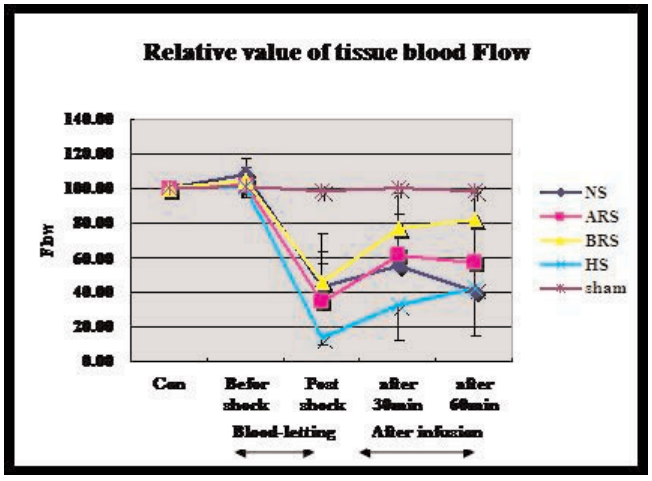
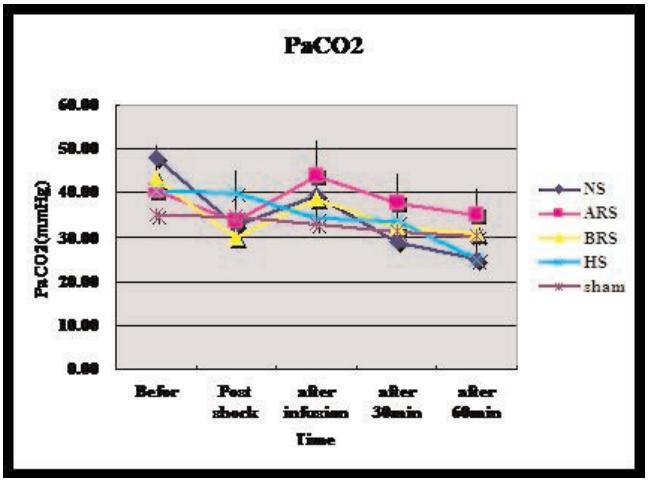


Figure 2 (abstract P178)



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P179

Ethyl pyruvate prevents acute lung injury in an experimental multitrauma model

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Introduction Ethyl pyruvate (EP) is a pyruvate derivative that has been reported to improve survival, to decrease proinflammatory cytokine expression (including high mobility group box-1) and to ameliorate organ dysfunction in animals who have lethal sepsis or were subjected to hemorrhagic shock. We examined the potential

Figure 1 (abstract P179)

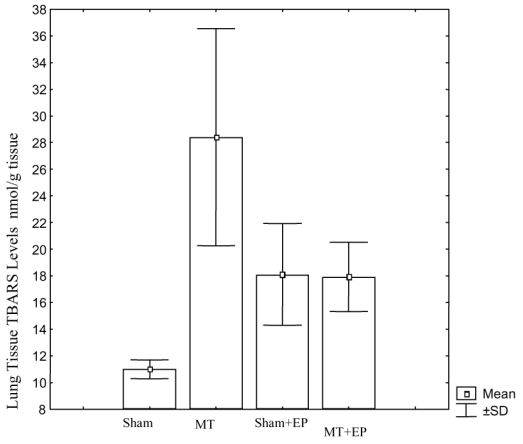
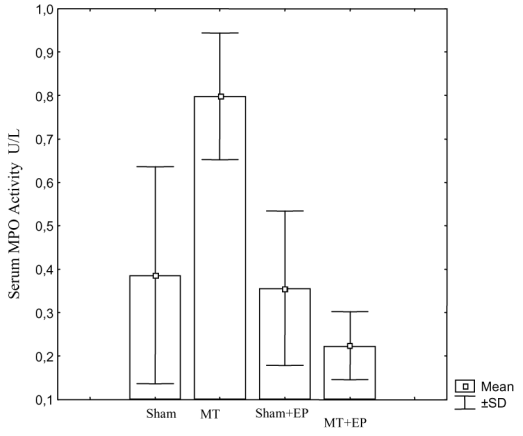


Figure 2 (abstract P179)



protective effects of EP administered after multi-trauma on lung oxidative damage and apoptosis in a rat model with delayed resuscitation.

Materials and methods Thirty-two male Wistar rats were equally divided into sham-control, multi-trauma, EP and multi-trauma + EP treatment groups. Anesthesia was performed with ketamine hydrochloride (60 mg/kg, intramuscularly) in all groups. Multi-trauma was applied as a moderate head trauma, left femur and tibia fractures under anesthesia. Head trauma was created using impaction model; a 450 g weight was dropped on to a metal plate fixed to the head of the subjects from a 1 m height through a Plexiglas guide tube [1]. The fractures of the tibia and femur were created by dropping a blunt guillotine with a weight of 500 g [2]. The first and third groups were resuscitated with Ringer lactate solution. EP (as a Ringer ethyl pyruvate solution; Sigma) was administered 40 mg/kg intraperitoneally 6 hours after the multi-trauma and animals were sacrificed at 24 hours. Post-trauma treatment with EP after the multi-trauma prevented the increase in lung tissue TBARS levels and serum MPO levels (Figs 1 and 2; $P < 0.05$). Lung tissue histopathology demonstrated a dramatic reduction in neutrophil infiltration and caspase-stained cells in the multi-trauma + EP group.

Discussion and conclusion These results suggest that a single dose of EP inhibits leukocyte infiltration and oxidative lung damage, even when given 6 hours after the multi-trauma. EP warrants further evaluation as a therapeutic agent to ameliorate multi-trauma-induced acute lung injury.

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P180

Effect of ethyl pyruvate against un-injurious spinal cord ischemia in rats

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Introduction Paraplegia is a complication that sometimes occurs after successful operations on the thoracic aorta with an incidence rate ranging from 0.9% to 40%. The primary cause of such spinal cord injury is ischemia. Pyruvate, a glycolytic intermediate, is a promising substance with a protective effect against ischemia. Its mechanism of action has been assumed to be an energy supply to augment the ATP level, and free radical scavenging. However, pyruvate is fragile in aqueous solution, and its use is thus restricted. Ethyl pyruvate (EP) is a novel ester derivative of pyruvate, which is stable in solution and dissolves immediately into pyruvate in blood. The objective of this study was to evaluate whether EP can improve the neurological outcome in a rat spinal ischemia/reperfusion model.

Methods We used male Sprague–Dawley rats, and spinal cord ischemia was induced for 9 min, in which most rats tend to become paraplegic, using an intra-aortic balloon occlusion. EP was dissolved in saline under sonication with a final concentration of 28 mmol/l. We administered 2 ml EP solution pre and post ischemic interval. For the control, saline (vehicle fluid) was administered at the same times. The neurological function of the lower extremities was assessed with the BBB scale at 24 and 72 hours after ischemia. A histochemical examination of the spinal cord was performed for neurons or apoptotic bodies.

Results and discussion The motor function of the lower extremities (BBB scale) of the EP group was better than the saline group at 24 and 72 hours after ischemia. The number of neurons stained for NeuN in the EP group was higher than those in the saline group, but less than the normal control (no treatment) ($P < 0.001$). The number of apoptotic bodies in the EP group was less than those in the saline group ($P < 0.001$). We demonstrated that the EP improved the neurological outcome after a transient ischemia and reperfusion model in rats. The histological findings supported the hypothesis that EP protected the neurons against ischemic injury. This is a first report to describe the neuroprotective effect of EP *in vivo*.

Conclusions EP improved the neurological outcome after transient ischemia and reperfusion, and also preserved the neurons. Although the mechanism for such neuroprotection is still unclear, inhibition of apoptosis may be related its preventive effect against neuronal damage.

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P181

Maintenance fluids should contain at least 77 mmol sodium per liter for critically ill pediatric patients

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Background Disorders of sodium and water metabolism are frequently encountered in hospitalized patients. Hyponatremia in critically ill patients can cause significant morbidity and mortality. It remains uncertain what should be the composition of maintenance fluids for critically ill pediatric patients. We conducted a prospective randomized trial to compare the effect of fluids composition on hyponatremia in a heterogeneous population of pediatric patients.
Methods We randomly assigned patients who had been admitted to hospital to receive maintenance fluids of 34 mmol/l (group I) or 50 mmol/l (group II) or 77 mmol/l (group III) sodium during the first 72 hours of hospitalization. The primary outcome measure was to determine the relation between hyponatremia and fluid composition, the secondary outcome was to identify the optimal maintenance fluids for critically ill children.
Results Of the 77 patients who underwent randomization, 24 were assigned to group I, 27 to group II and 26 to group III; the three groups had similar baseline characteristics. There were 41.7% ($n = 10$) with hyponatremia in group I, 37% ($n = 10$) in group II as compared with 15.4% ($n = 4$) with hyponatremia in group III. The risk of hyponatremia was increase 3.92 times in group I and 3.23 times in group II according to group III (95% CI, 1.03–14.9 and 0.86–12.1, respectively). There were no significant differences between the groups in the proportions of patients who were treated in the PICU: 45.8% ($n = 11$) in group I, 44.4% ($n = 12$) in group II and 42.3% ($n = 11$) in group III ($P = 0.78$). In all the groups hyponatremia developed especially in PICU patients: 70% ($n = 7$) in group I, 80% ($n = 8$) in group II and 100% ($n = 4$) in group III ($P < 0.001$).
Conclusions The most important factor for hospital-acquired hyponatremia is the administration of hypotonic fluid. Hyponatremia risk increases especially in critically ill pediatric patients. In patients in the PICU, for preventing of hyponatremia, maintenance fluids should contain at least 77 mmol/l sodium.

P182

The accuracy of tonicity balance formulas in predicting changes in plasma sodium in ventilated infants with respiratory syncitial virus bronchiolitis

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Objective Infants with respiratory syncitial virus (RSV) infection demonstrate avid renal water retention due to raised antidiuretic hormone activity and are at risk of hyponatraemia [1]. Fluid restriction (48 ml/kg/day) and diuretics are often required to prevent this occurrence and to maintain fluid and sodium balance. Many methods have been postulated for predicting tonicity balance and the resulting change in plasma sodium (Na) changes. These include calculating the tonicity balance using intake/output of water with net Na flux (tonoNa), Na and K flux (tonoNa+K), and more recently with the Nguyen–Kurtz method [2-4]. The objective of this study was to document the water and electrolyte balance, and to document the accuracy of these different tonicity balance methods to predict Na changes during the first day of intensive care admission in ventilated infants with bronchiolitis.
Method We prospectively enrolled 30 consecutive infants (median weight 4.3 kg) with bronchiolitis requiring mechanical ventilation to a tertiary PICU. Infants were placed on a fluid-restricted regime of 48 ml/kg/day 0.9% saline intravenously or oral feed when tolerated, and were studied over the first 24 hours following PICU admission. Blood samples were collected on admission and at 24 hours; urine collection over this period was analysed for osmolality and electrolyte content. The volume and content of all fluid inputs, including drugs, were recorded over the same time periods. Data are presented as the median (IQR).
Results The admission plasma Na was 140 mmol/l (138–141) and after 24 hours was 139 mmol/l (138–143). The net electrolyte and fluid balance is presented in Table 1 with almost neutral balance for Na, K and Cl and fluid, in keeping with the fact that plasma Na did not change over the 24-hour period ($P = 0.9$). Free water clearance predicted a net gain of water of 10 ml/kg/day (5–17). Electrolyte free water clearance using urine Na and K predicted a net gain of 17 ml/kg/day (7–26) free water. Consequently both the tonicity balance with Na and with Na and K predicted a significant fall in plasma Na at 24 hours: 137 mmol/l (136–139, $P = 0.1$), and 136 mmol/l (135–140, $P = 0.006$), respectively. The Nguyen–Kurtz method was most accurate and predicted no change in plasma Na: 142 mmol/l (136–147, $P = 0.06$). Bias with 95% limits of agreement for predicting plasma Na with the tonoNa, tonoNa+K and Nguyen methods were −2 (−9 to 13), −3 (−10 to 5) and 2 (−9 to 13) mmol/l, respectively.
Conclusion Fluid restriction of ventilated infants with bronchiolitis results in a neutral balance of water and elelctrolytes and no resulting change in plasma Na. Tonicity balance methods using the net Na balance or Na and K balance overestimate free water retention and predicted lower plasma Na values. The Nguyen–Kurtz method, although more complex, provides the most accurate method of predicting plasma Na changes in these patients.
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Table 1 (abstract P182)

Parameter	Intake/kg/day	Output/kg/day	Net/kg/day
Sodium (mmol)	1.7 (0.5–2.8)	2 (1.6–3.8)	0.3 (1.1–1)
Potassium (mmol)	0.6 (0.5–0.7)	0.9 (0.7–1.3)	0.3 (0.2–0.6)
Chloride(mmol)	1.8 (1–3)	3.7 (1.6–3.8)	1.9 (0.6–0.8)
Fluid (ml)	48 (46–53)	49 (40–70)	1.7 (−19 to 6.7)

P183

Therapeutic effects of hypertonic saline on peritonitis-induced septic shock with multiple organ dysfunction syndrome in rats

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Significant mortality in patients with sepsis results from the development of multiple organ dysfunction syndrome (MODS). More recently, small-volume resuscitation with 4 ml of 7.5% NaCl per kilogram of body weight of hypertonic saline (HS) has been proposed to restore physiological hemodynamics in hypotensive conditions such as hemorrhagic shock. We therefore hypothesized that HS resuscitation may alleviate the development of MODS in sepsis. In order to test this possibility, we evaluated effects of hypertonic saline in a rat sepsis model induced by cecal ligation and puncture (CLP). Our results demonstrated that CLP for 18 hours was associated with circulatory failure (i.e., hypotension and vascular hyporeactivity to norepinephrine), MODS (examined by biochemical parameters and histological studies) and severe 18-hour mortality. Animals treated with HS (7.5% NaCl, 4 ml/kg; at 3 hours after CLP surgery) not only ameliorated the deterioration of hemodynamic changes but also attenuated polymorphonuclear neutrophil (PMN) infiltration in the lung and the liver. In addition, HS increased the survival rate at 9 and 18 hours when compared with the CLP group. Moreover, HS reduced plasma nitric oxide (NO) and IL-1β and organ O_2^- levels in CLP-treated rats. In conclusion, HS prevented circulatory failure and alleviated MODS as well as decreasing the mortality rate in CLP-treated animals. These beneficial effects of HS may be attributed to reducing the plasma concentration of NO and IL-1β as well as the organ O_2^- level and decreasing lung PMN infiltration and liver necrosis, and thus decreasing the mortality rate in peritonitis-induced septic animals. Our study suggests that HS could be a cheap and novel therapeutic agent in the early sepsis animals or patients.

P184

Clinical practice of fluid resuscitation in severe sepsis and septic shock on German ICUs

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Objectives Intravascular fluid resuscitation is one of the mainstays of supportive therapy in severe sepsis or septic shock. However, despite decades of research, there is still ongoing controversy whether crystalloid or colloid fluids should be used. Therefore the choice of fluids varies widely. In order to describe current clinical practice, we analyzed the epidemiological data derived from the Prevalence Study of Severe Sepsis and Septic Shock in Intensive Care Units in Germany.
Methods The study was designed as a prospective observational cross-sectional study. A representative random sample of 454 ICUs out of a total 2075 ICUs was obtained. According to hospital size, five strata (<200, 201–400, 401–600, >600 beds and university hospitals) were established. All data were collected by specially trained physicians from SepNet who used ACCM/SSCP criteria. Visits were randomly distributed over a 1-year period to allow assessment of seasonal variations.
Results Four hundred and fifteen patients with severe sepsis or septic shock were identified, representing a total of approximately 1500 patients with severe sepsis and/or septic shock. Crystalloids were administrated in 87% of the patients. In this subgroup 57% received full electrolyte solutions (median: 1500 ml; 25/75 percentile: 1000–2000 ml), whereas in 30% of patients NaCl 0.9% was used (1000 ml; 500–1575 ml). A combination of 0.9% NaCl with full electrolyte solutions was administered in 12.8% of patients. Other crystalloid solutions such as 1/2 or 2/3 electrolyte solution or glucose 5% did not play a role in fluid therapy. Artificial colloids such as gelatins or hydroxyethyl starch (HES 6% or 10%) were used much less frequently. Gelatins, HES (6%) or HES (10%) were administered as follows: gelatins, 10.2% (500 ml; 500–1000 ml); HES (6%), 23.5% (500 ml; 500–1000 ml); HES (10%), 12.1% (500 ml; 500–1000 ml). A combination of crystalloids and colloids was observed in 36.3% of the patients. Albumin (HA) was used in 0.5% (HA 5%) and 4.0% (HA 20%) of the patients, respectively. There was no significant difference in hospital-size strata.
Conclusion There is a marked preference for crystalloid fluid resuscitation (87% of patients) in the treatment of severe sepsis in Germany, whereas colloids are used to a much lesser degree (46%), among them most frequently HES 6% (24%) and gelatins (10%). Human albumin does not play a role in volume replacement therapy. Fluid choice is not associated with hospital size. The relatively low amount of colloids administered may be explained by time delay between onset of sepsis and the visiting day (mean 7.7 days).
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P185

Survey of intravenous fluid maintenance therapy for surgical patients in the UK

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Introduction Surgical patients receive various intravenous maintenance fluids after major surgical procedures. Usually these fluids are prescribed by most junior surgical trainees with different levels of experience. We surveyed intravenous maintenance fluid therapy for post major abdominal surgery patients among surgical trainees in London, UK.
Objective To assess the current intravenous fluid optimisation practice among surgical senior house officers (SHOs), after major abdominal operations.
Methods Surgical SHOs were contacted by telephone. The answers for a set of questions regarding their level of experience, including intensive care training, and choice of intravenous fluids for major abdominal surgical procedures were recorded on a paper. The telephone interview was done by a single member, for all SHOs, and data were analysed.
Results One hundred and fifty surgical SHOs were contacted (response rate 100%) and the results are summarised in Tables 1 and 2. The majority (67%) of the surgical trainees did not have previous formal intensive care training. More than one-half of the SHOs (51%) preferred 0.9% sodium chloride (normal saline) as their first-choice intravenous maintenance fluid. When asked regarding awareness of central venous saturation ($ScvO_2$) monitoring for fluid optimisation, only 44% of the trainees regularly used $ScvO_2$ as a guide to fluid therapy. Only 27% of the surgical SHOs are aware of goal-directed therapy for surgical patients. The SHOs who had previous intensive care experience had better knowledge of $ScvO_2$ monitoring (88%) and goal-directed therapy.

Table 1 (abstract P185)

Awareness of post-operative fluid optimization among surgical trainees in the UK

Questions	Yes [*n* (%)]	No [*n* (%)]
Previous formal intensive care training	50 (33)	100 (67)
$ScvO_2$ monitoring for fluid optimisation	66 (44)	84 (56)
Awareness of goal-directed therapy	41 (27)	109 (73)

Table 2 (abstract P185)

Choice of intravenous maintenance fluid prescription for post major abdominal surgery patients among surgical trainees in the UK

Intravenous fluid	Number of surgical trainees [*n* (%)]
Normal saline	77 (51)
Hartman's solution	33 (22)
Dextrose saline	40 (27)

Sixty-one per cent of trainees monitor blood electrolytes only when they recognise or anticipate complications.

Discussion Currently there is no clear recommendation by the surgical or intensive care bodies regarding minimal formal intensive care training for surgical trainees in the UK. In spite of increasing evidence of hyperchloremic metabolic acidosis, caused by use of normal saline as maintenance fluid in surgical patients, the majority of the surgical SHOs prefer normal saline as the first-choice maintenance fluid. Introduction of regular intensive care teaching should be part of the curriculum for surgical training to improve the care of critically ill surgical patients in the wards.

P186

First-aid treatment of hydrofluoric acid skin burns with 2.5% calcium gluconate gel: an experimental controlled study

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Introduction Present in various industrial and household products, hydrofluoric acid (HF) is one of the most dangerous mineral acids. Extremely aggressive for the skin, HF is responsible for immediate tissue damage and potentially systemic complications, especially life-threatening hydro-electrolytic perturbations. Calcium gluconate in the form of a 2.5% gel is considered the first-aid treatment for accidental HF skin burns. In France, a ready-to-use form is produced and distributed to hospitals by the AGEPS. Although the use of this gel is based on clinical practice, there is no available controlled study on its efficacy.

Materials and methods Thirty male Wistar–Han rats of 250 g were burned with 60 µl of a 40% HF aqueous solution on two spots of 4 cm^2 (right flank) under pentobarbital anesthesia. After a 2 min contact with HF, one lesion was treated by repeated ($n = 10$) topical applications of 1 g of 2.5% calcium gluconate gel for 4 days; the other one was untreated (control). The AGEPS formulation and two other alternatives were evaluated in a blind fashion (10 rats/gel). Burn severity was assessed on days 1, 2, 3, 7, 10, 14 and 17 post-injury by a visual semi-quantitative scaling system (0–4). Treatment efficacy was evaluated by comparing burn severity scores and areas under the curve (AUC) of treated and untreated lesions for each animal. Statistical analysis was performed by analysis of variance followed by the Student–Newman–Keuls test.

Results The untreated lesion started to develop upon HF application; it reached a maximum between days 2 and 7 (median score: 3), before beginning to recover (day 17, median score: 1). Treatment significantly limited the severity of burns at all time intervals (median: −0.5 to −2) and for all scores (median: −1 for severity scores 1, 2 and 4, −2 for score 3 lesions, $P < 0.0001$). Treatment reduced the AUC days 1–17 of burn injury from 34.0 (untreated) to 17.7 ($P < 0.001$); there were only three cases of treatment failure (AUC of untreated/treated: 15/21, 53.5/58.5, 51.5/50.5). At day 17, full wound recovery was obtained in 14 cases by gel therapy compared with six cases in the absence of treatment. The efficacy of the three gel formulations was comparable (severity scores and AUC of burn injury, number of full recoveries).

Conclusion Calcium gluconate in the form of a 2.5% gel reduces the severity of skin burns induced by 40% HF in a rat model. These data support the use of the AGEPS gel as a rapid, safe, and economical 'first-aid' treatment for accidental HF skin burns; more severe burns may require additional injection of calcium gluconate.

P187

Selenium and its substitution in critically ill patients

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Introduction In patients in the ICU of the Anaesthesiological Clinic we find generally decreased selenium (Se) in serum, which does not normalise under supplementation with standard doses of Se. Some recently published papers demonstrate that supplementation of high doses of Se significantly decreases the mortality of patients in critical states. We therefore started in a prospective clinical trial the supplementation of Se in high doses and followed its influence on selected laboratory parameters, on the mean arterial pressure (MAP) and on the survival of critically ill patients.

Methods In a randomised clinical trial, 61 ICU patients were followed. Thirty-five of them (group 1) received standard daily doses of Se 0.4–0.8 mmol (30–60 mg) as part of nutritional support, 25 patients (group 2) received additional Na-selenite containing Se through infusions in the amount of 12.7 mmol (1000 mg) on the first day, and later 6.7 mmol (500 mg) daily until the 14th day. In blood samples, the following were examined every other day during this period: Se, prealbumin, albumin, cholesterol, C-reactive protein, procalcitonin, IgM. Altogether, 150 examinations in group 1 and 119 in group 2 were performed. Moreover, the glutation peroxidase (GSHPx) was investigated 67 times in group 1 and 34 times in group 2.

Results Presented as medians and 95% CIs. Serum Se levels (µmol/l) group 1 = 0.292 (0.27; 0.33), group 2 = 0.57 (0.51; 0.72), $P < 0.01$; GSHPx (U/l) group 1 = 4059 (3854; 4346), group 2 = 4668 (4213; 4878), $P < 0.01$. Reference ranges: Se 0.58–1.82 mmol/l, GSHPx 4170–10,880 U/l. There was no statistically significant difference between both groups for all the other biochemical parameters followed. In the supplemented group 2, the MAP could more frequently be kept above 70 Torr ($P < 0.01$). Fifty-nine per cent of patients from group 1 and 72.7% from group 2 survived their ICU stay. Neither at the dismissal from the ICU or 1 month later was this difference statistically significant.

Conclusion Patients with high Se supplementation had significantly higher levels of Se in serum and GSHPx in blood. There was no significantly higher surviving rate in the supplemented group. The MAP was positively influenced. No side effects were registered with high Se dosing. The study continues.

P188

N-terminal pro-B-type natriuretic peptide in patients after cervical spine surgery

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Objective The aim of the study was to evaluate levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP) and its correlation to sodium biochemical parameters in patients after elective cervical spine surgery.
Methods We prospectively measured NT-proBNP and serum sodium immediately after the operation, urinary loss of sodium, creatinine clearance, sodium clearance, sodium fractional excretion, diuresis, intake of fluids and sodium on day 1 in 50 patients and NT-proBNP on day 2 in 30 patients after elective cervical spine surgery for spondylosis. All patients were classified as New York Heart Association (NYHA) I, they did not receive diuretic or osmotic therapy and had an uneventful postoperative period.
Results Immediate postoperative NT-proBNP values were normal (51 ± 28 pg/l), but they increased significantly on day 2 (230.5 ± 160 pg/l, $P < 0.001$). There was a significant correlation between NT-proBNP on days 1 and 2 ($P = 0.002$), NT-proBNP and daily urinary loss of sodium ($P = 0.049$) on day 1, and no other correlations were found.
Conclusion NT-proBNP values were not increased on day 1 in patients after elective cervical spine surgery, but they were significantly increased on day 2 and there was a significant correlation to daily urinary loss of sodium.

P189

NT-proBNP levels in the ICU do not predict the etiology of respiratory distress

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Introduction BNP and NT-proBNP are hormones released by the ventricular myocardium in response to pressure and volume overload. Their levels help differentiate cardiac from noncardiac etiologies of dyspnea. For example, NT-proBNP above 1000 pg/ml is as a cutoff value indicating CHF is a more likely cause of dyspnea in non-ICU patients. The applicability of this test to a mixed ICU population is unclear and there is no known correlation between PCWP and BNP levels in these patients. In addition, there is no known correlation between elevated NT-proBNP and the incidence of respiratory failure.
Methods A retrospective review of our combined medical/surgical ICU between 1 July 2004 and 30 June 2005 using Project IMPACT (Cerner Corporation) to generate a list of patients admitted for a variety of potential causes of dyspnea along with NT-proBNP levels. The Kruskal–Wallis test was used to determine significant differences between five specific diagnoses; CHF/pulmonary edema (both cardiogenic and noncardiogenic), pneumonia, COPD exacerbation, ARF and sepsis. A receiver–operator curve (ROC) was used to examine the sensitivity and specificity of CHF at different NT-proBNP cutoff values.
Results A total of 47 patients out of 199 (23.6%) surveyed had NT-proBNP measured. Forty-two of 199 (21.1%) fit into the diagnostic categories used for comparison. The Kruskal–Wallis test showed among the five diagnoses that only CHF and pneumonia had significantly different NT-proBNP levels ($P = 0.0025$). The difference in NT-proBNP levels between patients with and without respiratory failure was not significant. Results are presented in Table 1. The ROC analysis showed a ROC AUC of 0.774, but to achieve a specificity >0.9 requires a cutoff value of approximately 15,000 pg/ml.
Conclusion The generally accepted cutoff for NT-proBNP supporting the diagnosis of CHF is 1000 pg/ml. The average values in this ICU population (14,114.6 pg/ml) are well above this cutoff value; 85% were above 1000 pg/ml but only 12/47 (25.5%) of the patients were diagnosed with CHF. This suggests either a higher cutoff value may be required to properly utilize the test in an ICU population or it should be abandoned completely for patients admitted to the ICU, especially in light of such large standard deviations about the mean. Moreover, the data suggest that NT-proBNP does not play a role in differentiating the etiology of respiratory compromise.

P190

Relationship between B-type natriuretic peptide plasma levels and echocardiography parameters in decompensated chronic heart failure patients treated with levosimendan

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Background B-type natriuretic peptide (BNP) plasma levels have recently been demonstrated as significant neurohormonal markers of chronic heart failure (CHF) progression and prognosis. Additionally, clinical studies have shown that the calcium sensitizer levosimendan beneficially affects the central hemodynamics of CHF patients and improves their long-term prognosis.
Purpose To investigate whether levosimendan-induced hemodynamic improvement, as confirmed by echocardiogram of CHF patients, is related to respective changes in BNP levels.
Methods Circulating levels of BNP were measured by ELISA in 37 patients with decompensated advanced CHF at baseline and 72 hours after the initiation of levosimendan treatment. Echocardiographic parameters – pulmonary artery pressure (PAP), end-diastolic volume (EDV), end-systolic volume (ESV) and left ventricular ejection fraction (LVEF) – were also measured at baseline and 72 hours after infusion initiation. We used the threshold of 500 pg/ml for BNP, 30 mmHg for PAP and 50% for LVEF to define patients as having altered results.
Results We retrospectively analyzed 37 consecutive CHF patients to whom levosimendan was prescribed by the attending physician besides standard measures. BNP levels were significantly lower

Table 1 (abstract P189)

	Total	ARF	CHF/pulmonary edema	COPD	Sepsis	Pneumonia
n; mean (pg/ml) (SD)	42; 14,115 (20,093)	3; 22,504 (23,240)	11; 33,219 (29,104)	11; 6126 (5718)	3; 7024 (5831)	14; 5102 (5489)

within 72 hours of levosimendan treatment ($P < 0.01$). A significant reduction of PAP ($P < 0.05$) was also found during the same period. A good correlation between the levosimendan-induced changes in LVEF and the respective reduction of BNP levels ($P < 0.01$) was observed.
Conclusions Our results indicate that changes in BNP levels may be useful as biochemical markers of levosimendan-induced improvement in echocadiographic and clinical parameters.

P191

Significance of B-type natriuretic peptide in acute cerebrovascular disease

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Introduction Increased serum N-terminal pro-B-type natriuretic peptide (N-BNP) has been observed in congestive heart failure (CHF), acute coronary syndromes, pulmonary embolism and septic shock. N-BNP elevation has also been linked with ischemic stroke (IS) and aneurysmal subarachnoid hemorrhage (SAH); however, the significance of N-BNP in this setting is unknown. We hypothesized that elevated serum N-BNP may occur independently of CHF in patients with acute cerebrovascular disease.
Design A case–control study.
Methods Patients hospitalized with acute IS, SAH, or spontaneous intracerebral hemorrhage (ICH) were evaluated with serum N-BNP testing and transthoracic echocardiography. Patients were classified into two groups (presence or absence of CHF) using modified Framingham criteria.
Results Sixty-seven patients were evaluated, 37 with IS, 20 with SAH, and 10 with ICH. CHF was present in 36 patients (53%), while elevated N-BNP (>500 pg/ml) was detected in 57 (85%). Patients with and without CHF were not significantly different with regard to demographics, cardiovascular risk factors, stroke subtype, fluid balance, and administration of diuretic, antihypertensive, or vasoactive medications. Systolic and diastolic dysfunction and increased serum troponin I were more common in the CHF group, but these differences were not significant. N-BNP was markedly elevated in both groups, and significantly higher in patients with CHF. At a 500 pg/ml cutoff, the sensitivity, specificity, positive predictive value, and negative predictive value of N-BNP for CHF were respectively 94%, 25%, 58%, and 80%.
Conclusions Serum N-BNP has limited value for diagnosing CHF in patients with acute cerebrovascular disease. Elevated levels in patients without CHF point to alternative mechanisms of N-BNP production. More work is needed to explore the pathophysiology, diagnostic role, and prognostic significance of N-BNP in this patient group.

Table 1 (abstract P191)

	CHF ($n = 36$)	No CHF ($n = 31$)	*P* value
Age (years)	65	62	0.8
Males (number of patients)	18	11	0.05
SAH (number of patients)	9	11	0.7
ICH (number of patients)	6	4	0.7
IS (number of patients)	21	16	0.6
N-BNP (pg/ml)	8032 ± 10,110	3014 ± 3823	0.007
Systolic dysfunction (number of patients)	14	6	0.08
Diastolic dysfunction (number of patients)	14	7	0.1
Tropinin I (number of patients)	15	9	0.2
Hospital LOS (days)	17	17	0.8
Death (number of patients)	12	4	0.04

P192

Can N-terminal pro-B-type natriuretic peptide and troponin T predict ICU and hospital mortality in patients with septic shock?

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Introduction The counter-regulatory neurohormone N-terminal pro-B type natriuretic peptide (NT-proBNP) is predominantly released from the left ventricle in response to increasing wall tension and is a useful prognostic marker in patients with-established cardiac failure [1]. Myocardial dysfunction commonly occurs in septic patients. Cardiac biomarkers, including NT-proBNP, have been shown to be predicators of mortality in unselected critically ill patients [2].
Objectives To evaluate the role of NT-proBNP and troponin T (TnT) as predictors of mortality in patients with severe sepsis and septic shock.
Methods A prospective observational study was carried out on patients admitted to a noncardiothoracic tertiary ICU within 24 hours of the development of severe sepsis or septic shock. Plasma samples were taken on all patients on admission. NT-proBNP and TnT were determined using commercially available assays. Data were compared after logarithmic transformation, where appropriate.
Results Thirty-four patients met the entry criteria (mean age 61.3 ± 14.9 years, male $n = 19$, all patients were mechanically ventilated). The APACHE II score of ICU survivors (median [range]) was 19 (12–33) and for nonsurvivors was 22.5 (14–38) ($P = 0.19$). Of the 34 patients, 11 died during their ICU admission (32%). Hospital mortality was 15/34 (44%). NT-proBNP was elevated (>150 ng/l) in all patients and TnT (>0.1 ng/ml) in 13 patients. Results are summarised in Table 1.
Conclusion NT-pro-BNP and TnT are frequently elevated in severe sepsis. However admission values are not prognostic markers of ICU and hospital survival.
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Table 1 (abstract P192)

ICU and hospital outcomes related to admission NT-proBNP and TnT levels

	Outcome	Survivors	Nonsurvivors	*P* value
NT-proBNP	ICU	8514 (1943–31,290)	8171 (4279–28,269)	0.7
TnT	ICU	0.05 (0.01–0.18)	0.07 (0.04–0.22)	0.37
NT-proBNP	Hospital	6291 (1943–30,345)	23541 (4279–30,416)	0.4
TnT	Hospital	0.05 (0.01–0.15)	0.07 (0.03–0.28)	0.37

Data presented as median (interquartile range).

P193

Should natriuretic peptide B-type be used to predict weaning failure in mechanically ventilated patients?

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Background Heart failure and pulmonary edema have been implicated as causes for weaning failure in mechanically ventilated patients; however, the identification of these conditions could be challenging in critically ill patients. The natriuretic peptide B-type (BNP) level has been used to evaluate volemia and cardiac function in patients with heart failure, but no data have been published about the use of BNP to guide weaning in mechanically ventilated patients.
Objective This study was performed to evaluate whether the BNP level could be useful to predict weaning failure or success in patients mechanically ventilated for more than 48 hours.
Methods Sixty-three consecutive patients mechanically ventilated for more than 48 hours in a medical/surgical ICU and who were included in our weaning protocol had their BNP level (pg/ml) recorded immediately before a T trial. The decision about extubation or reintubation was made by an attending physician not involved in this study and blinded for the BNP level. Weaning failure was defined by the T-trial intolerance or need for reintubation in the first 48 hours after extubation.
Results Weaning failure was observed in 16 patients (25%), seven who failed during the T trial and nine who were extubated but needed reintubation within 48 hours. The BNP level was greater in the failure group when compared with the success group (712.6 ± 151.9 vs 295.3 ± 42.4 respectively, $P = 0.02$). The patients who were reintubated had a BNP level (864 ± 128.8) higher than the success group ($P < 0.001$) but there were no differences between the reintubation group and T-trial failure (517.8 ± 146).
Conclusion BNP recorded before a T trial can be helpful to predict weaning outcome in patients mechanically ventilated for more than 48 hours.

P194

N-terminated natriuretic propeptide type B is a better prognostic factor than MB isoenzyme of creatine kinase in patients after cardiac arrest

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Background and goals The aim of our study was to assess concentrations of N-terminated propeptide type B (NTBNP), a marker of cardiac insufficiency, and MB isoenzyme of creatine kinase (CKMB), which level is adequate to the area of acute myocardial necrosis, and to compare their predictive values of survival in patients after cardiac arrest (CA).
Participants Fifty-two patients after CA (CA-patients) of age 62 ± 13 years. In 34 patients CA appeared during acute coronary syndrome. Twenty-six patients died after CA (CA-D), and 26 patients survived and were discharged from hospital (CA-S).
Methods The state of patients after CA was assessed by scales of proven values of survival after CA used in critical care: Glasgow Coma Scale (GCS), Multiple Organ Dysfunction Score (MODS), Simplified Acute Physiology Score II (SAPS II) and Acute Physiology and Chronic Health Evaluation II (APACHE II). In CA-patients the concentrations of NTpBNP and CKMB were measured in venous blood samples taken just after CA (day 0) and on two consecutive days (day 1 and day 2) at 8:00 am. In CA-D and CA-S patients the concentrations of NTBNP and CKMB were compared. In regression and survival analysis, predictive values of concentrations of NTBNP and CKMB were assessed. Correlations among concentrations of NTBNP, CKMB and values of the scales used in critical care were estimated by Spearman's correlation coefficient.
Results The mean concentrations of NTBNP and CKMB were higher in CA-D than in CA-S patients 3 days running but were significantly higher only for NTBNP on day 1 (114,000 ± 112,000 vs 45,100 ± 58,000 pmol/l, $P < 0.027$). On day 1 similar values of the OR of survival after CA of concentrations of NTBNP (OR 5.7 for concentrations >50,000 or ≤50,000 pmol/l, $P < 0.02$) and concentrations of CKMB (OR 7.5 for concentrations >40 or ≤40 U/l, $P < 0,02$) were found, but it was only concentrations of NTBNP whose OR was significant in blood on day 0 (OR 5.8 for concentrations >50,000 or ≤50,000 pmol/l, $P < 0.02$). The relationship to survival of concentrations of CKMB on day 1 and concentrations of NTBNP on day 0 and day 1 was also confirmed in Kaplan–Meyer survival analysis. Only concentrations of NTBNP revealed good correlation with values of the scales used in critical care.
Conclusions On day 1 after CA, concentrations of NTBNP and CKMB are of predictive values of survival. In blood taken just after CA, only the concentration of NTBNP reveals a predictive value of survival. NTBNP is a better predictor of survival after CA than CKMB because its concentration is of predictive value in the first 2 days after CA and of good fit with scales concerning the severity of state of patients after CA.

P195

Cardiopulmonary exercise testing and NT-proBNP before major vascular surgery: do they correlate?

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Introduction The counter-regulatory neurohormone N-terminal pro-B type natriuretic peptide (NT-proBNP) is predominantly released from the left ventricle in response to increasing wall tension and is a useful prognostic marker in patients with cardiac failure [1]. Cardiopulmonary exercise (CPX) testing is an objective method of assessing functional cardiac status. The anaerobic threshold (AT), the point at which anaerobic metabolism supplements aerobic metabolism, correlates with the severity of cardiac failure [2].
Objective and methods An ongoing, prospective, observational study, to determine the correlation between preoperative CPX testing and measurement of NT-proBNP (Roche) in patients undergoing elective abdominal aortic aneurysm (AAA) repair (open or endovascular [EVAR]). All patients were preassessed by a consultant vascular anaesthetist with particular emphasis on cardiac risk factors and functional capacity (metabolic equivalents [METs]). CPX testing was performed preoperatively, by a blinded investigator, in a standardised manner [3] with calculation of AT made by the V-slope method. NT-proBNP levels were also measured preoperatively, a level >150 pg/ml considered elevated.
Results Forty-three patients were recruited, mean (SD) age 71.8 ± 8.9 years. The mean (SD) AT was 10.7 ± 3.2 ml/min/kg. There was no significant correlation between age and AT ($r = -0.12$, $P = 0.45$). The median level (range) of NT-proBNP was 322.8 (52–5085) pg/ml. Over 85% of patients had an NT-proBNP level >150 pg/ml. There was a weak negative association between

Table 1 (abstract P195)

	Open AAA	EVAR	*P* value
n	21	22	
Age (years)	68.3	74.8	0.02
AT (ml/min/kg)	9.6	11.9	<0.02
NT-proBNP (pg/ml)	292	368	0.9

NT-proBNP and AT ($r = -0.24$, $P = 0.18$). Results between open repair and EVAR are summarised in Table 1. There was a positive correlation between AT and METs ($r = 0.41$, $P < 0.01$).

Conclusion There is no correlation between anaerobic threshold and NT-proBNP levels in patients undergoing elective abdominal aortic aneurysm repair but there was a definite positive correlation between AT and functional capacity (METs). Whether CPX or cardiac biomarkers influences outcome requires further study.

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P196

Plasma levels of pro-atrial natriuretic peptide, pro-adrenomedullin, and pro-endothelin-1 correlate with the severity of organ dysfunction in critically ill patients

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Introduction Prohormones of cardiovascular active mediators may add important information to the clinical status of patients with systemic inflammation. However, only little information is available of how serum levels of such prohormones are affected by the clinical status of critically ill patients. The goal of this study was to identify factors that independently influence prohormone plasma concentrations in an ICU setting.

Methods Citrate plasma samples of 185 patients with either severe sepsis/septic shock ($n = 120$) or systemic inflammatory response syndrome (SIRS, $n = 65$) after coronary bypass surgery have been obtained daily, resulting in 2385 samples. The Sequential Organ Failure Assessment (SOFA) score was also determined daily. Midregional pro-atrial natriuretic peptide (MR-proANP), midregional pro-adrenomedullin (MR-proADM), and C-terminal pro-endothelin-1 (CT-proET-1) have been measured by an immunoassay (BRAHMS AG, Germany). For each patient, the maximum values of MR-proANP, MR-proADM and CT-proET-1 were identified. These maximum levels were analyzed with multiple regression using demographic parameters and parameters of inflammation (leukocytes [WBC], C-reactive protein [CRP], procalcitonin) as well as the SOFA score as independent factors.

Table 1 (abstract P196)

	MR-proANP	MR-proADM	CT-proET-1
Age	0.31	0.18	0.27
Gender	0.16	0.34	
SOFA score	0.42	0.55	0.22
Creatinine	0.37	0.30	
Procalcitonin		0.25	0.26
WBC		0.16	

Results The mean age was 63.5 years. The mortality rate was 27% at a mean APACHE II score of 17.5. Table 1 presents individual regression coefficients if statistically significant. CRP levels did not correlate with any of the measured prohormones.

Conclusions Variations in the levels of measured prohormones are only slightly affected by parameters of inflammation. However, development of organ dysfunction is well reflected by proANP and MR-proADM but only to a lesser degree by CT-proET-1.

P197

Prognostic value of pro-atrial natriuretic peptide, pro-adrenomedullin, and pro-endothelin-1 in critically ill patients

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Critical Care 2006, **10(Suppl 1):**P197 (doi: 10.1186/cc4544)

Introduction Systemic inflammation is accompanied by cardiovascular dysfunction. Prohormones of cardiovascular active mediators may therefore add important information to the clinical status of these patients. The goal of this study was to describe the prognostic value of three different prohormones in an ICU setting.

Methods Citrate plasma samples of 185 patients with either severe sepsis/septic shock ($n = 120$) or systemic inflammatory response syndrome (SIRS; $n = 65$) after coronary bypass surgery have been obtained on admission to the ICU. Midregional pro-atrial natriuretic peptide (MR-proANP), midregional pro-adrenomedullin (MR-proADM), and C-terminal pro-endothelin-1 (CT-proET-1) have been measured by an immunoassay (BRAHMS AG, Germany). The prognostic value for ICU survival was estimated by the area under the curve (AUC) of the receiver–operating characteristics (ROC).

Results The mean age was 63.5 years. The mortality rate was 27% at a mean APACHE II score of 17.5. AUC values and 95% CIs are presented in Table 1. The AUC of the APACHE II score to predict survival in this study was 0.70 (0.61; 0.80).

Table 1 (abstract P197)

	Admission value	ROC AUC	95% CI
MR-proANP	199.7 pmol/l	0.66	0.57; 0.74
MR-proADM	2.3 nmol/l	0.68	0.59; 0.77
CT-proET-1	70.5 pmol/l	0.64	0.56; 0.73

Conclusion Elevation of all three parameters is significantly associated with a poor prognosis in critically ill patients. Outcome prediction is similar to the APACHE II score.

P198

Impact of positive fluid balance on ICU outcome is influenced by the severity of illness

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Introduction Less fluid gain has been suggested to be associated with better survival of ICU patients. We investigated whether the positive fluid balance itself or rather the severity of illness is the major determinant of ICU mortality.

Materials and methods Four hundred and seventeen medical and surgical adult patients admitted to the general ICU of Tartu University Clinics during 2004 and 2005 were retrospectively studied. Eighty patients were excluded due to missing data.
Results The total ICU mortality was 29%. The survivors had significantly smaller fluid gain during the admission day than nonsurvivors (2.6 ± 3.3 l vs 4.7 ± 6.4 l; $P < 0.001$). The fluid gain was significantly smaller in survivors who had SOFA score ≤10 (2.4 ± 3.3 l vs 3.8 ± 5.6 l in nonsurvivors; $P = 0.026$), but not for those with SOFA score >10 (4.3 ± 3.7 l vs 5.3 ± 6.9 l; $P = 0.525$). The fluid balance had no impact on the outcome of the latter subgroup of patients, having lactate >4 mmol/l. However, if these patients had lactate <4 mmol/ they significantly benefit from positive fluid gain (Table 1).

Table 1 (abstract P198)

Fluid gain on the day of admission to the ICU in subgroups of patients (liters)

SOFA score (points)	Lactate (mmol)	Survivors	Nonsurvivors	*P* value
< 10	< 4	2.3 ± 3.1	3.6 ± 2.8	0.074
< 10	> 4	4.0 ± 4.3	4.8 ± 8.0	0.695
> 10	< 4	4.4 ± 3.3	1.5 ± 1.5	0.011
> 10	> 4	4.0 ± 4.6	6.3 ± 7.5	0.296

Data presented as mean ± SD.

Conclusions The fluid gain during the admission day is associated with increased mortality of ICU patients. Subgroup analysis revealed that this was true for less severely ill patients (SOFA score ≤10), but not for patients with SOFA score >10. The positive fluid balance *per se* is not necessarily fatal and its effect on outcome is mainly dependent on the severity of illness.

P199

Determination of 'unmeasured' anions in acidotic ICU patients

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Metabolic acidosis is one of the most frequent acid–base disorders occurring in the ICU. Major causes of metabolic acidosis in critically ill patients are hyperchloremia, hyperlactatemia and the presence of anions of unknown identity, the so-called 'unmeasured' anions. The latter is associated with increased mortality and several diseases: sepsis, shock, liver dysfunction and renal failure. The physicochemical approach described by Stewart can be applied to quantify metabolic acidosis. Accordingly, the strong ion gap (SIG) is a quantitative measure of 'unmeasured' anions. We hypothesised that derangements in amino acid and organic acid metabolism and abnormal uric acid concentrations could be an explanation for the SIG.
From 32 adult ICU patients with metabolic acidosis, defined as a pH less than 7.35 and a base excess less than −5 mmol/l, the SIG was calculated in a single arterial blood sample. Two groups were compared: patients with SIG <2 mEq/l and patients with SIG >5 mEq/l. 'Unmeasured' anions were examined quantitatively by ion-exchange column chromatography, reverse-phase HPLC and gas chromatography/mass spectrometry measuring, respectively, 25 amino acids, uric acid and organic acids. Some organic acids were determined semi-quantitatively. The Mann–Whitney U test was applied for significance (considered $P < 0.05$) in all cases. For nominal data, the chi-square test was used.
Aspartic acid, isoleucine, ornithine, uric acid, succinic acid, fumaric acid, p-OH-phenyllactic acid and the semi-quantified organic acids 3-OH-isobutyric acid, pyroglutamic acid and homovanillic acid were all significantly elevated in the SIG >5 group ($n = 12$, mean = 8.3 mEq/l) compared with the SIG <2 group ($n = 8$, mean = 0.6 mEq/l). Generally, no major differences in organic acid spectra between both groups were observed. However, in one patient in the SIG >5 group who was in a prolonged fasted state at ICU admission, 3-OH-butyric acid was extremely high: 4.0 mEq/l, corresponding to 25% SIG. Overall, the averaged difference between both groups in total amino acid, uric acid and organic acid concentration contributed to the SIG for, respectively, 3.5% (268 μEq/l, not significant), 2.2% (169 μEq/l, $P = 0.021$) and 1.0% (79 μEq/l, $P = 0.025$). The total organic acid concentration consisted of glycolic acid, oxalic acid, methylmalonic acid, succinic acid, fumaric acid, malic acid, adipic acid and p-OH-phenyllactic acid. Comparison of patient characteristics of both groups showed that age, sex, APACHE II score, pH, base excess and lactate were not significant. However, renal insufficiency, sepsis and mortality were more prominent in the SIG >5 group. Also, the apparent strong ion difference (due to a significantly lower plasma chloride), phosphate and urea were significantly elevated in the SIG >5 group.
This study demonstrates that total amino acids, uric acid and organic acids form a minor contribution (6.8%, corresponding to 517 μEq/l) to the SIG in acidotic ICU patients.

P200

Hyperchloremic metabolic acidosis after cardiac surgery

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Background Hyperchloremic metabolic acidosis (HCMA) after cardiac surgery is iatrogenic and is due to large volumes of saline infused perioperatively [1]. The aim of the study was to determine the incidence, the clinical implications and the duration of this acid–base disorder in cardiac surgery.
Methods One hundred patients who underwent cardiac surgery with cardiopulmonary bypass (CPB) were included prospectively. Exclusion criteria were: diabetes mellitus, pre-existing acid–base abnormalities, postoperative renal failure or low cardiac output syndrome. All patients received crystalloid (0.9% saline or Ringer's) and colloid solutions (gelatin). Sampling of arterial blood for gas, acid–base parameters and serum electrolytes were performed at four time points: 30 min after induction of anesthesia (T1), after completion of CPB (T2), at 6 hours (T3) and at 24 hours postoperatively (T4). Values are given as the mean ± SD. We registered the volume of solutions administered intraoperatively and in the first 24 hours postoperatively as well as complications: bleeding, cardiac arrhythmias and organ dysfunctions. (renal, pulmonary or neurological). For statistical analysis we used a *t* test ($P < 0.05$).
Results Sixty-six patients (66%) presented a simple normal-anion gap hyperchloremic acidosis. Twenty-seven patients had no acidosis. The results of the arterial blood sampling are presented in Table 1. The infused volumes are presented in Table 2.
Cardiac arrhythmias were more frequent in patients with HCMA compared with those with no acidosis. There were no statistical differences in the incidence of bleeding or organ dysfunctions.
Conclusions HCMA due to saline infusion is common after cardiac surgery. However it is transient (less than 24 hours). Due to the low number of patients in our study, the clinical relevance of

Table 1 (abstract P200)

	T1	T2	T3	T4
Chloride (mmol/l)	103 ± 3.5	113 ± 5.1	111.8 ± 3.6	108.5 ± 4.1
pH	7.4 ± 0.04	7.34 ± 0.06	7.35 ± 0.06	7.4 ± 0.03
$paCO_2$ (mmHg)	37.2 ± 5.01	34.8 ± 4.5	37.3 ± 5.9	37.5 ± 4.6
Base excess (mmol/l)	−1.4 ± 1.2	−5.9 ± 2.1	−6.33 ± 2.3	−0.9 ± 3.5
Bicarbonate (mmol/l)	22.7 ± 2.0	19.2 ± 1.8	20.6 ± 3.7	23.8 ± 2.9
Anion gap (mmol/l)	11.4 ± 3.1	8.4 ± 2.1	12.7 ± 2.5	10.6 ± 2.9

Table 2 (abstract P200)

	Intraoperative (ml)	Postoperative (ml)
Crystalloids	2680 ± 853	1687 ± 696
Colloids	500 ± 254	805 ± 420
Bicarbonate	40 ± 15	35 ± 25
Tromethamol	0	613 ± 156

this metabolic acidosis is not clear. The major risk is of undesirable interventions.

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P201

Prediction of arterial blood gas values from earlobe blood gas values in patients receiving mechanical ventilation

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Background Arterial blood gas (ABG) sampling represents the gold standard method for acquiring patients' acid–base status. The most common complications associated with arterial puncture are pain, arterial injury, and thrombosis with distal ischemia, hemorrhage, and aneurism formation. Earlobe blood gas samplings (EBG) may be useful alternatives to ABG sampling. This study evaluates whether the pH, partial pressure of oxygen (PO_2), partial pressure of carbon dioxide (PCO_2), base excess (BE), and bicarbonate (HCO_3^-) values of EBG accurately predict their ABG analogs for patients treated by mechanical ventilation in an ICU.
Methods Sixty-seven patients who were admitted to the ICU and treated by mechanical ventilation were included in this descriptive study. Blood for ABG analysis was sampled from the radial or brachial arteries. Blood for EBG analysis was sampled simultaneously from ear lobe by contact with a capillary tube tip. Regression equations and mean percentage-difference equations were derived to predict arterial pH, PCO_2, PO_2, BE, and HCO_3^- values from their EBG analogs.
Results A total of 67 simultaneous arterial and earlobe blood samples were obtained from 67 patients. The pH, PCO_2, BE, and HCO_3^- ere all significantly correlated in ABG and EBG. In spite of a highly significant correlation, the limits of agreement between the two methods were wide for PO_2. Earlobe values of PO_2 were usually lower than arterial values, with larger differences in the range of normal arterial PO_2. On the other hand, the error and the limits of agreement were smaller for PCO_2. Regression equations for prediction of pH, PCO_2, BE, and HCO_3^- values were: arterial pH (pHa) = 1.81 + 0/76 × earlobe pH (pHe) [r = 0.791, $P < 0.001$]; $PaCO_2$ = 11/44 + 0/7 × earlobe PCO_2 ($PeCO_2$) [$r = 0.774$, $P < 0.001$]; arterial BE (BEa) = 1/14 + 0/95 × earlobe BE (BEe) [$r = 0.894$, $P < 0.001$], and arterial HCO_3^- (HCO_3^-a) = 1/41 + earlobe HCO_3^- (HCO_3^-e) [$r = 0.874$, $P < 0.001$]. The predicted ABG values from the mean percentage-difference equations were derived as follows: pHa = pHe × 1.001; $PaCO_2$ = $PeCO_2$ × 1.04; BEa = BEe × 0.57; and HCO_3^-a = HCO_3^-e × 1.06.
Conclusions Earlobe blood gas can accurately predict the ABG values of pH, PCO_2, BE, and HCO_3^- for patients receiving mechanical ventilation.

P202

Does the arterial–central venous lactate gradient correlate with the P/F ratio in mechanical ventilated critically ill patients?

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Introduction There is evidence about pulmonary production and release of lactate during acute lung injury. The aim of this study was to evaluate whether the arterial–central venous lactate gradient (AVLG) is correlated with the P/F ratio in general ICU patients.
Methods Twenty-four patients requiring mechanical ventilation for at least 72 hours were enrolled. During the first 72 hours, we prospectively collected and recorded central venous and arterial blood samples to analyse blood gases and serum lactate every 24 hours. Ventilator settings as well as general patient characteristics were also recorded. Data are shown as the median and interquartiles. The Spearman correlation test was used and $P < 0.05$ was considered significant.
Results Eleven females and 13 males were evaluated. Median age was 49 (42, 65) years old and the APACHE II score was 23 (19, 33). One-half of patients were admitted with septic shock diagnosis. Four patients had the diagnosis of acute lung injury or acute respiratory distress syndrome at enrollment. The median PEEP was 10 (8, 12) cmH_2O, FiO_2 was 0.4 (0.3, 0.5) and the P/F ratio was 229 (159, 315). The AVLG was evaluated as the variation [(arterial – venous lactate) / arterial lactate] and its median was 0.00 (–0.20, 0.08). In overall group analysis ($n = 70$), the P/F ratio and AVLG correlation was –0.05 ($P = 0.670$). In the P/F ≤ 200 subgroup analysis ($n = 25$), the P/F ratio and AVLG correlation was 0.08 ($P = 0.709$).
Conclusions Even though the lungs may produce and release lactate in some patients as sepsis and acute respiratory distress syndrome subjects, we could not find a correlation between the AVLG and the P/F ratio in a general population of critically ill patients. However, our results are probably underpowered.

P203

Plasma lactate and base excess as independent prognostic factors

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Objective To investigate the levels of lactate and base access (BE) as independent prognostic factors of the mortality of newly admitted patients compared with the existing scoring systems (SAPS II and APACHE II).

Table 1 (abstract P203)

	n	SAPS II	APACHE II	Plasma lactate
Survived	50	43.49 ± 15.45	18.22 ± 7.74	20.74 ± 15.15
Died	38	63.68 ± 17.1	26.37 ± 6.14	32.60 ± 25.32

Table 2 (abstract P203)

	n	SAPS II	APACHE II	Base excess
Survived	70	43.49 ± 15.45	18.22 ± 7.74	−13.46 ± 42.84
Died	53	63.68 ± 17.1	26.37 ± 6.14	−33.60 ± 39.40

Participants All the newly admitted patients in an eight-bed ICU regardless of the cause of admission.
Methods Lactate and BE levels were measured at the time of admission along with the SAPS II and APACHE II scores. Patient outcome at 28 days was also documented.
Results See Tables 1 and 2. Statistical analysis using a paired *t* test was performed, indicating a statistical significant difference $P < 0.001$ for SAPS II and $P < 0.000$ for the APACHE II score, and $P < 0.008$ for the lactate and BE levels between the two groups.
Conclusion Lactate levels and BE appear to be independent prognostic factors for the 28-day mortality of the newly admitted patients in the ICU.

P204

Osmolar gap as an individual prognostic factor (revised data)

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Objective The assessment of the validity of the osmolar gap (OG) as an independent prognostic factor for the mortality of the newly admitted patients compared with the SAPS II and APACHE II scores.
Participants All the newly admitted patients in two 12 (6 + 6)-bed ICUs regardless of the cause of admission.
Method Measurement of the freezing point and simultaneous calculation (using the known formula) of plasma osmolarity in every patient at the time of admission. Patient data and the overall outcome at 28 days were documented.
Results See Table 1. The findings were statistically analysed using a paired *t* test and a statistically significant difference was obtained ($P < 0.001$ for SAPS II and OG scores, and $P < 0.000$ for APACHE II and OG scores, respectively). In addition ROC analysis disclosed for OG an area under the curve of 0.745 ± 0.040 (SE).

Table 1 (abstract P204)

	n	SAPS II	APACHE II	Osmolar gap
Survived	90	43.49 ± 15.45	18.22 ± 7.74	11.06 ± 8.83
Died	70	63.68 ± 17.1	26.37 ± 6.14	24.81 ± 24.82

Conclusion The OG appears to have good correlation with the existing clinical scoring systems and therefore it might be used as an independent prognostic factor. To find out the appropriate cutoff point for the OG obviously requires a greater number of patients in the present study, which is still underway.

P205

Assessment of stress oxidative modulation when conventional parenteral solutions were used compared with nutrition based on an olive oil compound in multiple trauma patients

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Critical Care 2006, **10(Suppl 1):**P205 (doi: 10.1186/cc4552)

Introduction We studied metabolic parameters from oxidative stress response in trauma patients when using intravenous nutrition with Oliclinomel (an olive/soybean oil mixture characterized by an essential fatty acids content of 20%) or Nutriflex (an soybean oil composition).
Methods A prospective, randomized study was conducted in a 16-bed ICU during an 8-month period: family informed consent and institutional agreement were obtained in 43 consecutive intubated multiple traumatic patients with Injury Severity Scores of 23.2 ± 10.6; 22 patients received Oliclinomel N7 (O group [Og]) and 21 patients received Nutriflex Energy (N group [Ng]) to reach equal caloric support in the two groups (50% of the energy demand at day 1 to 100% at day 3). Oxidative parameters were measured every day by blood sample analyses and capnography was used continuously. Every patient was sedated and ventilated (Vc: 6 ml/kg; rate: 12/min; PEEP 5 ± 3 mmHg) by the same approach. The study stopped on day 4 at the beginning of enteral nutrition. For statistical analysis, a Shapiro–Wilk test, a Wilcox test and a Student *t* test were used.
Results The ratio between the total energy intake and the energy expenditure was similar in both groups (Og: 0.75 ± 0.17; Ng: 0.86 ± 0.26, $P = 0.24$). The nitrogen balance was negative for all patients and showed no significant difference ($P = 0.08$). The daily amino supply showed no significant difference (Og: 0.7 ± 0.2; Ng: 0.8 ± 0.2 kcal/kg; $P = 0.17$).
The daily glucose intake was similar in both groups, but with a lower significant trend in Og showing a more stable glucose/insulin ratio ($P < 0.05$) with a significant lower average PCO_2 production (Og: 38 ± 5 mmHg; Ng: 68 ± 12 mmHg) ($P < 0.01$). The daily lipid intake was higher in Og (Og: 0.8 ± 0.3; Ng: 0.5 ± 0.1 g/kg; $P < 0.001$). The ratio triglyceride/cholesterol level was not different between groups. No fat emboly occurred in all the study population. Infection rates where similar in both groups.
Conclusion The main purpose for controlling stress oxidation is to diminish eicosanoide production [1]. By modifying the n-6/n-3 ratio in new parenteral solution we can protect the cellular membrane and promote a glucose/insulin ratio stability avoiding also further CO_2 production.
Reference
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P206

Utilisation of structured triglycerides (Structolipid®) in surgical ICU patients receiving parenteral nutrition

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Background Within the frame of postoperative total parenteral nutrition, a frequent consequence due to postaggression metabolism is an inhibition of lipoprotein lipase leading to hypertriglyceridemia. The aim of this study was to investigate whether the administration of structured triglycerides (TGs) compared

with conventional lipid emulsions led to a better utilisation of the lipids.
Methods A prospective randomized study. After approval of the ethical committee, 45 postoperative surgical patients with an indication for parenteral nutrition therapy were included in the study. Nonprotein calories were given as 60% glucose and 40% lipid emulsion. The total energy intake per day was 25 kcal/kg body weight. Sedation regimen was standardized. Patients were divided into three groups: Group A ($n = 15$) received structured TGs (Structolipid® 20%), group B ($n = 15$) received a MCT/LCT physical mixture (Lipofundin® 20%) and group C ($n = 15$) received a pure LCT lipid emulsion (Lipovenoes® 20%). Lipid emulsions were administered for 5 days postoperatively, corresponding to the observation time. TG levels were measured before the start of infusion (d0), at day 1 (d1), day 2 (d2), day 3 (d3) and day 5 (d5) after the start of infusion. The significance level was defined at $P < 0.05$.
Results There were no significant differences in TG levels at d1 and d2, whereas at d3 and d5 the TG levels in group A (d3: 140 ± 31 mg/dl; d5 134 ± 36 mg/dl) were significantly lower than in group B (d3: 220 ± 91 mg/dl; d5 177 ± 52 mg/dl) and group C (d3: 239 ± 136 mg/dl; d5 256 ± 156 mg/dl).
Conclusions The administration of structured lipid emulsions within a parenteral nutrition regimen led at d3 and d5 of the nutrition regimen to significantly reduced TG levels compared with a MCT/LCT physical mixture or a pure LCT lipid emulsion.

P207

Immunonutrition with eicosapentaenoic acid and γ-linolenic acid as a new strategy to reduce mortality and improve outcomes in patients with severe sepsis

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Introduction Enteral diets enriched with EPA (fish oil), GLA (borage oil) and elevated levels of antioxidant vitamins are capable of ameliorating several outcomes in patients with ARDS. Several studies using animal models of sepsis point towards a possible role of enteral nutrition enriched with omega-3 fatty acids in the reduction of mortality.
Hypothesis This study investigates whether an enteral diet enriched with EPA, GLA and elevated levels of antioxidants can improve outcomes and reduce 28-day all-cause mortality in patients with severe sepsis or septic shock under mechanical ventilation.
Methods This is a prospective, double-blind, placebo-controlled, randomized trial. One hundred and sixty-five patients with either severe sepsis or septic shock were enrolled. Patients were randomized and continuously tube-fed either EPA, GLA and elevated antioxidants or a control diet isonitrogenous and isocaloric to the study diet and delivered to achieve a minimum of 75% of basal energy expenditure × 1.3 during a minimum of 4 days.
Results Septic patients fed EPA, GLA and elevated antioxidants showed a significant reduction in mortality rate, with an absolute reduction of 19.4% ($P = 0.037$). The EPA+GLA-fed group also presented significant improvements in oxygenation status from baseline to study days 4 and 7, more ventilator-free days (13.4 vs 5.8, $P < 0.001$), more ICU-free days (10.8 vs 4.6, $P < 0.001$) and significantly less development of new organ dysfunctions during the follow-up period ($P < 0.001$).
Conclusions An enteral formulation enriched with EPA, GLA and elevated antioxidants can contribute to better ICU and hospital outcomes, and is also associated with lower mortality rates of septic patients under mechanical ventilation. The beneficial effects of this diet suggest that this enteral nutrition formula would be a useful adjuvant therapy in the clinical management of sepsis.

P208

Continuous L-arginine infusion does not deteriorate the haemodynamic condition in patients with severe sepsis

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Introduction Septic patients have reduced plasma arginine (ARG) levels, and have been considered ARG deficient. This has resulted in the use of ARG-enriched enteral formulas, which recently raised much concern. These formulas, however, also contain other components besides ARG. ARG is the precursor for nitric oxide, a known vasodilator. Since little is known about the haemodynamic effects of continuous i.v. ARG supplementation as a single component in sepsis, we aimed to study dose–response effects of ARG in severe septic patients.
Methods Eight ICU patients with severe sepsis/septic shock (<48 hours) were included. APACHE II scores ranged between 27 and 43. Norepinephrine dose ranged between 0.05 and 0.8 μg/kg/min. After 2 hours baseline, L-ARG-HCl was infused continuously in three stepwise increased doses (0.6, 1.2 and 1.8 μmol/kg/min), each dose for 2 hours. Haemodynamics were recorded at 30-min intervals. Plasma arginine levels were analysed by HPLC. Repeated-measurements ANOVA was used to compare doses; data are means ± SEM.
Results No significant changes in systemic blood pressure were observed. Compared with plasma ARG levels of age-matched healthy subjects (81 ± 5 μM), levels were reduced in our patients ($P < 0.05$). The heart rate decreased during ARG supplementation and the stroke volume increased (Table 1).

Table 1 (abstract P208)

	Baseline	0.6	1.2	1.8	*P*
Plasma arginine (μM)	49 ± 2	86 ± 5	136 ± 7	192 ± 9	<0.01
MAP (mmHg)	75 ± 7	80 ± 6	79 ± 4	80 ± 4	
HR (beats/min)	101 ± 6	101 ± 7	96 ± 6	95 ± 6	<0.05
Stroke volume (ml/beat)	78 ± 3	81 ± 3	83 ± 5	88 ± 4	<0.05

Conclusions ARG infusion does not affect systemic and pulmonary blood pressure, but increases the cardiac stroke volume. This indicates that continuous ARG supplementation does not deteriorate the haemodynamic condition in severe septic patients, despite its vasodilating effect.
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P209

Cellular immunity changes after total parenteral nutrition enriched with glutamine in patients with systemic inflammatory response syndrome

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The immune status is altered in patients with systemic inflammatory response syndrome (SIRS). Nutrition is one of the most important

treatments for these patients, improving body protein and immune function, reducing the rate of infection and shortening hospitalization. In this study, we administered intravenous glutamine supplementation to patients with SIRS in order to investigate the effect of glutamine supplementation on immune states.

This study is a prospective, randomized clinical trial. The APACHE II score and the SAPS II were used to evaluate the patients after admission. All patients received total parenteral nutrition (TPN) given continuously during 6 days. Thirty patients with SIRS were allocated to either a glutamine group (L-glutamine 0.4 g/kg/day) or a control group (glutamine-free, isonitrogenous, isocaloric formula). Blood samples were collected on day 1 and day 6 after admission for C-reactive protein, IgM, IgG, IgA, C3, C4 and lymphocyte analysis.

Although there was tendency to decrease T-sitotoxic cells and natural killer cells in the control group, no significant difference was observed between the two groups. However, an increase in lymphocyte and lymphocyte subgroups in the glutamine group was observed but there was no difference between groups. A low SAPS II was observed on the sixth day in the glutamine group whereas no difference in SAPS II and the APACHE II score were observed between the two groups.

The administration of TPN supplemented with glutamine causes enhancement in T-cell function in SIRS patients.

P210

Preoperative nutrition support with or without glutamine can reduce ICU admissions

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Background Malnourished elective major surgery patients are not routinely given nutrition support (NS) preoperatively in the Philippines owing to financial constraints and lack of evidence of benefit in the local patient population. Such patients frequently develop postoperative complications that may necessitate admission to the ICU. This pilot study was conducted to demonstrate the benefit of NS in such patients in terms of reduced ICU admissions.

Methods Thirty-six malnourished and lymphopenic elective abdominal surgical patients (BMI <18.5 kg/m^2 or weight loss >10% or SGA grade C) were given NS preoperatively for 5 days without (n = 18, group A) or with (n = 18, group B) parenteral glutamine. NS was given orally, enterally or parenterally in combinations to ensure delivery of energy 25–30 kcal/kg/day and of proteins 0.8–1.5 g/kg/day. For ethical reasons at the research centres, a control group (no NS) was not included.

Results Postoperatively, only one (2.7%) patient required ICU admission. Compared with historical data in similar patients (>20% incidence; $P < 0.05$) the difference was significant. Complications included one (2.7%) each of wound infection, respiratory infection and wound dehiscence. Unlike group A, group B showed significant ($P < 0.05$) increases in granulocyte, lymphocyte and monocyte counts, which returned to normal at 7 days post-operation. See Table 1.

Conclusions Preoperative NS resulted in a reduction in postoperative complications requiring ICU admission, at least in comparison with historical data of similar patients at the same institutions. Addition of glutamine to NS resulted in indicative immunologic benefits that may be worth further exploration.

P211

Role of preoperative nutritional assessment on early postoperative wound infection

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Objectives To study the prevalence of malnutrition in surgical patients. To identify the patients at risk of early postoperative wound infection. To observe the pattern of wound healing in various groups of surgical patients based on their preoperative nutritional status.

Design A descriptive study in the surgical department at Jinnah Hospital Lahore, Pakistan.

Participants One hundred patients presenting to surgical OPD since 1 January 2001.

Methods Serum albumin levels and the BMI of these patients were evaluated and patients were assigned to a group according to their nutritional status.

Main outcome measures Adding all patients in groups II, III, and IV and dividing by the total number of patients in the study determined the prevalence of malnutrition. Wounds of all patients were examined on the third postoperative day and the wound category was recorded. Wound infection was observed in various nutritional status groups.

Results The prevalence of malnutrition in surgical patients is 70%. Wound infection was present in all groups of patients except group I. Patients in groups II and IV had more severe wound infection.

Conclusions Malnutrition is common in surgical patients. Hypoalbuminemia is associated with increased risk of early postoperative wound infection. The BMI has no direct effect on early postoperative wound infection. Further studies are needed to explore the role of other parameters of nutritional assessment on early postoperative wound infection in patients with different demographic factors.

Table 1 (abstract P210)

	WBC (/mm^3) [median (IQR)]					
	Group A			Group B		
	Preoperative day 7	Day of operation	*P* value	Preoperative day 7	Day of operation	*P* value
Granulocytes	4406.5 (3418–6221)	5019 (4455–7368)	0.07	6179 (4344–8664)	9124 (6154–12,920)	0.04
Lymphocytes	1689 (879–2326)	1624 (790–2347)	0.33	1486 (974–1711)	1773 (1361–2285)	0.02
Monocytes	526 (382–769)	569 (395–790)	0.39	613 (440–818)	648 (392–912)	0.02
Total WBC	6655 (5690–8640)	7440 (6120–9670)	0.14	8760 (5900–11,270)	11,490 (8430–15,200)	0.06

P212

Impact of synbiotics (Synbiotic 2000 Forte) on monocyte function in long-term ICU patients

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Critical Care 2006, **10(Suppl 1):**P212 (doi: 10.1186/cc4559)

Introduction The impact of synbiotics on enteral feeding tolerance and immune function has been studied. We designed a protocol monitoring impact of synbiotics on these variables in long-term ICU patients.
Patients and methods Patients estimated on D1 (D0 = admission) to stay in the ICU >3 days were randomized (according to age, sex, SOFA score and diagnosis group) to postpyloric placebo (tea) or treatment (Synbiotic) groups. Monocyte function was monitored on D1 and then at 5-day intervals; enteral nutrition (EN) was given according to the standard ICU protocol.
Preliminary analysis of early development (D1–D5–D10) of $CD14^+HLADR^+$ expression and tolerance of enteral feeding is reported. Data are presented as the median (Q25; Q75). Kruskal–Wallis ANOVA and Wilcoxon tests were used when appropriate, $P < 0.05$ considered significant.
Results Twelve patients (10 male, two female; age 54 [39; 63] years) were randomized and 11 were eligible for analysis (Synbiotic $n = 6$, placebo $n = 5$). Ten patients survived the ICU stay (S), and one did not (NS). The APACHE II score on admission was 22 (21; 26.5). The course of $CD14^+HLADR^+$ did not differ in the Synbiotic/placebo groups (Table 1). In two placebo and no Synbiotic patients a significant drop of 15% was measured. The amount of EN (10 days) is higher in the Synbiotic than the placebo group (6930 ml [6490; 7292] vs 5010 ml [4747; 5237], $P < 0.05$), as was the frequency of stool (9 [4; 14] vs 1 [0; 4], $P = 0.13$).

Table 1 (abstract P212)

	$CD14^+HLADR^+$		
	Day 1	Day 5	Day 10
Synbiotic ($n = 6$)	49 (33; 59)	60 (56; 72)	71 (65; 79)
Placebo ($n = 5$)	54 (33; 66)	57 (44; 57)	53 (51; 57)

Conclusion Preliminary data do not show a major impact of synbiotics on monocyte function. Tolerance of EN seems to be better in the synbiotics group.

P213

The effect of enteral synbiotics on the incidence of ventilator-associated pneumonia in mechanically ventilated critically ill patients

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Introduction Ventilator-associated pneumonia (VAP) affects between 8% and 28% [1] of mechanically ventilated patients. A novel way of reducing the incidence of VAP may be the use of enteral synbiotics. Synbiotics may reduce VAP directly (reducing pathogenic organisms in the proximal gut) or indirectly (improving host immunity) [2].
Objective To determine the effect of enteral Synbiotic 2000 FORTE® (a mixture of lactic acid bacteria and fibre) on the incidence of VAP in critically ill patients.
Design A prospective, randomised, double-blind, placebo-controlled trial in the 14-bed general ICU of a UK university hospital.
Participants Mechanically ventilated, enterally fed, critically ill patients were recruited over a 13-month period.
Methods Patients were enterally fed as per the ICU protocol and were randomly assigned to receive either synbiotic 2000 FORTE® (twice a day) or a cellulose-based placebo, throughout the ICU stay. Oropharyngeal swabs were obtained on days 0, 4 and 7.
Measurements and results The treatment group ($n = 130$) was well matched with the placebo group ($n = 129$) for age (median 53 and 50 years) and APACHE II score (median 17 for both). Oropharyngeal microbial flora and colonization rates were unaffected by synbiotics. The overall incidence of VAP was lower than anticipated (11.2%) and no statistical difference was demonstrated between synbiotic or placebo in the incidence of VAP (9% and 13%, $P = 0.31$), VAP rate per 1000 ventilator-days (13 and 14.6, $P = 0.73$) or hospital mortality (27% and 33%, $P = 0.32$), respectively.
Conclusions The incidence of VAP and mortality were not significantly decreased by the administration of Synbiotic 2000 FORTE®. These preliminary data indicate that synbiotics are unlikely to be harmful, although trends to benefit suggest a larger multicentre study may be warranted.
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P214

Erythromycin or metoclopramide for feed intolerance in the critically ill

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Critical Care 2006, **10(Suppl 1):**P214 (doi: 10.1186/cc4561)

Introduction In critical illness, nasogastric (NG) feeding is frequently compromised by delayed gastric emptying. This is usually treated by administration of prokinetics, such as metoclopramide or erythromycin. Data on the relative and individual effects of these agents, in critically ill patients, are limited. In addition, erythromycin has been reported to cause hypotension, which could compromise splanchnic perfusion.
Objectives To compare metoclopramide (M) and erythromycin (E) in the initial treatment of feed intolerance in critical illness, to determine the success of combination treatment in patients who fail to respond to a single agent, and to examine the effect of E on blood pressure (BP).
Methods Ninety feed-intolerant (6-hourly NG aspirate >250 ml) mechanically ventilated patients (mean APACHE II score = 21.4 ± 0.6) were randomly allocated to receive either M ($n = 45$; 10 mg i.v. four times daily) or E ($n = 45$; 200 mg i.v. twice daily) in a prospective, double-blind randomized fashion. Age, sex, APACHE II scores and initial gastric residual volumes were similar between the two groups. After the first dose of prokinetic therapy, NG feeding was restarted at 40 ml/hour and increased in a standardized fashion and 6-hourly NG aspirates were performed. If NG aspirate >250 ml recurred, combination therapy was commenced. Patients were studied for 7 days. The BP was recorded.

Results Inotrope, opioid and benzodiazepine usage, and blood glucose concentrations were similar in the two groups. After 24 hours of treatment, both M and E significantly reduced 24-hour gastric residual volumes (M: 830 ± 32 ml to 435 ± 30 ml, $P < 0.0001$; E: 798 ± 33 ml to 201 ± 19 ml, $P < 0.0001$) and improved the proportion of patients with successful feeding (no aspirate >250 ml; M: 62% and E: 87%). Treatment with E was more effective than with M ($P < 0.05$). The effectiveness of both treatments on subsequent days declined rapidly. In patients who failed single-agent therapy, combination therapy was highly effective (day 1, 92%) and its effectiveness was maintained for the duration of the study (day 6, 77%). Predictors of poor response to single or combined prokinetic therapy included increased age, APACHE II score, pretreatment gastric residual volume, trauma, and abnormal renal function. E caused a nonsignificant reduction in systolic BP (+1.0 ± 0.9 vs −3.6 ± 0.9 mmHg, P = NS) and diastolic BP (−0.1 ± 0.9 vs −1.7 ± 1.1 mmHg, P = NS).
Conclusions Erythromycin is safe and more effective than metoclopramide in treating feed intolerance in critical illness; however, rapid tolerance occurs to both agents when used individually. In patients who develop feed intolerance on a single agent, combination therapy is effective with little evidence of tolerance. The role of combined therapy as initial treatment requires further evaluation.

P215

Prospective observational study of self-placing nasojejunal tubes (Tiger Tube) on the ICU

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Introduction Nutritional support is vital to improving the clinical outcomes in patients on the ICU. Enteral nutrition should be administered early and aggressively, thereby reducing the need for parenteral nutrition (TPN). Nasogastric (NG) feeding may not be tolerated due to gastroparesis, small and large bowel ileus associated with drugs and/or surgery.
Objectives We hypothesised that if NG feeding was not tolerated within 24 hours, following suitable use of prokinetics, then a self-propelling nasojejunal (NJ) tube (Tiger Tube [TT tube]; Wilson Cook, USA) would be placed and NJ feeding commenced reducing TPN requirements.
Design A prospective observational study.
Methods We prospectively monitored patients with NG feeding intolerance. If enteral feed was not tolerated, patients were commenced on prokinetic agents (metaclopramide 10 mg three times daily i.v. and or erythromycin 250 mg i.v.). Despite prokinetic therapy, if still intolerant a TT tube was placed. One hour pre-TT and 4 hours post-TT placement patients received erythromycin (500 mg i.v.). The TT tube was placed according to the manufacturer's protocol. (The NG tube was also left *in situ* for aspirate assessment.) Abdominal X-ray was performed 6 hours after initiation of TT placement to confirm location and NJ feeding commenced.
Results NJ feeding was commenced promptly on medical and surgical patients intolerant of standard NG feeding, and placement of the TT tube was successful (35/40 patients, 87.5%). Estimated savings in patient days of TPN have been illustrated in Table 1 ($n = 40$).
Conclusion The TTs were easily placed aided by prokinetics (87.5%). All tubes were placed by the nurse/doctor at the bedside and did not require endoscopic placement. Significant financial and manpower resources have been saved by a simple bedside technique. No clinical complications were noted with the use of TT tubes in our study. A randomised study is now planned.

P216

Sonography as a tool to confirm the position of the nasogastric tube in ICU patients

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Introduction More than 80% of ICU patients are fed enterally via nasogastric or nasoenteric tubes. Incorrect placement of these tubes, however, can have fatal consequences for these patients. Several methods have been used to ensure proper placement of the nasogastric tube before starting enteral feeding. Our aim was to estimate the value of bedside sonography (ATL, ultramark9) in confirming the position of a common radio-opaque nasogastric tube (NG-Levin) and compare this procedure with simple radiography.
Methods A prospective study in a five-bed ICU over a 5-month period from May to September 2005. Confirmation of the nasogastric tube position was made by sonographically identifying the air bubble that comes out of the Levin after injecting a 10 cm^3 mixture of 5% dextrose and air as well as by standard radiography. All NG tubes where inserted by the same individual. The success and the accuracy of the procedure, as well as the procedure times for both sonography and radiography, were recorded and compared. The APACHE score was estimated for every patient.
Results Sixteen patients were included in the study, nine of them men and seven women, with a mean age of 66.3 ± 7.1 years and a mean APACHE II score of 21 ± 5.2. All patients were intubated and mechanically ventilated. The nasogastric tube position was confirmed sonographically in 15 out of 16 patients. In one case the ultrasound failed to produce results due to gas interposition. The nasogastric tube position was also confirmed radiographically. The median procedure time was 14.93 ± 1.71 min for sonography and 84 ± 30.64 min for radiography ($P < 0.001$). No case of mispositioning occurred.
Conclusion Bedside sonography is a sensitive method for confirming the position of nasogastric tube. It is easy to perform by ICU physicians, it is an easy procedure to be learned and it is quicker than conventional radiography.

Table 1 (abstract P215)

	Patient groups		APACHE score		Days of NJ feeding		Negative TPN days	
Percentage placed	Surgical patients	Medical patients	Surgical patients	Medical patients	Surgical patients	Medical patients	Surgical patients	Medical patients
87.5	25/40	15/40	20 ± 3	19 ± 3	15.0 ± 10.4	10.7 ± 1.7	125	75

P217

Effects of hypocaloric feeding on clinical outcome in ICU patients

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Introduction The risk of a severe malnutrition is particularly high in critically ill patients. On the other hand, to administer feeding overcoming the metabolic need should be considered a significant risk factor and not a useful approach in improving the outcome of ICU patients. To this purpose, a hypocaloric nutritional support has been proposed. It may satisfy the patient's caloric–proteic needs, and supply energy enough aimed to avoid the adverse effects of the stress-related metabolic response. The present study aimed to evaluate the nutritional support management in our ICU, and to assess the relative role of the enteral nutritional therapy on morbidity.
Methods One hundred and fifty-one out of 194 adult patients admitted to our polyvalent ICU from 1 January 2005 to 30 September 2005 were retrospectively analyzed. Patients younger than 18 years, those requiring a length of stay less than 3 days, patients with an ideal body weight >30%, and those on parenteral nutritional therapy were excluded from the study. The enteral nutritional support contained 55% carbohydrates, 30% lipids and 15% proteins, and was administered by means of either a nasogastric or orogastric probe. The estimated total caloric need for each patient was calculated with the Harris–Benedict formula. The correction factor of 1.2 was used for patients admitted to the ICU after severe head injury. Multivariate and receiver–operating characteristic (ROC) curve analyses were applied.
Results The daily average of theoretical kcals provided was 26.4 ± 6 kcals, with respect to 21.8 ± 3.4 kcals actually administered. Only 22% of patients received the amount of 90% of the theoretically calculated kcals. The ROC analysis identified a threshold of 70% for the theoretical/administered nutritional support ratio (T/A-NSR) value related to morbidity (the area under curve was 0.76; 95% CI = 0.681–0.843, $P < 0.05$). By using the threshold of 70% for the T/A-NSR value, we were able to split our patient population into two groups: group A, patients receiving a T/A-NSR value ≤70%, and group B receiving a T/A-NSR value >70%. The statistical analysis showed that morbidity, duration of mechanical ventilation, and ICU length of stay were higher in group A ($P < 0.05$).
Conclusion Our findings showed that administering a lower nutritional support (i.e. hypocaloric nutritional support) than the theoretically calculated calories is associated with increased morbidity. However, hyponutrition should be considered not only a direct risk factor for morbidity, but a result of bad outcomes. In fact, gastrointestinal problems often occur in critically ill patients, and the enteral nutrition may not be sufficiently adequate. In such cases, the only alternative to enteral nutrition is total parenteral nutrition. In conclusion, proof that limiting the hyponutrition improves outcomes in this setting awaits a sound prospective goal-oriented trial investigating one or more strategies to improve the nutritional management of the critically ill patient.

P218

Nutritional markers as a surrogate of severity of illness: association with ICU length of stay and mortality

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Introduction Nutritional status has been associated with several outcomes in critically ill patients, including prolonged ventilatory dependence, increased infection rate, prolonged ICU length of stay (ICU LOS) and mortality.
Objective To study the influence of several markers of nutritional status on ICU LOS and mortality.
Methods An observational study regarding several nutritional markers (serum albumin, nitrogen balance and caloric deficit) routinely recorded on our ICU and their association with ICU LOS and mortality. Appropriate descriptive statistics are presented Comparisons between groups were performed using the chi-square test, Student's *t* test or the nonparametric Mann–Whitney U test or Kruskal-Wallis test as appropriate. Analysis of the association between nutritional markers and mortality, estimated by the OR, unadjusted and adjusted for sex and SAPS II, were calculated using logistic regression. Multiple logistic regression modelling was performed, using the stepwise forward method, with mortality as the dependent variable and age, sex, nutritional markers and ICU variables (reason for ICU admission, SAPS II, ICU LOS) as independent variables. For the analysis of ICU LOS, and because of the right skewness of its distribution, a logarithmic transformation of this variable was used. Simple and multiple linear regression models were then used to study the association between nutritional and other factors and the ICU LOS, with the log-transformation of ICU LOS as the dependent variable. For hypothesis testing a value of $P < 0.05$ was considered significant. Statistical analysis was performed using SPSS 13.0® software package.
Results Ninety-one patients were included, of which 53 were male; mean age was 62 years. The reason for admission was medical in 68 patients, surgical in 16 patients and trauma in seven patients. The mean SAPS II was 45 and the median ICU LOS was 11 days. Patients surviving, patients with serum albumin lower than 2.5 g/dl, and those with a caloric deficit higher than –500 kcal/day exhibit a significantly shorter ICU LOS. In the linear regression model, however, these variables were no longer significantly associated with ICU LOS. Severity of illness (SAPS II) (OR 1.052; 95% CI 1.014; 1.091), nitrogen balance (OR 1.115; 95% CI 1.013; 1.228) and the need for parenteral nutrition plus enteral nutrition (OR 6.255; 95% CI 1.277; 30.645), were significantly associated with mortality in the logistic regression model. Caloric deficit was also significantly associated with mortality after adjustment for sex and SAPS II.
Conclusion Nutrition markers were associated with a longer ICU stay and a higher mortality. This hypothesis should be evaluated with more appropriate methodological approaches.

P219

Persistent hypoproteinemia is an independent risk factor for critical illness polyneuromyopathy

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Introduction Critical illness polyneuromyopathy (CIPM) is the leading cause of failure to wean in ICU patients without concomitant cardiorespiratory disease, resulting in a prolonged ICU stay and increased morbidity and mortality.
Objectives To estimate the epidemiologic characteristics of CIPM in a general ICU and to investigate the risk factors.
Patients and methods We prospectively evaluated 474 (323 male/151 female, age 55 ± 19 years) consecutive patients from August 2004 to September 2005 who were admitted to a general ICU and stayed for >24 hours. All patients were assigned admission APACHE II (15 ± 19) and SOFA (6 ± 3) scores and were subsequently evaluated for newly developed neuromuscular weakness. We examined muscle strength according to the Medical Research Council scale, deep tendon reflexes, sensory function and muscle wasting. Laboratory values and medical therapy were recorded daily. Other potential causes of new-onset generalized weakness after ICU admission were excluded before the diagnosis of CIPM was established.
Results Fifty (11%) out of 474 patients developed generalized weakness that met the criteria for CIPM. Patients with CIPM had a higher admission APACHE II score (19 ± 7 vs 14 ± 7, $P < 0.001$), SOFA score (8 ± 3 vs 6 ± 3, $P < 0.001$) and a higher mortality rate (30% vs 18%, $P < 0.05$). Multivariate logistic regression showed that risk factors independently associated with the development of CIPM were the duration of hypoproteinemia and APACHE II score during admission at the ICU. Other factors studied were the SOFA score at admission, use of inotropic and pressor agents, duration of enteral and parenteral nutrition, administration of colistin and the development of ventilator-associated pneumonia.
Conclusions CIPM has a high incidence in the general ICU population. The severity of illness and persistent hypoproteinemia are associated with an increased risk of the development of CIPM.

P220

Neuroimmune interactions for the prognosis the risk for stress ulcer formation in patients with peritonitis

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Introduction Acute gastroduodenal stress disorder-related ulcer is a major problem for treatment in patients with generalized peritonitis. Numerous studies have tried to identify some of the risk factors for stress ulcer formation in patients with peritonitis. The aim of this study was to investigate the most important changes of the immune system and neuroimmune interactions for the prognosis of the risk for stress gastroduodenal ulcer formation in patients with acute generalized peritonitis.
Methods We studied prospectively 320 patients aged 18–86 with acute generalized peritonitis of different etiology after an emergency operation. All patients were treated with broad-spectrum antibiotics and supportive therapy. Blood was collected 1, 3, 7 and 14 days after operation to determine lymphocyte subsets, plasma concentrations of IgA, IgM, IgG, and neuroreceptors (β-adrenoreceptors and cholinoreceptors) on the surface of lymphocytes.
Results Although most patients with acute peritonitis (94%) did not demonstrate clinical signs of ulcer, the incidence of stress ulcer was significantly higher (32% in nonsurvivors). Our findings revealed four types of neuroimmune interactions in patients with generalized peritonitis. Type I – patients (only 8% of patients) with active adrenoreceptors and cholinoreceptors; type II – patients (61%) with active cholinoreceptors in combination with blockade of β-adrenoreceptors on the surface of sensitized lymphocytes; type III – patients (16%) with active β-adrenoreceptors in combination with blockade of cholinoreceptors; type IV – patients (15%) with blockade of both β-adrenoreceptors and cholinoreceptors. Among the patients with proinflammatory complications in the postoperative period we observed mostly the III (40%) and IV (34%) types of neuroimmune interactions; and among the patients with an uncomplicated course of the postoperative period, type II (62%). In patients with stress ulcer formation in the postoperative period we diagnosed II and IV types of neuroimmune interactions. The index of stimulation of β-adrenoreceptors activity by adrenaline was decreased to 1.7 ± 0.09, and the index of stimulation of cholinoreceptors on the surface of lymphocytes by carbocholine was normal (1.62 ± 0.09 in type II) or below the normal level (0.8 ± 0.07). We did not reveal stress gastroduodenal ulcers in patients with I and III types of neuroimmune interactions.
Conclusions Dysfunction of neuroimmune interactions may explain a proneness towards weaker defense and formation of the stress disorder-related acute gastroduodenal ulcer. One of the contributing factors to the development of the stress ulcer in patients with acute generalized peritonitis is the condition of β-adrenoreceptors and cholinoreceptors on the surface of the lymphocytes.

P221

Effect of proton pump inhibitors on gastric volume, gastric pH and gastric intramucosal pH in critically ill patients in the ICU

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Objective In our study, we aimed to compare the effects of proton pump inhibitors in ICU patients with a control group for: hemodynamic parameters (heart rate, mean arterial pressure), hematologic parameters, gastric intramucosal pH, gastric volume, gastric pH, duration of stay in the ICU and mortality.
Materials and methods Seventy-five patients were included in our study. Cases of Group C ($n = 15$) were given only 100 ml serum physiologic, cases of Group O ($n = 15$) were given 20 mg omeprazole, cases of Group P ($n = 15$) were given 40 mg pantoprazole, cases of Group E ($n = 15$) were given 20 mg esomeprazole, and cases of Group R ($n = 15$) were given 20 mg rabeprazole from nasogastric with 100 ml serum physiologic. Demographic findings, the duration of stay in the ICU and mortality were recorded in all groups. Before any medicine was given, and after giving the medicine, in the second, fourth and sixth hours, the gastric pH, gastric volume, gastric intramucosal pH, hemodynamic parameters, and PaO_2 were recorded. Before any medicine was given, and after giving the medicine, in the second, fourth and 24th hours, hematologic parameters were recorded.

Results There were no differences regarding demographic findings, duration of stay in the ICU, mortality, hemodynamic parameters, hematologic parameters, gastric intramucosal pH, and PaO_2 between all groups. The initial gastric volume and gastric pH values were not statistically significantly different between all groups. In the second, fourth and sixth hours, after giving medicine, in the pantoprazole, esomeprazole and rabeprazole groups the gastric pH increased and the gastric volume decreased statistically significantly compared with the omeprazole and control groups. In the gastric volume and gastric pH values, changes in the pantoprazole, esomeprazole and rabeprazole groups were not statistically significantly different between these groups.
Conclusion The proton pump inhibitors pantoprazole, esomeprazole and rabeprazole were more effective in increasing the gastric pH and decreasing the gastric volume than omeprazole. In all the proton pump inhibitors we used, there were no effects on the gastric intramucosal pH.

P222

Implementation of an evidence-based stress ulcer prophylaxis protocol in the ICU

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Stress ulcer prophylaxis is one of the most common medications used in the intensive care setting. Despite well-established risk factors and guidelines, most critical care physicians use prophylaxis therapy inappropriately. In the absence of a standard of care, we evaluated the efficacy, safety, and potential cost savings of an evidence-based stress ulcer prophylaxis protocol in the surgical ICU (SICU).
We conducted a prospective, clinical study at a tertiary care teaching hospital in Chicago. One hundred and nine patients admitted to the SICU were screened daily for 12 risk factors of stress ulceration and followed until discharge from the unit. Patients with at least one identified risk factor were started on famotidine. Prophylaxis was discontinued when risk factors were no longer present and/or the patient tolerated at least 50% of his/her daily caloric need. Data collected included patient demographics, daily risk factor assessment, number of doses received, nutritional intake, estimated creatinine clearance, and adverse outcomes. Comparison data was collected for the 109 patients admitted to the SICU prior to the adoption of our protocol. Of the 109 patients meeting inclusion criteria, 99 required stress ulcer prophylaxis per our protocol. The most common risk factors were major cardiovascular or abdominal operation within 48 hours, mechanical ventilation greater than 48 hours, and intolerance to enteral feeding. A comparison of pre-protocol versus post-protocol implementation revealed an average SICU length of stay of 5.2 vs 8 days ($P = 0.003$), an average duration of prophylaxis therapy of 5 vs 4 days ($P = 0.02$), and an average number of doses administered per patient of 8.6 vs 5.7 ($P = 0.001$), respectively. This translated into a cost difference per patient of $4.53 vs $3.84 ($P = 0.02$). Efficacy and safety analysis revealed six adverse drug reactions, with one treatment failure documented by a clinically significant bleed requiring transfusion (0.92% incidence), and five incidents of thrombocytopenia (0.01% incidence) for which famotidine could not be ruled out as a causative agent. These findings are consistent with previously established adverse reactions associated with histamine-2 receptor blockers. Pantoprazole was subsequently initiated in all six cases.
Our midpoint data analysis suggests that our evidence-based protocol is a safe and efficacious tool for the standardization of stress ulcer prophylaxis in an ICU. Although potential cost savings may be minimal, the reduction of unnecessary medication administration, prevention of potential drug–drug interactions, and recognition of patient risk factors through the use of a stress ulcer prophylaxis protocol are achieved.

P223

Factors associated with excessive bleeding in cardiopulmonary bypass patients

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Background Excessive postoperative bleeding (>1 l/24 hours) and transfusion requirements for major cardiac surgical interventions vary widely. Factors such as preoperative status and medication, cardiopulmonary bypass (CPB), activation of coagulation, fibrinolysis and complement all play a determinant role in postoperative bleeding.
Objective To determine the incidence and host factors associated with EB in CPB patients without antifibrinolytic prophylaxis.
Patients and methods We performed a cross-sectional study of 26 patients (15 men; mean age 64.5 years, SD 1.4), from a clinical trial of 50 CPB patients, who did not receive antifibrinolytic prophylaxis. Surgery performed was: 12 CABG, 10 valvular replacement and four patients underwent both procedures. Variables were collected preoperatively, at ICU admission, and at 4 and 24 hours after surgery. The associations of excessive bleeding with demographic, clinical and genetic factors were analyzed. We used SPSS-12.2 software for statistical purposes.
Results The incidence of excessive bleeding (EB) was 50%. BMI <26.4 (25–28) was associated with EB ($P = 0.026$). Preoperative levels of leptins ($P = 0.059$) and PAI-1 ($P = 0.014$) were predictors for EB. Body temperature <30.7 (30–32)°C during CPB ($P = 0.037$) and at ICU admission ($P = 0.029$) was associated with EB. We found greater activation at admission of C1q ($P = 0.019$), C1-inhibitor ($P = 0.029$) and B factor ($P = 0.005$), C7 ($P = 0.005$), with lower levels of PAI-1 ($P < 0.001$), prothrombin time (PT) ($P = 0.039$), leptins ($P = 0.014$) and leptin/BMI ($P = 0.019$) in those patients with EB. In the same patients at 4 hours, we found lower levels of C1q ($P = 0.004$), C1-inhibitor ($P = 0.046$), C3 ($P = 0.010$), B factor ($P = 0.016$), C7 ($P = 0.004$), PT ($P = 0.034$), leptins ($P = 0.004$) and leptin/BMI ($P = 0.011$). In addition lower levels at 24 hours of C1q ($P = 0.039$), leptins ($P = 0.005$) and leptin/BMI ($P = 0.003$) were found in patients with EB. These patients showed a hyperdynamic state and greater transfusion requirements.
We observed a statistically significant positive correlation between the complement system (alternative and final pathway: C3, B factor and C7) and the following variables: sTNF, PAI, PT and leptins; and an inverse correlation with bleeding.
Conclusion The incidence of excessive bleeding was 50%; coagulation, fibrinolysis, complement and inflammation parameters were involved. Our results suggest that patients admitted with low BMI, PAI and leptins together with higher activation of the complement system had greater transfusion requirements over 24 hours.

P224

Blood urea nitrogen and endoscopic pattern relationship in patients with gastrointestinal bleeding

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Introduction Blood urea nitrogen (BUN) increased in active upper gastrointestinal bleeding. The relationship between BUN and endoscopic pattern is not fully investigated.
Patients and methods From January 2001 to October 2004, 157 (male/female, 123/34; mean age 69.3 years) were admitted to our hospital because of signs of gastrointestinal bleeding (hematemesis and/or melaena). At admission to the Emergency Department, haemodynamics parameters (cardiac rate, arterial pressure) and laboratory blood tests (complete blood count, creatinine, electrolyte, BUN, albumin) were measured. All patients underwent endoscopy within 8 hours and Forrest's criteria for gastrointestinal bleeding were used: F1, active bleeding; F2, signs of recent bleeding (clot); F3, healing ulcer. During hospitalization, the history, past treatment, haemotransfusion, rebleeding and surgical treatment were also recorded. Data were analyzed in a statistical manner and *t* tests for unpaired data and univariate analysis were performed.
Results Among 157 upper gastrointestinal bleeding cases, 128 were peptic ulcer and classified, according to Forrest's criteria, as: 23 F1, 61 F2 and 44 F3. Bleeding recurrence occurred in 10/128 (7.7%); no patients underwent surgery. There was a significant difference between the three groups for: number of blood units transfused, BUN, BUN/creatinine ratio, systolic blood pressure, and length of hospital stay ($P < 0.05$) (see also Table 1).
Conclusion BUN levels and the BUN/creatinine ratio correlate with Forrest's different ulcer patterns. These could identify patients who need an early endoscopic evaluation and more intensive treatment.

Table 1 (abstract P224)

	Forrest 1 (23 patients)	Forrest 2 (61 patients)	Forrest 3 (44 patients)
Hct (%)	26.9 ± 7.2	28.7 ± 7.3	28.2 ± 7.0
WBC (mmc)	11,217 ± 4884	11,944 ± 4573	10,381 ± 4749
PLT (mmc)	243,147 ± 79,587	252,923 ± 84,948	225,590 ± 86,796*
Creatinine (mg/dl)	1.6 ± 1.0*	1.1 ± 0.4	1.2 ± 0.5
BUN (mg/dl)	53.1 ± 16.6*	45 ± 15.3	40 ± 10.9
BUN/creatinine	39.9 ± 14.1*	39.4 ± 14.2*	34.6 ± 11.2
Na (mEq/l)	139.8 ± 5.7	138.7 ± 3.5	139.7 ± 4.1
DBP	72.6 ± 14.8	70.1 ± 13.0	75.8 ± 12.9
SBP	125.4 ± 31.1	117.7 ± 21.1*	133.0 ± 25.5
Heart rate (bpm)	93.9 ± 20.8	95.1 ± 19.1	90.0 ± 13.7
Number of blood transfusions	3.8 ± 2.9*	3.2 ± 2.7	2.1 ± 1.9
Hospital stay (days)	12.0 ± 6.7*	7.1 ± 4.8	8.6 ± 8.1

*$P < 0.05$. DBP, diastolic blood pressure; SBP, systolic blood pressure.

P225

Predictive genetic factors for bleeding in cardiac surgery patients with cardiopulmonary bypass

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Background The incidence of excessive postoperative bleeding and transfusion requirements for major cardiac surgical interventions varies between 10% and 70%. Not all the mechanisms involved are as yet understood.
Objective To investigate the possible role of several genetic polymorphisms associated with coagulation, fibrinolysis and inflammation, in patients with excessive bleeding after elective cardiopulmonary bypass (CPB).
Patients and methods We performed a cross-sectional study of 26 patients, from a clinical trial of 50 CPB patients, who did not receive antifibrinolytic prophylaxis. For these patients we recorded clinical variables associated with bleeding, and the following polymorphisms: insertion/deletion (I/D) of angiotensin-converting enzyme (ACE) gene; G1691A of the Leiden factor gene; G20210A of the factor II gene; 4G/5G of plasminogen activator inhibitor-1 (PAI-1); Alu repeat I/D of the plasminogen tissular activator (tPA) gene; and finally the first intron of TNF-β (TNF-β +250). In addition, seven neutral markers were genotyped to follow genomic control strategies that would detect spurious associations due to population substructure [1]. The neutral markers chosen are biallelic Alu repeats distributed in different chromosomes. We used SPSS-12.2 software for statistical purposes.
Results Greater bleeding in the 24-hour postoperative period was associated with: ACE (DD: 891 [SD 531] ml; ID: 512 [SD 458] ml, II: 1125 [SD 735] ml; $P = 0.046$), TNF-β +250 (AA: 747 [SD 459] ml; AG: 568 [SD 482] ml; GG: 1350 [SD 775] ml; $P = 0.029$), and PAI-1 (4G/4G: 792 [SD 477] ml; 4G/5G: 554 [SD 376] ml; 5G/5G: 1036 [SD 694] ml; $P = 0.037$). Homozygous 5G showed lower levels of PAI-1 (36.98 [7.68] vs 120.3 [14.3], $P = 0.02$), lower levels of leptins preoperatively (11.15 [2.15] vs 25.56 [3.93], $P = 0.016$), at admission (3.54 [0.84] vs 18.67 [3.72], $P = 0.02$), and at 4 hours (3.43 [1.12] vs 15.48 [3.27], $P < 0.001$) and 24 hours postoperatively (11.12 [4.36] vs 29.57 [4.82], $P = 0.013$) and greater coagulation factors consumed. Those patients achieved a greater advantage of antifibrinolytic prophylaxis with tranexamic acid.
Conclusion We found three polymorphisms associated with excessive postoperative bleeding. This may enable us to identify patients at risk before CPB intervention and to optimize prophylactic therapy.
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P226

Tranexamic acid decreased postoperative bleeding and systemic inflammatory response syndrome associated with cardiopulmonary bypass: a prospective, randomized, double-blind controlled study

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Background Postoperative bleeding reflects haemostatic alterations associated with cardiopulmonary bypass (CPB), which may lead to

systemic inflammatory response syndrome (SIRS). We evaluated the efficacy of tranexamic acid (TA) for SIRS and postoperative bleeding.
Patients and methods We performed a prospective, randomized, double-blind controlled study of 50 consecutive patients who underwent elective CPB. Twenty-four patients received TA, and 26 received saline solution before and after CPB. We performed an intention-to-treat analysis, comparing SIRS incidence, post-operative 24-hour bleeding, and the need for haemoderivatives. We used SPSS-12.2 software for statistical purposes.
Results No significant differences were found between groups for demographic, biochemical, and surgical characteristics. The incidence of post-CPB SIRS was significantly lower in the TA group than in the placebo group (17% vs 42%; $P = 0.048$). Fifty-three per cent of SIRS patients had vasoplegic shock vs 0% in non-SIRS patients ($P < 0.001$), and SIRS patients required more red blood cell (RBC) transfusions ($P = 0.013$), and more fresh plasma ($P = 0.014$) in the first 4 postoperative hours. The SIRS group showed an hyperfibrinolytic state, TA reduced fibrinolysis parameters such as D-dimer ($P < 0.001$). The TA group lost less blood than the placebo group (492 ± 387 ml vs 1036 ± 147 ml; $P = 0.001$) and required less RBC (475 ± 146 ml vs 962 ± 165 ml; $P = 0.021$) and less fresh plasma (33 ± 33 ml vs 409 ± 144 ml; $P = 0.012$). In the TA group the incidence of vasoplegic shock was significantly lower ($P = 0.013$), as was the use of norepinephrine ($P = 0.029$) and the mechanical ventilation time ($P = 0.018$).
Conclusions We observed a significant reduction of SIRS and postoperative bleeding in the group of CPB patients who received tranexamic acid.

P227

The erythropoietin neuroprotective effect: assessment in coronary artery bypass graft surgery (TENPEAKS) — a randomized, double-blind, placebo-controlled, proof-of-concept clinical trial

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Introduction Human recombinant erythropoietin (rh-Epo) may be a potent neuroprotectant [1]. It is approved in Canada to reduce blood transfusions in coronary artery bypass graft (CABG) surgery, which is complicated by neurocognitive dysfunction (NCD) in 50–80% of patients at discharge, 10–36% at 6 weeks and 42% at 5 years [2]. We conducted a randomized, double-blind, placebo-controlled study in 32 first-time CABG patients to investigate the feasibility and safety of three doses of rh-Epo with the ultimate goal of reducing NCD in patients following CABG.
Methods Patients were randomized to receive placebo or a total of 375 U/kg, 750 U/kg, or 1500 U/kg rh-Epo divided into three doses: the day before, the time of, and the day after surgery. A battery of 10 neuropsychological tests was performed pre-operatively, at discharge and at 2 months. The primary outcomes were feasibility and safety, including recruitment rates, 28-day all-cause mortality, ICU and hospital length of stay (LOS), incidence of pure red cell aplasia (PRCA) and thrombotic complications (stroke, myocardial infarction, deep vein thrombosis and pulmonary embolism). The secondary outcome was the incidence of NCD defined as a 20% reduction in 20% of the tests.
Results Consent was obtained in 32/101 of eligible patients. All subjects were male with mean age 60 years (range 46–73 years). Hypertension was present in 66%, diabetes in 22%, dyslipidemia in 81%, CHF in 6% and COPD in 6%. The mean pump time was 76 min (SD 23), and the mean cross-clamp time was 56 min (SD 22). The median ICU LOS was 1 day (IQR range 1–2). The median hospital LOS was 6 days (IQR 5–6.5). Mortality, PRCA and thrombotic complications were not observed. NCD was present in 66% of patients at discharge and 16% at 2 months. One patient declined 2-month follow-up. NCD at discharge, by group, was: placebo 75%, 375 U/kg 50%, 750 U/kg 75% and 1500 U/kg 63%. NCD at 2 months, by group, was: placebo 38%, 375 U/kg 13%, 750 U/kg 13% and 1500 U/kg 0%. Patients receiving rh-Epo at any dose had an incidence of NCD of 8.3%, compared with 38% for placebo ($P = 0.085$). The comorbidity, mean pump time and mean cross-clamp time were not significantly different between the two groups, nor were the ICU and hospital LOS.
Conclusion This study of rh-Epo as a neuroprotectant in patients undergoing CABG surgery is feasible and safe. rh-Epo was associated with a trend in the reduction of NCD at 2 months. These data support a multicentre study of rh-Epo to reduce NCD in CABG patients.
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P228

Large changes in renal microvascular PO_2 during acute normovolemic hemodilution

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Introduction Large differences in tolerance of organ systems for conditions of decreased O_2 delivery such as hemodilution exist. The kidney is an organ receiving a high amount of oxygen and is generally regarded as being less prone to reduced oxygen delivery. In a model of acute normovolemic hemodilution (ANH) we studied the total oxygenation of the rat kidney.
Methods In 12 anesthetized and mechanically ventilated (FiO_2 0.4) male Wistar rats, the arterial blood pressure (MAP) and renal blood flow (RBF) were recorded. After infusion of Oxyphor G2 the renal cortical (c) and medullary (m) microvascular PO_2 (μPO_2) and the renal venous PO_2 were continuously measured by oxygen-dependent quenching of phosphorescence. Six animals underwent four steps of ANH (hematocrit 25%, 15%, 10% and <10%). Six animals served as time controls. Data are presented as means ± SD. $P < 0.01$ was considered significant.
Results Baseline values: RBF 6.0 ± 0.5 ml/min, $c\mu PO_2$ 71 ± 12 mmHg, $m\mu PO_2$ 53 ± 3 mmHg, DO_2ren 1.4 ± 0.2 ml/min and VO_2ren 0.13 ± 0.04 ml/min/g. Despite a significant increase in RBF in the first two steps of ANH (7.9 ± 2.5 and 7.5 ± 1.1 ml/min, respectively), $c\mu PO_2$ and $m\mu PO_2$ dropped immediately (hematocrit 25%: 37 ± 6 and 29 ± 2 mmHg; hematocrit 15%: 20 ± 4 and 15 ± 2 mmHg, respectively). VO_2ren became dependent on supply when DO_2ren fell below 0.5 ml/min (hematocrit 15%). With impairment of μPO_2 during progressive hemodilution (lowest values $c\mu PO_2$ and $m\mu PO_2$ 12 ± 4 and 10 ± 3 mmHg, respectively), a significant correlation between $c\mu PO_2$ and $m\mu PO_2$ and VO_2ren could be observed (hematocrit ≤15%). Furthermore there was a high correlation between VO_2ren and RBF over a wide range of different flows.
Conclusion Our data provide evidence that the oxygen supply to the renal tissue is already becoming critical in an early stage of acute normovolemic hemodilution.
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P229

Low hematocrit causes worsened cerebral injury after prolonged hypothermic circulatory arrest in rats: possible involvement of C-Fos, Bcl-2 and Bax

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Background Although experience with cardiovascular surgery in adults refusing transfusion suggests that very low hematocrit levels can be tolerated, the optimal hematocrit level for cerebral protection during CPB and HCA has not been defined. Gaining insights into the cerebral consequences of HCA and CPB, and in particular the molecular pathways possibly involved, has been limited by the relative inability to study brain tissue after recovery from HCA and CPB. With the development of a rat model of CPB, we have been able to sample brain tissue after HCA and CPB for molecular analysis with well-established molecular tools. In this study, we hypothesized that low hematocrit causes worsened cerebral injury after prolonged hypothermic circulatory arrest in rats, with possible involvement of C-Fos, Bcl-2 and Bax.
Methods A rat HCA model was developed and animals were randomly distributed into four groups: sham operation group (sham op); hematocrit (Hct) 10% group; Hct 20% group and Hct 30% group ($n = 10$ each). All animals except those of the sham op group underwent HCA for 90 min at 18°C. Physiologic values such as Hct, pH and so on were monitored. Brain damage after HCA was evaluated with the light microscopy and electron microscopy. RT-PCR and imunohistochemistry techniques were used to measure the transcription and translation of the C-Fos, Bcl-2 and Bax in various brain parts.
Results After beginning CPB, Hct was decreased to the target levels. The number of injured neurons in the hippocampus CA1 and parietal cortex in the Hct 10% group (CA1: 11.44 ± 2.52; cortex: 13.65 ± 2.31) was higher than that of the Hct 20% group (CA1: 8.29 ± 1.31; cortex: 10.68 ± 1.24; $P < 0.05$), and the Hct 20% group was higher than that of the Hct 30% group (CA1: 4.40 ± 1.98; cortex: 7.38 ± 2.11). The mean score of mitochondrial injury in the Hct 10% group (34.05 ± 1.56) was higher than that of the Hct 20% group (29.30 ± 0.68; $P < 0.05$) and the Hct 20% group was higher than that of the Hct 30% group (18.65 ± 0.53; $P < 0.05$). The ratio of mRNA transcription of C-Fos and Bax to that of β-actin in the Hct 10% group (C-Fos: 1.94 ± 0.19; Bax: 1.41 ± 0.12) was higher than that of the Hct 20% group (C-Fos: 1.66 ± 0.13; Bax: 1.22 ± 0.14, $P < 0.05$) and the Hct 20% group was higher than that of the Hct 30% group (C-Fos: 1.33 ± 0.16; Bax: 0.99 ± 0.14, $P < 0.05$). On the other hand, the transcription of the Bcl-2 mRNA in the Hct 30% group (0.97 ± 0.04) was higher than that of the Hct 20% group (0.76 ± 0.10) and the Hct 10% group (0.75 ± 0.12, $P < 0.05$). The numbers of C-Fos and Bax immunoreactive cells in the hippocampus CA1 and parietal cortex in the Hct 10% group (C-Fos in CA1: 14.00 ± 2.45; C-Fos in cortex: 18.67 ± 2.16; Bax in CA1: 22.50 ± 1.87; Bax in cortex: 24.33 ± 3.88) were higher than those of the Hct 20% group (C-Fos in CA1: 10.83 ± 1.94; C-Fos in cortex: 12.50 ± 1.87; Bax in CA1: 14.67 ± 2.94; Bax in cortex: 14.00 ± 2.83; $P < 0.05$), and the Hct 20% group was higher than that of the Hct 30% group (C-Fos in CA1: 5.83 ± 0.75; C-Fos in cortex: 7.50 ± 1.05; Bax in CA1: 10.83 ± 1.47; Bax in cortex: 9.17 ± 1.72; $P < 0.05$). The number of Bcl-2 immunoreactive cells in the HCT 30% group (CA1: 13.33 ± 2.16; cortex: 15.50 ± 1.87) was higher than that of the Hct 20% group (CA1: 11.00 ± 1.41; cortex: 11.83 ± 2.04) and the Hct 10% group (CA1: 9.33 ± 1.21; cortex: 9.67 ± 1.03, $P < 0.05$).
Conclusions Low hematocrit resulted in evidence of worsened cerebral injury after prolonged HCA and CPB in rats, which is possibly due to the regulation of the C-Fos, Bcl-2 and Bax transcription and translations.

P230

Impact of critical illness severity on transfusion requirements

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Background Among the common problems in critically ill ICU patients is anemia, the consequences of which on mortality and morbidity are not adequately studied.
Objectives To describe the anemia incidence and the red blood cell transfusion strategy in critically ill patients and their relationship to clinical outcome.
Patients and methods The study period lasted from July 2003 to December 2004. The patients were enrolled within 48 hours of ICU admission. The follow-up time was 30 days, until hospital discharge or death.
Results A total of 169 patients (116 male, 53 female, mean age 57.6 ± 2.1 years, range 15–96 years) were included in the study. The mean hemoglobin level at baseline was 11.2 ± 2.1. Overall, 63.9% (108/169) of the patients received one or more RBC units while in the ICU (mean 3.1 ± 3.8 units per patient). The mean pretransfusion Hb was 8.7 ± 1.8 g/dl and the mean time to first ICU transfusion was 2.6 ± 4.1 days. More RBC transfusions were given in the first week of the ICU stay (331units vs 110, 61 and 36 units in the second, third and fourth week, respectively). The number of RBC units transfused during the study were positively associated with a longer ICU length of stay and increased mortality ($r = 0.19$, $P < 0.05$ and $r = 0.26$, $P < 0.05$, respectively). The baseline Hb level was significantly related to the number of RBC transfusions ($r = 0.55$, $P < 0.001$), but was not an independent predictive risk factor of length of stay or mortality ($r = 0.16$, $P > 0.05$ and $r = 0.13$, $P > 0.05$, respectively). The mean baseline APACHE II and SAPS scores were 19.6 ± 7.4 and 49.8 ± 17.4, respectively. Furthermore, both baseline APACHE II and SAPS scores were significantly higher in patients with a baseline Hb level <10 g/dl (23.2 ± 7.9 vs 18.3 ± 6.7 and 54.6 ± 18.8 vs 48.1 ± 16.5, respectively), while the APACHE II values were positively associated with a significantly increased likelihood of RBC transfusion (Pearson correlation $P < 0.005$).
Conclusions In ICU patients the commonly occurring anemia appears early in their ICU course and conveys them throughout their ICU stay. More RBC transfusions are given during the first week of the ICU stay. The severity of illness seems to have a positive relation to transfusion requirements. Although a strong enough statistical correlation emerges from our study, further prospective studies with larger cohorts are required in order to definitively address the issue.

P231

Effect of red blood cell transfusion on cerebral oxygenation and metabolism following severe traumatic brain injury

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Introduction Following severe traumatic brain injury (sTBI), cerebral hypoxia is a common secondary insult that is associated

with worsened neurological outcome. Traditionally, red blood cell (RBC) transfusion has been employed in patients with sTBI to improve oxygen delivery to the brain. The objective of this study was to determine the effect of RBC transfusion on cerebral oxygenation and metabolism in patients with sTBI.

Methods Adult patients with sTBI were randomized to one of three transfusion thresholds: 8, 9, or 10 g/dl. Patients with active hemorrhage or coronary ischemia were excluded. A tissue oxygen monitor and cerebral microdialysis catheter were placed in the nondominant frontal region. When the patient's hemoglobin concentration fell below their assigned threshold, 2 units packed RBCs were transfused, each over 1 hour. Following transfusion, a 1-hour period of stabilization was observed prior to final data collection. The primary outcome was change in brain tissue oxygen (PbO_2). Secondary outcomes included dependence of baseline hemoglobin concentration and baseline PbO_2 on the relationship of transfusion and PbO_2, and the effect of transfusion on lactate/pyruvate ratio and brain pH as markers of cerebral metabolic state. Analysis was performed using a population-averaged panel-data model developed using a generalized estimating equation (GEE) variant of the generalized linear method.

Results Thirty patients (21 male) with a mean (SD) age of 39 (15) years were studied. The median (IQR) pre-intubation GCS was 7 (6, 10). Transfusion occurred on median (IQR) day 4 (3, 6) after injury. Patients received a mean (SD) of 551 (58) ml packed RBCs. Transfusion resulted in a significant increase in hemoglobin concentration (pre-transfusion mean [SD] 8.4 [0.8], post-transfusion 10.2 [0.9]; $P < 0.0001$). Multivariable GEE analysis revealed the following variables to be positively associated with an increase in PbO_2: [Hb] 0.10 kPa/(g/dl) (95% CI: 0.03–0.17, $P = 0.003$); PaO_2 0.09 kPa/kPa (95% CI: 0.04–0.13. $P < 0.001$); and CPP 0.02 kPa/mmHg (95% CI: 0.008–0.031, $P = 0.001$). Probe location, age, GCS, time of transfusion from injury, pH_b, $PbCO_2$, and temperature were not significantly related to the change in PbO_2. Improvement in PbO_2 was not associated with the baseline Hb, assigned transfusion threshold group or low baseline PbO_2 (<1 kPa). The lactate/pyruvate ratio and pH_b did not change during the course of the study.

Conclusion RBC transfusion improved PbO_2 without an effect on the cerebral metabolism.

P232

Red cell pack use and mortality rate in Brazilian septic patients: Sepsis Brazil study

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Background Anemia in the setting of critical illness is quite prevalent, with 37–44% of patients receiving at least one blood transfusion during their ICU stay [1,2]. In one representative study [3], 85% of patients with an ICU length of stay greater than 1 week received at least one blood transfusion. In more than two-thirds of these cases blood transfusion was not associated with acute blood loss.

Objective To compare packed red blood cell (RBC) transfusion in septic patients and the mortality rate in septic patients.

Methods We conducted a prospective cohort study in 65 hospitals of all regions of Brazil. The patients who were admitted or who developed sepsis during September 2003 were enrolled. They were followed until the 28th day. Sepsis diagnosis was made in accordance with the criteria proposed by ACCP/SCCM in 1992. We evaluated demographic features, APACHE II score, SOFA score, mortality, sources of infections, microbiology and interventions. We also recorded underlying diseases and length of stay.

Results A total of 3128 patients were identified and 526 (16.8%) filled the criteria of sepsis, severe sepsis or septic shock. Two hundred and thirty-three patients (44.7%) received a RBC transfusion and 288 did not (55.3%). Five patients were excluded (three lost to follow-up and two lack RBC transfusion registry).

One hundred and eighteen patients (50.6%) of the transfused group were dead on the 28th day; 115 (49.4%) were alive. One hundred and twenty-five patients (43.4%) of the nontransfused group were dead on the 28th day; 163 (56.6%) were alive. The APACHE II score in both groups was 20, with an expected mortality rate of 40%.

Conclusions RBC transfusion made no difference in the 28-day mortality rate (the number of patients dead or alive with RBC transfusion was almost the same). In the nontransfused group the number of patients alive on the 28th follow-up day is greater then the number of dead patients.

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P233

Prothrombin complex concentrate versus fresh frozen plasma in patients on oral anticoagulant therapy undergoing cardiac surgery: a randomized study

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Introduction To reverse oral anticoagulant (OAC) therapy, a number of treatment modalities is available. Fresh frozen plasma (FFP) is effective and is currently used for coagulation factor replacement, carrying a risk of volume overload, transmission of infective agents and being time consuming. Variable and frequently low potency of clotting factors results in minor haemostatic effects compared with prothrombin complex concentrates (PCC), which are considered very effective and safe. PCC PPSB-SD® has constant, highly concentrated levels of factors II, VII, IX and X compared with FFP. We studied the efficacy of the intraoperative administration of PCC and FFP in patients on OAC therapy undergoing heart surgery with cardiopulmonary bypass (CPB).

Method After Ethical Committee approval and informed consent, 40 patients (P group, $n = 20$; FFP group, $n = 20$) with a preoperative INR ≥2.1 were studied. PCC was supplied as 500 IU factor IX (20 ml) vials. The dose was calculated on the basis of body weight, the initial INR and the target INR aiming at an INR of 1.5 after protamine. One-half of this dose was administered before the start of CPB. After weaning from CPB and protamine, the second half-dose was given in order to reach a postoperative INR ≤1.5. In case the INR value was still too high a further dose of PPSB was given. In the FFP group, each patient received 4 units: one-half of this dose was given before CPB and the other half after CPB. Additional FFP was given until the INR had reached a satisfactory level. In cases of poor response and/or if there was a danger of volume overload, PCC was given. A portable coagulation monitor (CoaguChek) was used for INR measurements. Blood sampling was preoperative (T−1), preincision (T0),

preadministration and postadministration before CPB (T1,T2), during CPB at 15 and 45 min (T3, T4), at the end of CPB (T5), after protamine administration (T6), and 15 and 60 min and 3 and 16 hours post-CB (T7–T10).
Analyses performed were: INR, PT, Hct, ACT, aPTT, ad factors II, VII, IX, X and FV. The amount of blood lost in the chest tube drainage and the blood products administered was also registered. Statistical evaluations were performed using the Student *t* test, repeated-measurements ANOVA and Fisher's exact test.
Results The P group was more successful in reaching the target INR. In the FFP group 16/20 (80%) patients received an additional dose of PPSB vs 6/20 (30%) in the PCC group. The INR with PCC treatment dropped sooner below 1.5 than that in the FFP group. More patients in this group reached the target INR in the first hour after ending CPB (T7, $P < 0.007$). We found a significant difference between groups in factor II ($P = 0.023$) and factor X ($P = 0.008$) levels over time.
Conclusion The results of our study support the use of PCC in patients on OAC therapy facing semi-urgent or urgent cardiac surgery. Treatment with PCC reverses anticoagulation safely, more rapidly and more effectively than FFP.

P234

Clinical application of an integrated multiparameter system in perioperative body stress assessment

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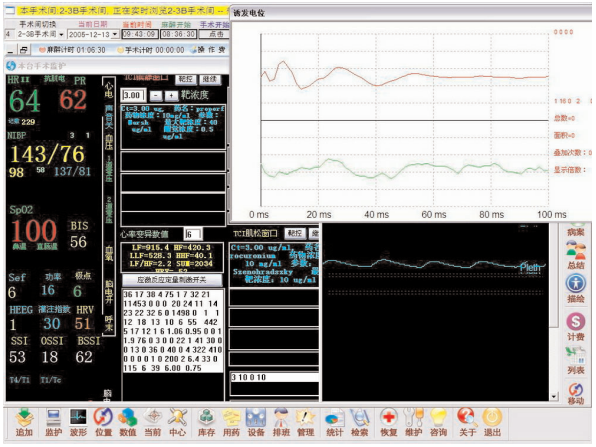
Objective As an important reaction against nociceptive stimulus, perioperative stress response has important predictable effects during operation. A moderate stress reaction can protect patients from excessive injury and enable them to safely live through the operation. However, to evaluate perioperative stress levels properly and maintain the reaction in a suitable range to decrease post-operative complications remains a problem. In the present study, we applied a novel system that integrated life multiparameters into a composite index to evaluate patients' reactions to body stress, and the stability and accuracy of the system was further estimated by modifying the intensity of body stress with electroacupuncture.
Method Volunteers were randomly selected. Multiparameters were recorded respectively. The physiological parameters, including heart rate (HR), variety of HR, pulse tracings (PT), variety of PT, blood pressure (BP), variety of BP, high frequency of electro-encephalogram (HFECG), electric resistance of skin, bispectral index (BIS) and perfusion index (PI), were recorded continually. In addition, blood samples were collected at different time points (including preoperation, onset time of operation, and every 15 min postoperation) to acquire biochemical indicators, such as adnephrin, noradrenalin, 5-hydroxytryptamine (5-HT) and so on.
The aforementioned parameters were analyzed with the algorithms of ambiguity mathematics according to the principle of evidence-based methods of cybernetics, combined with modern intelligence technology, integrating into a physiological and a biochemical stress index, respectively, which tended to reflect the intensity of the body reaction to nociceptive stimulus. Electroacupuncture was then applied to modify the intensity of body stress. Stress indexes were acquired accordingly.
Results (1) Every parameter in this system contributed to certain weight in the stress index. Changes of stress indexes paralleled with a variety of perioperative stress intensities. A preliminary estimation of the stimulus level can thus be achieved from the stress indexes. (2) The multiparameter system was designed based on modern mathematical methods including fuzzy theory, grey system and neural networks, and bioinformation reflecting the intensity of stress reaction in these parameters was excavated with the algorithms of ambiguity mathematics. (3) Correlation between the physiological index and biochemical stress index was validated in the multiparameter system, with the conclusion that there was positive concordance between them. So the system using integrated physiological multi-indexes can replace the blood sample analysis to estimate body stress more promptly and, feasibly, with less injury. The multiparameter system provided a platform for evaluating stress reaction standardly and optimally. (4) In this study, the effects of electroacupuncture significantly modulated the body reaction to stress, and the effect can be estimated with a multiparameter system timely and accurately.
Conclusion In this study, a life multiparameter system was explored with a combination of medicine, mathematics and bioengineering. The body reaction to stress was estimated by integrated multi-indexes, including physiological parameters and blood bio-chemistry parameters. The biochemical analysis can be replaced by an integrated physiological multiparameter system, as the latter can assess stress continuously and promptly. The system provided a platform and an objective reference standard to evaluate the stress reaction. In addition, the effects of electroacupuncture modulating stress were validated and estimated by the multi-parameter system.
Acknowledgement The study was funded by the Shanghai science and technology community (04dz19840).

Figure 1 (abstract 234)

Figure 2 (abstract 234)



P235

Phosphodiesterase 4D disruption causes β2 adrenergic receptors to behave like β1 adrenergic receptors *in vivo*

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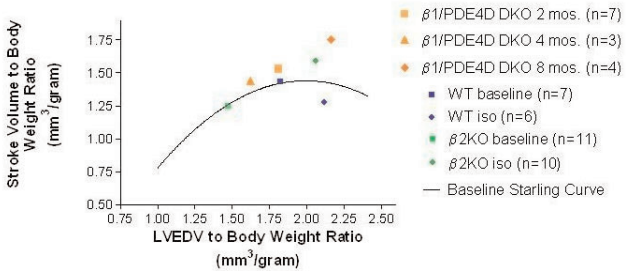
Background β1 and β2 adrenergic receptors (βARs) are G-protein-coupled receptors that mediate physiologic responses to catecholamines in the heart. β1ARs couple to stimulatory G protein (Gs) and elicit increases in inotropic and chronotropic performance during acute activation. Continuous activation of β1ARs is cardiotoxic, causing ventricular remodeling. β2ARs couple first to Gs then to inhibitory G protein (Gi). Continuous β2AR activation may protect the heart from continuous β1AR stimulation.
Distribution of cAMP within myocytes differs after β1AR stimulation relative to β2AR stimulation. β1AR activation results in a global increase in cAMP while β2AR activation generates an increase only within restricted cellular subdomains. Phosphodiesterase 4D (PDE4D) degrades cAMP and is recruited to activated β2ARs after agonist-induced internalization of the receptors. In cultured myocytes, inhibition of PDE4D leads to a global rise in cAMP levels after β2AR stimulation and causes β2AR signaling to resemble that of the β1AR.
Hypothesis We hypothesized that mice with disruption of both β1AR and PDE4D (β1/PDE4D DKO) would experience myocardial remodeling similar to that associated with continuous β1AR stimulation.
Methods Seven β1/PDE4D DKO, 11 β2KO, and seven wild-type mice were evaluated. The wild-type and β2KO mice received 14-day infusions of the βAR agonist isoproterenol. ECG-gated magnetic resonance imaging was used to determine the left ventricle end diastolic volume (LVEDV), left ventricle end systolic volume, and heart rate. The stroke volume and cardiac output were calculated.
Results See Fig. 1.
Conclusions Disruption of PDE4D causes β2ARs to behave like β1ARs *in vivo*, just as it does *in vitro*.

Figure 1 (abstract 235)



Starling axis. Measurements of LVEDV and stroke volume were obtained using electrocardiogram-gated MRI and plotted on a Starling axis. By 8 months of age the β1/PDE4D DKO mice demonstrated left ventricular dilatation similar to that experienced by β2KO mice during continuous catecholamine (isoprotenerol) administration. In β2KO mice, the dilatation has been attributed to cardiac remodeling caused by continuous β1 adrenergic receptor activation in the absence of β2 adrenergic receptor-mediated protective effects. The absence of the β1 adrenergic receptor in the β1/PDE4D DKO mice suggests that the PDE4D disruption causes β2 adrenergic receptors to behave like β1 adrenergic receptors *in vivo*, a phenomenon that has been shown to occur *in vitro*.

P236

Long-term alcoholic patients have decreased perioperative cAMP levels

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Background Patients with chronic alcohol misuse have an increased risk of postoperative bleeding complications compared with non-alcoholic individuals [1]. Serotonin increases [2], and cAMP and cyclic guanosine monophosphate (cGMP) decrease, platelet aggregation [3]. The aim of our study was to examine platelet-rich plasma levels of the mentioned substances in long-term alcoholic patients undergoing surgery.
Methods We included 33 consecutive patients with chronic alcohol misuse scheduled for tumor resections of the upper digestive tract and postoperative intensive care. We defined long-term alcoholic patients as having a daily alcohol intake of at least 60 g and fulfilling the DSM-IV criteria of the American Psychiatric Association for alcohol abuse or dependence. Blood samples were collected before and 1 day after surgery. Serotonin was measured by ELISA, cAMP and cGMP by radioimmunoassay. Additionally, we measured standard coagulation tests and determined platelet aggregation induced by ADP, collagen, epinephrine and ristocetin before and after surgery. Statistics: Mann–Whitney U test.
Results Basic patient characteristics and platelet aggregation responses induced by the mentioned agonists did not significantly differ. Data are presented in Table 1.

Table 1 (abstract P236)

Parameter	Alcoholics	Nonalcoholics	*P* value
cAMP preoperatively (nmol/l)	1.8 (1.6–2.6)	3.2 (2.2–5.3)	<0.01
cAMP postoperatively (nmol/l)	1.8 (1.5–2.3)	2.7 (2.1–3.9)	0.03
cGMP preoperatively (nmol/l)	4.0 (2.3–5.8)	5.6 (1.6–14.4)	0.77
cGMP postoperatively (nmol/l)	2.9 (2.3–7.8)	3.7 (1.4–9.3)	0.94
Serotonin preoperatively (ng/10^9 platelets)	381 (194–573)	386 (180–905)	0.98
Serotonin postoperatively (ng/10^9 platelets)	288 (193–380)	460 (225–923)	0.10

Data presented as median (25th–75th quartiles).

Conclusion In contrast to previous studies, there were no significantly altered aggregation responses in long-term alcoholic patients. A possible explanation might be the decreased inhibition through diminished cAMP levels. Our findings may suggest that cGMP and serotonin do not influence the perioperative hemostasis.
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P237

Effect of inspired oxygen concentration on central venous oxygen saturation

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Introduction A recent study has fuelled interest in the use of central venous oxygen saturation ($SCVO_2$) as a target for

resuscitation in early sepsis [1]. There has been no published study examining the effect of inspired oxygen concentration (FiO_2) on $SCVO_2$. We performed a study to examine the effect of increasing FiO_2 on $SCVO_2$.

Methods We studied 20 stable critical care patients who had arterial and central venous lines *in situ* and who were not due to undergo any events that would affect their oxygen consumption or delivery. After consent was obtained, basal arterial and central venous gases were obtained. Their FiO_2 was then increased to 1.0. After 30 min further arterial and central venous gases were taken and the patient's FiO_2 was returned to baseline.

Results The mean baseline FiO_2 was 0.35. The mean SaO_2 increased from 97.5% (SD 1.6) to 99.5% (SD 0.6), mean increase 2% (95% CI 1.3–2.6, $P < 0.001$ [paired *t* test]). The mean $SCVO_2$ increased significantly from 73.3% (SD 6.6) to 80.0% (SD 7.0), mean increase was 6.7% (95% CI 4.8–8.7, $P < 0.001$ [paired *t* test]).

Discussion This study has two implications. First, $SCVO_2$ should be interpreted with knowledge of FiO_2. Patients receiving high inspired oxygen concentrations may have elevated $SCVO_2$ values leading to false reassurance. Second, in early resuscitation many of our strategies are aimed at increasing tissue oxygen delivery. We measure $SCVO_2$ as a marker of oxygen extraction and thereby oxygen delivery. Our study showed that $SCVO_2$ can be significantly increased by increasing FiO_2, which implies better tissue oxygen delivery. Other investigators have shown that increasing FiO_2 can increase tissue oxygen delivery in surgical patients [2] and in patients with traumatic brain injury [3]. It is possible that increasing FiO_2 during the resuscitation of patients with sepsis may improve tissue oxygen delivery while other resuscitation is ongoing.

Conclusion Increasing FiO_2 significantly increased $SCVO_2$ in our study.

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P238

Contribution of perfusion-related, metabolic and respiratory components to gastric mucosal acidosis in acute cardiorespiratory failure

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Introduction Local mucosal acidosis in acute circulatory and respiratory failure is influenced by three main components: local perfusion and metabolism (mucosal–arterial pCO_2 gradient), systemic metabolic acidosis (arterial bicarbonate), and respiration (arterial pCO_2). The aim of this study was to determine the effect of primary resuscitation on these components of gastric mucosal pH in surviving and nonsurviving patients admitted to the ICU.

Patients and methods One hundred and three patients with acute respiratory or circulatory failure (age 63 ± 15 years [mean ± SD], APACHE II score 20 ± 6, SOFA score 8 ± 3) were studied during the first 24 hours after ICU admission. Gastric air tonometers were inserted and arterial blood gases for the calculation of pHi and $DpCO_2$ were taken ≥4 times daily. The effects of bicarbonate, and arterial and mucosal pCO_2 on pHi were calculated using the Hendersson–Hasselbach equation.

Results The pHi increased from 7.27 ± 0.14 at admission to 7.30 ± 0.12 after 24 hours ($P < 0.005$). Twenty-three patients died in hospital. In nonsurvivors, ΔpCO_2 contributed more to pHi at admission than in survivors (0.04 ± 0.10 vs −0.02 ± 0.09, $P = 0.023$) and this effect persisted for 24 hours. Arterial bicarbonate altered pHi at admission twice as much as ΔpCO_2 (nonsurvivors: 0.08 ± 0.10 vs survivors: 0.03 ± 0.09, $P = 0.006$) but this effect decreased during the first 24 hours (in nonsurvivors to 0.04 ± 0.10 and in survivors to 0.01 ± 0.09, $P < 0.001$ both). In nonsurvivors, hypocapnia increased pHi both at admission and after 24 hours ($P = 0.013$ both).

Conclusions Persistent inadequate gastric mucosal perfusion (increased ΔpCO_2) during primary resuscitation is associated with increased mortality. Arterial bicarbonate contributes more to gastric mucosal acidosis than the ΔpCO_2 at admission, and increases in both survivors and nonsurvivors. The severity of mucosal acidosis is partially masked by hyperventilation. These results support the concept that inadequate microcirculatory perfusion may persist despite normalization of systemic hemodynamics and that this contributes to poor outcome.

P239

Comparison of arterial haemoglobin and electrolyte measurements between an arterial blood gas analyser and the laboratory on the critical care unit

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Introduction Arterial blood gas analysers are commonly used in ICUs to provide a measurement of haemoglobin and electrolytes to determine progress and titrate therapy. Comparison between these analysers and formal laboratory measurement has not previously been undertaken in a large number of samples in the setting of a critical care unit. Anecdotal evidence suggests possible poor correlation.

Hypothesis To compare and contrast two methods of haemoglobin and electrolyte evaluation, expecting a significant difference.

Design A prospective, paired observational study.

Methods Patients had paired samples taken from their arterial line for arterial blood gas analysis via a Radiometer PICO 70 arterial sampler, and also samples taken into Vacutainer collection bottles for formal laboratory analysis. A Radiometer Copenhagen ABL700 or ABL625 blood gas analyser measured the total haemoglobin, sodium, potassium and chloride. Formal laboratory samples were analysed on GenS (haemoglobin) and LX20 (sodium, potassium and chloride) analysers (Beckman-Coulter). Samples were compared via a paired *t* test.

Results Two hundred and thirty-eight paired samples were collected over a 2-month period. The correlation coefficients between arterial blood gas analysis and formal laboratory analysis for haemoglobin, sodium, potassium and chloride were 0.934, 0.945, 0.817 and 0.922, respectively. There was no significant difference between the two methods of measurement in this study when measuring these variables ($P < 0.001$)

Conclusion Arterial blood gas analysis is an accurate method of measuring haemoglobin, sodium, potassium and chloride in the critical care unit. The transfusion practice and electrolyte or fluid resuscitation can therefore be accurately guided by the arterial blood gas measurements. This will be dependent on the accurate and regular calibration of the measuring device.

P240

Potential pharmacobiological and hormonal effects on resuscitation

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Objectives Studies have now clearly shown sex-related differences in the clinical presentations of women (vs men) with out-of-hospital cardiac arrest (OOHCA) and, more importantly, differences in the ability to resuscitate them. Presumably, these observations indicate potential pharmacobiological and/or hormonal factors. However, almost all out-of-hospital cardiac arrests (OOHCAs) occur in postmenopausal women aged >60 years. The purpose of this investigation was therefore to delineate any further stratification in sex-related differences when examining the outcomes of younger women and men (<50 years old) prospectively entered into a very large OOHCA registry.
Methods A prospective, population-based, 7-year study of all adult (>18 years) OOHCAs in an urban-EMS system with centralized protocols and medical direction using Utstein-style data guidelines. In terms of ability to resuscitate, the endpoints evaluated were return of spontaneous circulation (ROSC) and short-term survival (SURV) for those <50 years of age vs those >50 years.
Results Of the nearly 10,000 consecutive OOHCAs studied, 3926 were women (with 839 <50 years) and 5519 were men (with 1653 <50 years). Although OOHCAs for women were witnessed less often, were fewer in ventricular fibrillation (VF) presentations (21% vs 29% for men) and were less frequent with bystander CPR, they still achieved ROSC (46% vs 39%; $P < 0.001$) and SURV (21% vs 17%; $P < 0.001$) more often than men, especially if they were <50 years of age (ROSC = 52% for women vs 41% for men, $P < 0.001$; SURV = 28% vs 17%; $P < 0.001$). Also, for younger women, VF SURV was 31% vs 16% for men ($P < 0.001$) while VF SURV for older patients was 29% vs 20%. For pulseless electrical activity (PEA) cases, SURV was 29% vs 18% ($P < 0.001$) for younger ages, but was not different for the older women and men (18% vs 19%). For asystole presentations, it was 21% vs 11% (younger group; $P < 0.001$) and was 10% for both women and men >50 years of age.
Conclusions Relative to men, younger women (<50 years of age) are strikingly easier to resuscitate from cardiac arrest than older counterparts, especially with PEA and asystole presentations. Regardless of eventual neurological outcomes, these findings significantly strengthen the argument that there may be either hormonal and/or pharmacobiological differences between men and women that facilitate the ability to resuscitate. While these findings still ostensibly suggest genetic links to ROSC (and possible sex-related differences in the effects and dosing of interventions), the data here now strongly infer hormonal (e.g. estrogenic) differences as a key factor in these observations.

P241

Protection of mitochondria by intensive insulin therapy in critical illness: blood glucose control or insulin?

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Strict blood glucose control with intensive insulin therapy reduces the mortality and morbidity of critically ill patients [1]. To elucidate the relative impact of maintaining normoglycemia and glycemia-independent actions of insulin, we independently manipulated blood glucose (normal NG, high HG) and insulin levels (normal NI, high HI) in a rabbit model of prolonged critical illness [2]. We here focus on the mitochondrial compartment, which in the liver was shown to be protected by intensive insulin therapy [3].
In the liver, activities of all respiratory chain complexes are statistically similar for control and NI/NG rabbits. HI/NG rabbits have lower complex I activity than control or NI/NG animals and lower complex V activity than controls. Complexes I, II and V are further reduced in the NI/HG group and are even more severely affected in the HI/HG rabbits, with residual activities of 46%, 44% and 25% of control values, respectively. Complex III is only affected in HI/HG rabbits (62% of controls), whereas complex IV levels are similar in all groups. Complexes I, II, III and V are lower in HG vs NG groups. HI may negatively affect mitochondrial function and as such does not contribute to the protective effect of intensive insulin therapy on this cellular compartment. Compromised hepatic mitochondrial enzyme activities correlate with the degree of liver damage evaluated by serum ALT levels. Mitochondrial enzyme activities in the left ventricle are statistically equal for control, NI/NG and HI/NG rabbits. Complex III and V activities are lower in NI/HG than in NI/NG rabbits. Mitochondria of HI/HG rabbits are the most affected also in the heart, with residual activities of 76%, 84%, 61% and 47% compared with the NI/HG group for complexes I, II, III and V, respectively. Electron microscopic analysis confirmed the presence of severely damaged mitochondria in cardiac myocytes of HI/HG rabbits and is ongoing for liver.
In conclusion, the beneficial effect of intensive insulin therapy on hepatocytic mitochondria [3] is explained by avoiding glucose toxicity. The deleterious effect on both liver and cardiac mitochondria in the HI/HG group may be particularly important in view of the controversy surrounding glucose–insulin–potassium infusion and highlights the need for simultaneous glucose control when applying this therapy.
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P242

Hyperglycemia in a rat CLP model of sepsis is associated with mitochondrial uncoupling

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Background Tight glucose control was shown to greatly improve the morbidity and mortality of septic ICU patients [1]. The mechanism by which hyperglycemia is detrimental is not clearly understood.
Hypothesis Hyperglycemia is associated with hepatic dysfunction of the mitochondrial respiratory chain (MRC).
Methods Male Sprague–Dawley rats, 250–400 g, were used. We followed glucose levels in rats made septic by cecal ligation and perforation (CLP) over time (tail puncturing). We also evaluated MRC in isolated liver mitochondria at different time-points post-CLP. Enzymatic activities of MRC complexes I–IV were measured by spectrophotometry and respiration was measured by an oxygen electrode with glutamate + malate as substrates. The respiratory control ratio (RCR), calculated as the ratio of oxygen uptake in the presence and absence of ADP, served as an indicator for coupling. Sham laparotomy rats served as controls.

Figure 1 (abstract P242)

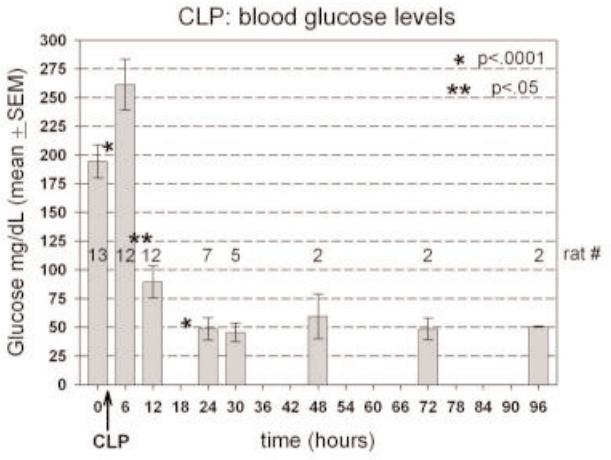
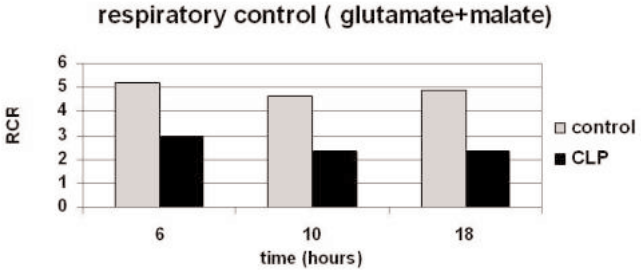


Figure 2 (abstract P242)



Results Hyperglycemia was evident 6 hours post-CLP, followed by a significant decrease of the blood glucose level (Fig. 1). Mitochondrial dysfunction was manifested as an up to 48% reduction of the RCR (Fig. 2). A mild reduction of oxygen consumption and MRC complexes I, II and IV (70%, 77%, 57% and 73% residual activity respectively, compared with controls) was observed at 6 hours post-CLP.

Conclusions This rat CLP model of sepsis, in its early hours, mimics human septic hyperglycemia. Impaired function of a septic rat's liver mitochondria (markedly decreased coupling and moderately decreased MRC activities) is evident following the time-period of hyperglycemia in this model.

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P243

Relationship between blood glucose level and outcome in acutely ill severe patients with glucose intolerance evaluated by means of a bedside-type artificial pancreas

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Objective To verify the significance of strict blood glucose (BG) control and to clarify the beneficial BG level in acutely ill severe patients with glucose intolerance.

Materials and methods Ninety patients were retrospectively investigated in whom BG control was performed by means of the bed-side type artificial pancreas (AP), STG22 (NIKKISO Corp., Japan). The patients were evaluated at two phases, that is, early phase or just after admission (E phase) and late phase (L phase: about 1 week after the E phase). Based on the daily mean BG level (BGm), patients were classified into two groups (i.e. high group and low group), which were compared with the three selected BGm values, or 150, 175, and 200 mg/dl. The patients with BGm below 150 mg/dl was group 150b and those above 150 mg/dl was group 150a, as well as those below 175 mg/dl being group 175b and those above 175 mg/dl being group 175a, and those below 200 mg/dl being group 200b and those above 200 mg/dl being group 200a. Parameters studied were as follows: sex, age, underlying diseases including diabetes mellitus, the amount of administered glucose (G [kcal/kg/day]), the amount of administered insulin (I [U/kg/day]) from the AP, the rate of septic patients, the severity (SOFA score), and the mortality (%). Nutritional support for all the patients was performed with total parenteral nutrition.

Results (1) E phase (1.2 ± 0.8 days [mean ± SD] after the operation of AP, $n = 84$): group 200b (BGm: 173 ± 19, $n = 68$) had lower G (23.4 ± 6.8 vs 27.4 ± 8.3, $P < 0.05$), I (1.11 ± 0.73 vs 2.47 ± 1.34, $P < 0.001$), and lower mortality (29 vs 56, $P < 0.05$) as compared with group 200a (BGm: 224 ± 22, $n = 16$). Other parameters were not significantly different between group 200b and group 200a. However, regarding the mortality, there was no statistical difference between groups 175b and 175a, and between groups 150b and 150a. (2) L phase (7.6 ± 1.4 days after the operation of AP, $n = 88$): group 175b (BGm: 155 ± 18, $n = 58$) had lower I (0.76 ± 0.58 vs 2.30 ± 1.19, $P < 0.001$) and lower mortality (28 vs 50, $P < 0.05$) as compared with group 175a (BGm: 197 ± 17, $n = 30$). Other parameters were not significantly different between group 175b and group 175a. In this phase the mortality was not statistically different both between groups 200b and 200a, and between groups 150b and 150a.

Interpretation BG control has recently been widely accepted as one of the most important therapies that improve outcome, which was reconfirmed by our strict BG control using the AP. However, the optimal BG goal remains to be elucidated. Our clinical trial suggested that we should change the goal chronologically.

Conclusions BG control aiming at a BG level lower than 200 mg/dl at the early stage and lower than 175 mg/dl at about 1 week later may link to the improvement of outcome of the acutely ill severe patients. The AP would be effective and essential for improving the outcome as well as for the evaluation of BG control and glucose tolerance through the strict BG control.

P244

Univariate and multivariate analysis of factors affecting tight glycaemic control

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Introduction Implementation of an intensive insulin protocol (IIP) aiming for tight glycaemic control (TGC) (blood glucose [BG] 4.4–6.1 mmol/l) resulted in a significant mortality reduction from 8% with conventional treatment to 4.6% in the IIP group [1].

Objective To determine the key factors that influence the degree of control achieved by IIP.

Method We implemented an IIP in mechanically ventilated surgical and medical patients, aiming for a target BG of 4.4–6.1 mmol/l.

Ethics approval was gained to conduct a prospective, observational study in 50 patients who were treated with the IIP. All measured BG results were analysed to calculate the time spent in predefined BG bands. Univariate and multivariate analyses were conducted on key baseline characteristics and the percentage time in the target band, using SPSS version 13 software.

Results In the univariate analysis, significant results were seen for BMI (R^2 = 13.1% P = 0.01), previous diabetes (R^2 = 10.2% P = 0.02) and gender (R^2 = 7.1% P = 0.06). The APACHE II score, age, drugs affecting glycaemia and percentage of correctly timed assays did not explain the variability in the percentage time in the target TGC range.

The multivariate analysis identified BMI as a significant factor (Table 1). Taken together, the factors in Table 1 explain 22.4% of the variability.

Table 1 (abstract P244)

	Coefficient	95% CI	*P* value
Constant	43.4		
Body mass index	−0.7	−1.4 to 0.0	0.044
Previous diabetes	−4.2	−16.9 to 8.4	0.501
Gender	−5.7	−12.5 to 1.1	0.096
Drug interactions	4.8	−2.4 to 12.0	0.184

Conclusion BMI was inversely related to control of glycaemia. Diabetics had worse glycaemic control than nondiabetics. Women had better TGC than men. The BMI, previous diabetes, gender and interacting drugs explained 22.4% of the variability in achieving TGC targets.

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P245

An altered glucose concentration increases plasma membrane injury in alveolar cells

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Introduction Lung injury has been associated with such insults as inflammation, infection, transfusion of blood products and mechanical ventilation with high tidal volumes (VALI). In the critically ill, intensive control of hyperglycemia with insulin results in decreased mortality and length of ICU stay. Whether or not abnormal glucose concentration contributes to VALI is unknown. The purpose of this study was to evaluate the role of an altered glucose environment in lung cell injury.

Methods In *in-vitro* experiments, rat type II alveolar cells were cultured on a flexible membrane in the presence of low (100 mg/dl), normal (400–500 mg/dl) and high (700 mg/dl) glucose concentrations (standard growth media = 400 mg/dl). Cells were stretched by deforming the membrane cyclically eight times per minute for 2 min. Cell stretch was performed in the presence of fluorescein isothiocyanate-dextran, a marker of plasma membrane injury and reseal. Following cell stretch, cells were labeled with propidium iodide (PI), a marker of cell death. Cell injury was expressed as the number of injured and dead cells over the total number of cells.

In *in-vivo* experiments, isolated rat lungs were mechanically ventilated with injurious tidal volumes (initial tidal volume 40 ml/kg, adjusted to initial peak airway pressure = 25 cmH_2O) for 25 min while perfused with Kreb's solution of normal (120 mg/dl) or high (500 mg/dl) glucose concentration. PI was added to the perfusate during injurious ventilation. The number of labeled subpleural cells was measured and reported as an injury index (labeled nuclei/number of alveoli in each view field).

Results At a glucose concentration lower than that found in standard type II cell growth media, there was increased injury following cell stretch (27.6% vs 18.9%, P = 0.01). At higher glucose concentrations cells no longer were adherent to the deformable membrane, which is a strong marker of nonviability. In rat lungs perfused with high-glucose Kreb's solution during injurious ventilation there was significantly greater injury than in lungs perfused with normal glucose Kreb's solution (28.0% vs 10.1%, $P < 0.01$).

Conclusions States of altered glucose homeostasis result in increased cell injury in both cell stretch and isolated lung models of injurious ventilation. These findings highlight the importance of tight glucose control in the lung cell environment to ensure the integrity of the alveolar capillary membrane. They also suggest that cell injury and resulting alveolar–capillary leakiness may explain the worse clinical outcome and increased incidence of bacteremia seen in critically ill patients with hyperglycemia. Further study is warranted to define the mechanism through which altered glucose homeostasis contributes to lung cell injury and VALI.

P246

Improved hepatic glucose production in mice lacking inducible nitric oxide synthase during hyperdynamic septic shock

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Introduction We recently showed in a hyperdynamic mouse model of septic shock that endogenous glucose production is depressed [1]. However, the mechanism for this depression remains unclear. In this context, the role of excess NO release due to activation of the inducible isoform of the NO synthase (iNOS) has been controversially discussed: while Stadler reported a direct relation between excess NO release and the inhibition of gluconeogenesis [2], other authors did not demonstrate any NO effect [3]. We therefore investigated the effects of genetic iNOS deletion on hepatic glucose production in a clinically relevant murine model of normotensive, hyperdynamic, volume-resuscitated septic shock. Wild-type mice served as controls.

Materials and methods Fifteen hours after induction of sepsis by cecal ligation and puncture, mice were anesthetized, mechanically ventilated and instrumented using a central venous line, ultrasound flow probes on the portal vein (PV) and the superior mesenteric artery (SMA), and combined laser Doppler flowmetry and remission spectroscopy to assess macrocirculatory and microcirculatory blood flows and tissue oxygenation. Normotensive, hyperdynamic hemodynamics were achieved by fluid resuscitation with colloids and intravenous noradrenaline (NA) titrated to maintain mean arterial pressure (MAP) >70 mmHg. Stable, nonradioactive isotope-labeled 1,2,3,4,5,6-^{13}C6-glucose was infused to calculate the rate of gluconeogenesis [1] from isotope enrichment in a liver specimen taken at the end of the experiment. Data are the median (range), analysed using Mann–Whitney rank sum tests (intergroup differences).

Results In iNOS knockout mice, the target MAP was achieved with less than 20% ($P < 0.001$) of the NA infusion rate required in wild-type mice. SMA and PV flow were significantly lower in iNOS-deficient mice; however, all parameters of gut and liver microcirculatory perfusion and oxygenation were well maintained.

Hepatic glucose production was significantly increased in iNOS knockout mice compared with wild-type mice in septic shock (4.3 [3.2–8.4] vs 1.9 [0.4–2.9] mg/g*hour, $P < 0.001$) despite reduced NA infusion rates.

Conclusions Since hepatic microvascular perfusion and oxygenation were well maintained in iNOS-deficient mice, our results of improved hepatic glucose production during hyperdynamic, volume-resuscitated septic shock support the concept that an iNOS-mediated inhibition of cellular energy metabolism rather than a deficiency in oxygen supply contributes to hepatic dysfunction in septic shock.

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P247

Parallel determination of glucose metabolism and fractional synthesis rates of individual hepatic proteins during hyperdynamic septic shock

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Introduction Proteomic platforms allow one to detect changes in the proteome of tissues. They can be combined with the use of stable isotope-labelled tracer amino acids to detect changes in the synthesis or breakdown rate of individual proteins. An ideal complement to these data would be a characterization of the metabolism. We focus on the defense against oxidative stress, which is closely related to energy metabolism. The latter can be assessed using isotope-labelled 1,2,3,4,5,6-^{13}C6-glucose and following the metabolic fate of the labelled carbons. We therefore investigated whether an *in-vivo* septic animal model with labelled glucose would provide useful data about glucose and energy metabolism and whether the same tracer set up could be used to reliably estimate the turnover of individual proteins.

Methods In a cecal ligation and puncture (CLP) model anaesthetized and mechanically ventilated mice were infused over 8–10 hours with labelled glucose and then liver samples were taken. Samples from five septic and five sham-operated mice were analysed by 2D-Page gel electrophoresis/Maldi TOF mass spectrometry, and the turnover of individual proteins was determined [1]. The same samples were also used for isotopomer analysis of glutamate and glucose to assess glucose production and oxidation via the Krebs or citric acid cycle [2]. Comparisons were based on Mann–Whitney rank sum tests.

Results Endogenous glucose production significantly decreased from 3.1 (CLP) to 1.6 (sham) mg/g/hour. Glucose oxidation via acetyl-CoA and subsequent use in the Krebs cycle was significantly reduced under sepsis. Metabolic labelling via glucose resulted in extensive labelling of glucose, glutamate and alanine such that 30–70% of the molecules had more than two carbons simultaneously labelled. It was sufficient to detect sepsis-induced changes in the protein labelling and their fractional synthesis rate: HSC71, a constitutive chaperone, had a reduced rate, the heat shock proteins HSP60 and HSP70 showed a minor increase, and protein disulfide isomerase, a protein repair enzyme, showed a significant increase.

Conclusions Metabolic labelling with glucose allows one to simultaneously assess key parameters of glucose metabolism and changes in the dynamics of individual proteins. The combined measurements allow a fine-grained characterization of sepsis and can be used to link changes in the energy metabolism to changes in the dynamics of individual proteins.

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P248

Organ dysfunction in critical illness: impact of maintaining normoglycemia and glycemia-independent insulin actions

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Introduction Tight glycemic control by intensive insulin therapy (IIT) reduces mortality and risk of organ failure in critically ill patients. The relative impact of maintaining normoglycemia and of glycemia-independent actions of insulin in explaining these clinical benefits remains unknown.

Methods In a TPN-fed rabbit model of prolonged (7 days) critical illness we assessed the impact of normoglycemia/normoinsulinemia, normoglycemia/hyperinsulinemia, hyperglycemia/normoinsulinemia and hyperglycemia/hyperinsulinemia on survival and organ function. Assessment of myocardial function (dp/dtmax) was performed under mechanical ventilation on day 7. Aortic rings were isolated to quantify endothelium-dependent relaxation by relaxation to cumulative doses of acetylcholine (Ach), Ach + L-nitro-arginine-methyl-ester and nitroprusside, respectively, of norepinephrine (NE)-induced vasoconstriction. Leukocyte function and plasma markers of kidney and liver function were measured.

Results Both normoglycemic groups revealed a mortality rate of 11%, whereas mortality was 36% in the HG/NI group and 47% in the HG/HI group ($P = 0.03$). Left ventricular contractility was increased by high insulin levels exclusively when normoglycemia was maintained ($P < 0.05$). The two normoglycemic groups revealed largely sustained endothelium-dependent vasorelaxation, as compared with both hyperglycemic groups ($P < 0.05$), independently of insulinemia. Nitroprusside-induced relaxation was not affected. Leukocyte function as well as kidney and liver function were protected only in both normoglycemic groups and deteriorated in both hyperglycemic groups ($P < 0.05$).

Conclusion Survival benefits and prevention of organ dysfunction by IIT largely depend on glycemic control rather than on glycemia-independent actions of insulin. When normoglycemia is maintained, insulin might exert a glycemia-independent effect on myocardial contractility.

P249

In-vitro effects of hyperglycemia on survival of neuroblastoma (SHSY) cells

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Objective It has long been known that chronic hyperglycemia results in severe neurological sequellae. Tight-regulated glycemia

has recently proven to ameliorate intensive care outcome and to prevent polyneuropathy. However, direct toxicity of glucose on neurons is hardly investigated

Methods Cultured neuroblastoma cells (with stauroporine for differentiation) were incubated with different amounts of glucose, starting from a concentration of 30 mM. Cultures were pretreated with placebo, nerve growth factor (NGF) or insulin-like growth factor-I (IGF-I). Survival was measured by the luminescent cell viability assay and the mitochondrial membrane potential (MMP) was measured using JC-1 fluoroscopy.

Results Differentiated SHSY cells died in 150 mM glucose over the 3-day period measured. Doses of mannitol to obtain comparable osmolality with the different glucose concentrations used resulted in a significant lower cellular mortality. MMP started to decrease at day 1 from 125 mM glucose. Cellular survival, measured at 1–3 days, was positively influenced by adding IGF-I (0.01–100 ng/ml) to the 200 and 300 mM glucose medium. NGF (same doses) also improved survival but was less potent, especially in the higher ranges of glucose. NGF, but not IGF-I, attenuated the MMP decrease elicited by high glucose concentrations.

Conclusion Neuroblastoma cell death is dose-dependently influenced by increasing doses of glucose. The decreased cellular production of ATP, as measured by MMP, possibly participates in cell death. Neuronal growth factors were able to improve cell survival, but their effects on MMP differ. The clinical relevance of these findings needs further investigation.

P250

Insulin inhibits IL-6 production in the kidneys in brain-dead pigs

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Introduction Kidneys transplanted from brain dead donors have a poorer function and a higher risk of rejection than kidneys from living donors [1]. This might partly be due to the inflammatory changes in the kidneys after brain death [2]. In a previous porcine study we found that a high-insulinaemic–euglucaemic clamp modulated the renal cytokine response to lipopolysaccharide infusion towards anti-inflammation [3]. We hypothesized that insulin in brain death would give a similar cytokine response, and tested this hypothesis in brain-dead pigs by studying the effect of insulin on renal IL-6 content.

Methods In 16 anaesthetized and mechanically ventilated pigs (38–42 kg bw) brain death was induced by inflation of an epidurally placed balloon catheter. Eight pigs received insulin at a constant rate (0.6 mU/kg/min). Blood glucose was clamped at 4.5 mmol/l by infusion of 20% glucose. The kidneys were removed 6 hours after brain death and biopsies from the renal cortex and medulla were taken for measurements of IL-6, by ELISA (pg/mg total protein) and of IL-6 mRNA by PCR (optimal density ratio IL-6/HRPT).

Table 1 (abstract P250)

	Minus insulin	Plus insulin	*P* value (*t* test)
IL-6 cortex	3981 ± 1373	2472 ± 1249	0.04
IL-6 mRNA	0.39 ± 0.23	0.63 ± 0.24	0.06
IL-6 medulla	2043 ± 1128	999 ± 293	0.05
IL-6 mRNA medulla	1.20 ± 0.24	0.92 ± 0.12	0.0002

Data presented as mean ± SD.

Results See Table 1. In the renal medulla IL-6 and IL-6 mRNA were lower in the treated group, whereas in the cortex only IL-6 was lower.

Conclusions Insulin inhibits renal IL-6 production in brain-dead pigs. This indicates that insulin treatment of organ donors might be beneficial for kidney graft survival after transplantation.

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P251

Hemoglobin A1c predicts outcome of sepsis in patients with diabetes

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Introduction Glycated hemoglobin (HbA1c) is a widely used marker of long-term glycoregulation in diabetes since it reflects levels of glucose in the 120 days prior to measurement. A positive impact of strict glucose control on the outcome of diabetic patients with sepsis has been well established, but the influence of glycoregulation prior to the occurrence of sepsis has not been investigated in relation to outcome. Nonenzymatic glycation and formation of advanced glycation end products (AGEs) are associated with chronic hyperglycemia in diabetes and have many biochemical and cellular effects, including changes in immune and inflammatory responses. Our hypothesis was that such changes could influence the outcome of sepsis.

Methods A prospective, single-center, observational study included adult patients admitted with sepsis and a history of diabetes during a 1-year period. HbA1c was measured on the first hospital day and the result did not influence treatment. APACHE II and SOFA scores were calculated for all patients at admission. Complications of diabetes (renal, vascular and ocular) were noted. WBC, CRP and blood culture results were recorded. The hospital mortality and hospital length of stay (LOS) were used as measures of outcome. Nonparametric tests, multiple regression and logistic regression were used in statistical analyses.

Results The study included 286 patients admitted to medical wards or the medical ICU. Hospital mortality for all patients with sepsis was 21.7% with a median LOS of 6 days (95% CI 6–7 days). Patients who survived had significantly ($P < 0.001$) lower HbA1c (median 8.2%; 95% CI 7.8–8.6%) than patients who died (median 9.75%; 95% CI 8.7–10.6%). A correlation was found between the HbA1c values and patient's LOS ($r = 0.289$, $P < 0.001$). In a logistic regression model HbA1c was found to be related to lethal outcome (OR 1.36; $P < 0.001$), together with APACHE II score (OR 1.08; $P = 0.014$) and SOFA score (OR 1.27; $P < 0.001$) and female sex (OR 2.223; $P = 0.032$). In a multiple regression model HbA1c was found to relate to LOS ($P < 0.001$) together with APACHE II ($P = 0.015$) and SOFA ($P < 0.001$) scores, age ($P = 0.032$), female sex ($P = 0.033$) and WBC ($P = 0.048$).

Conclusion HbA1c was shown to be predictive of mortality and hospital LOS of patients with sepsis and a history of diabetes. Chronic hyperglycemia and consequent increased AGE formation may influence inflammatory and immune responses, and thus be responsible. Proper glycoregulation in diabetic patients could reduce the risks in the event of infection.

P252

Expression of glucose transporters in critical illness

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Stress-induced hyperglycemia is a significant problem in critically ill patients, for whom the severity of hyperglycemia and insulin resistance reflects the risk of death. We recently demonstrated that strict maintenance of normoglycemia with intensive insulin therapy during intensive care reduced the morbidity and mortality of surgical ICU patients [1]. Normal cells respond to hyperglycemia by downregulating the insulin-independent glucose transporters (GLUT1, GLUT2 and GLUT3), thereby protecting themselves against passive glucose overload. Insulin is known to upregulate muscle GLUT4 expression, required for controlled glucose uptake in the muscle. We investigated expression levels of these four GLUTs in critical illness and assessed the impact of intensive insulin therapy.

We examined mRNA expression levels with real-time RT-PCR in muscle and liver tissue of 36 nonsurvivors, who had been randomized to intensive (normoglycemic) or conventional (hyperglycemic) insulin therapy and who were comparable for age and severity, duration and type of critical illness. The mean blood glucose levels were 5.6 ± 0.4 and 9.9 ± 0.9 mmol/l ($P < 0.001$) on a median daily insulin dose of 44.2 and 14.4 IU ($P = 0.005$), respectively. For comparison, we studied tissue harvested from patients undergoing acute surgical stress as well as tissue from healthy controls.

We demonstrated that in both the liver and muscle of patients with prolonged critical illness, the high-affinity insulin-independent glucose transporters GLUT1 and GLUT3 are substantially upregulated. In muscle the GLUT4 expression is reduced, reflecting insulin resistance. In liver, intensive insulin therapy suppresses GLUT2 with no effect on the other GLUTs. In muscle, intensive insulin therapy downregulates GLUT1 and GLUT3 expression whereas GLUT4 expression is normalized.

In conclusion, expression of GLUT1 and GLUT3 is upregulated and GLUT2 expression is normal in prolonged critical illness, a constellation that may predispose cells to glucose overload and toxicity, and that can be beneficially affected by intensive insulin therapy. Expression of GLUT4, by far the most dominantly expressed transporter in muscle, is low in the critically ill and is normalized by intensive insulin therapy. Together, these findings may offer an explanation for the high vulnerability to glucose toxicity during critical illness and how intensive insulin therapy may prevent this.

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P253

Plasma glucose levels and mortality in bacteremic ICU patients

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Introduction The influence of the plasma glucose levels on the prognosis of infection is unclear. The aim of this clinical trial is to study the impact of the plasma glucose levels at the onset of bacteremia (PGLOB) on the prognosis of bacteremia in ICU patients.

Methods We studied retrospectively 202 bacteremic ICU patients (143 men, 59 women). Mean age: 49.3 ± 16.9 years. Mean stay: 25.2 ± 11.1 days. Underlying diseases: multiple trauma 131, complicated surgery 52, other 19. All were mechanically ventilated and developed a nosocomial infection (NI) with at least one positive blood culture. From 202 patients, 34 (16.8%) were diabetic. The PGLOB (at the exact moment of the first positive blood culture) was measured and was related to prognosis of NI.

Results In diabetic patients the mean PGLOB was 244.5 ± 103.4 mg%, while in nondiabetic patients it was 141.3 ± 58.4 mg%. Global mortality rates (MR): 48/202 = 23.8%. From 48 patients who died, in 37 death was associated with NI with bacteremia; they had mean PGLOB 158.3 ± 91.1 mg%. The other 11 nonsurvivors had 153.4 ± 74.3 mg%. The related MR to NI and bacteremia according to PGLOB were: <75 mg%, MR 33.3%; 75–140 mg%, MR 20.1%; 141–200 mg%, MR 24.5%; >200 mg%, MR 27.1% ($P = 0.32$).

Conclusion There was no significant relationship between PGLOB and mortality attributed to NI and bacteremia. Multiple organ dysfunction syndrome was observed more frequently in patients with PGLOB >200 mg%, but not significantly. MR was similar in both diabetic and nondiabetic patients.

P254

Continuous glucose monitoring using the SCGM1 system in postcardiothoracic surgery patients

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Background and aims Tight glycaemic control (TGC) has proven to reduce mortality and morbidity in critically ill patients. However, in many ICUs implementation of TGC in daily practice is still suboptimal due to the risk of hypoglycaemia and the increased work demands for the ICU nursing staff. Continuous glucose monitoring (CGM) in the interstitial fluid (ISF) might be an alternative to improve the adjustment of insulin therapy without causing additional workload. The aim of the study was to investigate CGM in the ISF in ICU patients using a microdialysis-based monitoring system.

Materials and methods Twenty patients (male/female: 15/5; age 69 ± 7 years, nondiabetics/diabetics: 14/6; BMI 28.2 ± 4.9 kg/m^2, APACHE II score: 11.0 ± 3.5) with a glucose level higher than 6.7 mmol/l were investigated in ICU after cardiothoracic surgery. A

microdialysis catheter (CMA 60), which is part of the SCGM1 system (Roche Diagnostics, Mannheim, Germany), was inserted into the subcutaneous adipose tissue of the abdomen. In all patients, arterial glucose was measured hourly to describe the glucose profile until the end of the ICU stay, but for a maximum period of 48 hours.

Results The mean duration of glucose monitoring was 36 ± 15 hours. Eighteen out of 20 data could be analysed (two systems were excluded due to technical failure of the system). The mean blood glucose value was 7.2 ± 1.4 mmol/l (130 ± 25 mg/dl). The mean Pearson correlation coefficient between blood and the SCGM1 system reading was rBG-SCGM = 0.808. In addition the correlation for different calibration intervals (6–12–24 hours) of the SCGM1 system was quantified with several evaluation methods (method of residuals, modified error grid analysis [mEGA], predicted error sum of the squares [%PRESS], mean absolute difference [MAD], coefficient of correlation).

Table 1 (abstract P254)

	6 hours	12 hours	24 hours
Mean of residuals	0.17	0.30	0.31
System error (%)	2.49	4.03	3.97
%PRESS (%)	12.52	15.64	18.29
MAD (%)	0.76	1.27	2.71
EGA, A&B (%)	99.86	99.86	98.80

Conclusion Our data indicate that ISF is a promising site for CGM in critically ill patients. An implementation of this approach is microdialysis in combination with a glucose sensor. However, systems still have to be improved to be suitable for routine care in the ICU.

P255

Evaluation of a noninvasive blood glucose monitoring device for critically ill patients

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Introduction Critically ill patients frequently experience abnormalities in carbohydrate metabolism and a severe insulin resistance state. Hyperglycemia is a negative predictor of outcome in these patients, as high blood glucose (BG) values are associated with an increased risk of morbidity and mortality. Currently, BG monitoring methods cannot fulfill the need for continuous glucose monitoring in order to safely implement tight glucose control protocols. The purpose of this study is to evaluate the feasibility of the NBM-100 device (OrSense Ltd) for non-invasive (NI) continuous glucose monitoring in critically ill patients.

Materials and methods The NBM-100 uses a finger-based sensor shaped as a ring, located at the finger's base. Red/near-infrared occlusion spectroscopy detects and analyzes BG and hemoglobin concentrations. The NBM-100 utilizes an enhanced optical signal resulting from a temporary over-systolic occlusion, produced by a finger-based pneumatic cuff. The resulting changes in the optical signal create the sensitivity needed for measuring the glucose concentrations non-invasively.

A study was conducted on six patients (three female, three male, ages 44–88 years) in the ICU of Rabin Medical Center upon receipt of informed consent. The probe of the NBM-100 was placed on the patients' thumb, where it performed NI continuous measurements for up to 24 hours, with readings every 10–15 min. The results obtained from the NBM-100 device were compared with arterial blood samples taken through an arterial line every 30–60 min and analyzed with a blood gas machine (ABL 700; Radiometer, Copenhagen, Denmark).

Results A prospective analysis based on a uniform model with personal parametric adjustments was performed on the NBM-100 readings, for a total of 80 data points. The calibration phase lasted 1.5–2.5 hours. The reference BG range was 64–247 mg/dl. The resulting median relative absolute error was 11.5%, and the median absolute error was 18 mg/dl. A Clarke error grid analysis showed that 100% of the measurements fell within zones A (79%) and B (21%). In all these clinical settings there was good patient compliance and no adverse effects were identified. One of the trials did not meet a self-consistency criterion for the calibration, and was excluded.

Conclusion This study indicates the potential use of the non-invasive NBM-100 as a device for continual, accurate, safe, and easy-to-use BG evaluation for ICU. Consequently, it will improve patient care and survival, as well as reducing staff workload. It has the promise for trend analysis, hypoglycemia detection and closed-loop systems enabling automatic glycemic control.

P256

Does implementation of a computerised, decision-supported intensive insulin protocol achieve tight glycaemic control? A prospective observational study

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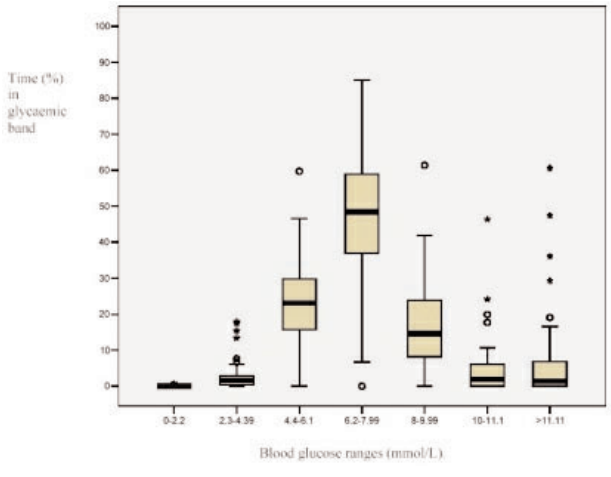
Introduction Implementation of an intensive insulin protocol, aiming for tight glycaemic control (TGC) (BG 4.4–6.1 mmol/l), has resulted in a significant mortality reduction from 8% with conventional treatment to 4.6% in the TGC group [1]. An observational study suggests that a less stringent target BG range of 4–8 mmol/l may achieve mortality benefits [2].

Objective To determine the degree to which TGC can be maintained using a TGC protocol.

Figure 1 (abstract P256)



Method At our general adult 22-bed ICU, we implemented a novel TGC protocol in mechanically ventilated patients aiming for a target glucose range of 4.4–6.1 mmol/l. The protocol was integrated on to the CIS by way of a decision support program. Ethics approval was gained. A prospective, observational study was carried out on 50 patients who were treated with the TGC protocol. All measured BG results were transferred and analysed to calculate the time spent in each predefined BG band. A linear trend was assumed between individual measurements.
Results Fifty consecutive patients were analyzed. This involved analysis of 7209 BG samples, over 9214 hours. The median time to reach glycaemic control was 10.4 ± 2.7 hours. The target TGC band (4.4–6.1 mmol/l) was achieved for a median of 23.1% of the time that patients were on TGC. For the majority of time (48.5%), BGs were within the band 6.2–7.99 mmol/l.
Conclusion Use of the computerised decision-supported intensive insulin protocol did not achieve TGC for a prolonged percentage of each patients stay, although it did deliver 'normoglycaemia' (4.4–7.99 mmol/l) for nearly three-quarters of the time. This observational examination of a 'real-life' situation reveals that TGC is difficult to achieve in critically ill patients.

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P257

Evaluation of function of pituitary gland in patients with septic shock and the effect of low-dose corticosteroid therapy

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Introduction There is evidence for the usefulness of low-dose corticosteroids for relative adrenal insufficiency in septic shock. Treatment with low-dose corticosteroid was found to have beneficial effects on hemodynamics and outcome. Relative adrenal insufficiency is often diagnosed by the adrenocorticotropic hormone (ACTH) stimulation test, but it is impossible to evaluate the function of the whole hypothalamus–pituitary–adrenal axis, so there might be possibility to miss the patients who need steroids due to disability of pituitary gland or hypothalamus.
Objectives We proposed a corticotropine releasing hormone (CRH) stimulation test to evaluate the function of the pituitary gland in patients with septic shock. We also examine the usefulness of low-dose corticosteroid in a nonresponder to the CRH stimulation test.
Methods One hundred micrograms of CRH is administered to a patient with septic shock. A patient was recognized to be a responder when the plasma concentration of ACTH raised up to 30 pg/dl or three times as high as the control level. For nonresponders, hydrocortisone of 200 mg/day was administered. We evaluated the 28-day mortality and the degree of reduction of cathecolamine and vasopressin, considered as an improvement in the circulatory status in each group.
Results Of 13 septic patients, three patients were determined as responders and 10 as nonresponders to the CRH stimulation test. For the latter group, hydrocortisone was used for nine patients and, particularly, there were four patients who responded to the ACTH stimulation test in this group. The 28-day survival rate was 33% (1/3) for responders and 60% (6/10) for nonresponders, 66% survived for 28 days who were given low-dose corticosteroid. We could reduce the dose of cathecolamine and vasopressin during 72 hours after the administration of hydrocortisone. Dopamine 7.0 ± 6.6 to 2.0 ± 3.0 μg/kg/min ($P = 0.077$), dobutamine 1.8 ± 2.4 to 1.0 ± 2.0 μg/kg/min ($P = 0.086$), noradrenaline 0.106 ± 0.088 to 0.004 ± 0.013 μg/kg/min ($P = 0.085$) and vasopressin 0.13 ± 0.25 to 0.0 ± 0.0 U/kg/hour ($P = 0.232$).
Discussion Based on this study, it is suggested that there are patients who need stress doses of corticosteroid due to malfunction of the pituitary gland even though they responded adequately to the ACTH stimulation test. We used hydrocortisone in all nonresponders. For further details, administration of hydrocortisone should be examined by randomized, double blind-test, but we think it is too critical to leave the nonreactive patient without corticosteroid.
Conclusion We propose that the CRH stimulation test is useful to assess the function of the pituitary gland of patients with septic shock.

P258

Cortisol levels fail to predict hemodynamic response to steroids and outcome in patients with septic shock

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Background Corticosteroid supplementation based on cortisol measurements was recently reported to decrease mortality in vasopressor-dependent septic shock patients and to predict hemodynamic response to corticosteroids. However, the prognostic value and clinical significance of basal cortisol levels remains controversial.
Objective To correlate basal cortisol levels with hemodynamic response to corticosteroids and hospital mortality in patients with septic shock
Design A prospective cohort study in a 19-bed medico-surgical ICU in a private hospital.
Patients All 24 patients admitted with septic shock with basal cortisol concentration measured, who received hydrocortisone as part of the treatment of septic shock.
Measurements and results Five hundred and twenty-seven patients were admitted to our ICU from September to November 2005; 24 (4.5%) were diagnosed with septic shock. After measuring a basal cortisol level, we started intravenous hydrocortisone, 50 mg every 6 hours. The patients were divided into two groups; those with hemodynamic response (HR+) to corticosteroids, defined as the reduction in noradrenaline dose greater than 50% in the next 24 hours, and those with no response to steroids (HR–). The mean age was 65 ± 15.75 years, and 58.3% were male. The mean cortisol level was 32.29 ± 13.7 μg/dl. Nine patients (37.5%) showed HR+ and seven (29.2%) patients died. APACHE II scores were similar in the HR+ and HR– groups, 21.33 ± 11.68 and 22.53 ± 11.39(P = NS), respectively. The mean cortisol basal level was 27.67 ± 13.75 μg/dl in the HR+ group and 35.06 ± 14.63 μg/dl in the HR– group ($P = 0.159$). Cortisol did not differ between survivors and nonsurvivors, 31.9 ± 12.9 and 33.2 ± 16.4 ($P = 0.7$), respectively. There was also no correlation between hemodynamic response and survival.
Conclusions In this small cohort, cortisol basal levels were not able to predict hemodynamic response to hydrocortisone in septic shock patients or to differentiate survivors from nonsurvivors.

P259

Predicting a low response to ACTH in the critically ill

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Objective To determine the risk factors for a low adrenocortical response to adrenocorticotropic hormone (ACTH) in critically ill patients.
Design A retrospective cohort study in the general ICU of a university hospital.
Patients Five hundred and twenty consecutive critically ill patients in a 3-year period, who underwent a 250 μg ACTH stimulation test for RAI, because of hypotension or prolonged need for vasopressor/inotropic therapy.
Methods The test was performed by i.v. injection of 250 μg synthetic ACTH and measuring cortisol immediately before and 30 and 60 min after injection.
Measurements and results A low adrenal response was defined as an increase in circulating cortisol <250 nmol/l and occurred in 60% of patients. Variables were collected at the onset of admission and at the day of testing. Risk factors, in multivariate analysis, included sepsis, positive local cultures if not from urine or sputum, mechanical ventilation and high inspiratory O_2 fraction, metabolic acidosis, low platelets, absence of prior cardiovascular disease or cardiac surgery, independently of baseline cortisol and albumin levels. The baseline cortisol/albumin levels, as an index of free cortisol, related directly and the increases inversely to the sequential organ failure assessment score.
Conclusions In the critically ill, sepsis and its sequelae are major risk factors of a low adrenocortical response to ACTH, independent of baseline cortisol values and cortisol binding capacity in blood. The data may help to delineate relative adrenal insufficiency.

P260

Reproducibility of the low-dose corticotropin (ACTH) stimulation test in ICU patients with sepsis and/or septic shock

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The low-dose ACTH stimulation test represents an accepted method to assess the adequacy of cortisol secretion. However, it remains currently unclear whether this test is reproducible in the setting of critical illness.
In this prospective study, we wished to investigate the reproducibility of the low-dose ACTH stimulation test in a group of severely ill patients.
To this end, 51 patients (40 men) with sepsis and/or septic shock, having a median age of 59 years (range: 17–82 years) were included. Two consecutive stimulation tests were carried out within 48 hours as follows: 1 μg freshly prepared tetracosactrin (1–24) was administered as an intravenous bolus and 30 min later a second blood specimen was obtained to measure stimulated cortisol levels.
The first test revealed that baseline and stimulation cortisol levels were 19 ± 7 μg/dl and 25 ± 8 μg/dl, respectively. The second test showed that baseline and stimulated concentrations were 19 ± 7 μg/dl and 24 ± 9 μg/dl, respectively. There was a good positive correlation between cortisol responses obtained following the two stimulation tests (Spearman's correlation coefficient, $r = 0.65$, $P < 0.005$).
We conclude that in critically ill patients with sepsis and/or septic shock, cortisol responses after stimulation with the low-dose test are fairly reproducible. This suggests that a single stimulation may be sufficient to assess adrenal function in such patients.

P261

Cortisol and dehydroepiandrosterone sulphate levels in ICU patients upon admission correlate with severity of disease

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To date, the relationship between cortisol and dehydroepiandrosterone sulphate (DHEAs) levels upon admission and the severity of disease in ICU patients remains controversial.
To further clarify this, 150 consecutive mechanically ventilated, critically ill patients (120 men), with diverse underlying diagnoses, having a median age of 50 years (range: 17–84 years) were investigated. Severity of illness was assessed by the APACHE II scoring system. Hypocortisolism was defined as cortisol below 15 mcg/dl. Upon admission to the ICU, blood was drawn to measure cortisol and DHEAs. Median APACHE II score was 11 (range: 1-35). Hormonal measurements were as follows: median cortisol and DHEAs levels were 16 μg/dl (range: 0–63 μg/dl) and 1335 ng/ml (range: 50–7238 ng/ml), respectively. Overall, 60 patients (40%) had hypocortisolism and 46 patients (31%) had DHEAs levels below the local reference ranges (normal values: 800–5600 ng/ml). For the entire patient population, there was a significant positive correlation between APACHE II scores and cortisol concentrations ($r = 0.33$, $P < 0.05$). Furthermore, APACHE II correlated negatively with DHEAs levels ($r = -0.30$, $P < 0.05$).
In conclusion, these data show a positive correlation between APACHE II scores and cortisol concentrations. Also evident is the negative correlation between severity of acute illness and DHEAs levels.

P262

Hypothalamic–pituitary–adrenal axis in mechanically ventilated critically ill patients: incidence of hyporesponsiveness to stimulation and relationship to cytokine levels

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The incidence of hypothalamic–pituitary–adrenal (HPA) axis hyporesponsiveness to stimulation and its relationship to cytokine levels in mechanically ventilated critically ill patients remain controversial. To further clarify these issues, 42 patients (33 men) with a median age of 57 years (range: 16–81 years) were enrolled. Underlying diagnoses included postoperative cases ($n = 20$), multiple trauma without head injury ($n = 12$), pancreatitis ($n = 4$), and miscellaneous

($n = 8$). Endocrine testing was performed 3–14 days (median: 6 days) after ICU admission. The median APACHE II score at the day of endocrine testing was 15 and the mean SOFA score was 9 ± 4.
Morning blood samples were collected for the determination of baseline cortisol, corticotropin (ACTH), and cytokines including IL-8, IL-1, IL-6, IL-12p70 and TNF-α. Immediately after, a low-dose stimulation test (LDST) was performed: 1 μg freshly prepared tetracosactrin (1–24) was administered as an intravenous bolus and 30 min later a second blood specimen was obtained to measure stimulated cortisol. Patients having stimulated cortisol levels less than 20 μg/dl were defined as nonresponders to the LDST.
The mean baseline cortisol was 16 ± 6 μg/dl (range: 3–32 μg/dl). The mean stimulated cortisol and the increment in cortisol were and 21 ± 6 μg/dl (range: 11–42 μg/dl) and 6 ± 4 μg/dl (range: 0–20 μg/dl), respectively. The median ACTH was 19.0 pg/ml (range: 2–300 pg/ml). Fifteen patients (36%) were nonresponders to the LDST.
In the entire patient population median cytokine levels were as follows: IL-8 = 133 pg/ml (range: 11–1010 pg/ml); IL-1 = 51 pg/ml (range: 0–282 pg/ml); TNF-α = 1 pg/ml (range: 0–16 pg/ml); and IL-12p70 = 8 pg/ml (range: 0–47 pg/ml). Nonresponders to the LDST had higher values for IL-1 (45 pg/ml vs 16 pg/ml, $P < 0.05$) and IL-12p70 (11 pg/ml vs 3 pg/ml, $P < 0.05$) compared with responders. The two groups did not differ with regard to the other cytokine concentrations.
In conclusion, adrenal cortisol secretion after dynamic stimulation is deficient in about two-thirds of critically ill patients; this disorder is associated with higher IL-1 and IL-12p70 levels.

P263

Relative adrenal insufficiency after major abdominal surgery

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Introduction Relative adrenal insufficiency has been described in diverse critical ill states; however, this issue has not been investigated following major abdominal surgery. The aim of the present study was to gain insight on this topic.
Methods Thirty-two consecutive patients (16 men), with a mean age of 69 ± 10 years, were enrolled. All patients underwent elective, major abdominal surgery. Underlying diagnoses included carcinoma of the intestine ($n = 12$), carcinoma of the stomach ($n = 8$), carcinoma of the pancreas ($n = 5$), carcinoma of the esophagus ($n = 1$) and abdominal aorta aneurysm ($n = 6$). Blood sampling was performed preoperatively to measure morning baseline corticotropin (ACTH) and cortisol levels. Furthermore, a low-dose (1 μg) corticotropin stimulation test was carried out to determine stimulated cortisol. The same measurements were performed on the first postoperative day. Relative adrenal insufficiency was defined as stimulated cortisol less than 18 μg/dl.
Results Preoperative measurements: median ACTH and mean baseline cortisol were 13 pg/ml and 15 ± 5 μg/dl, respectively, while stimulated cortisol was 25 ± 7 μg/dl. One patient (3%) had relative adrenal insufficiency (stimulated cortisol was 16 μg/dl). Postoperative results: median ACTH and mean baseline cortisol were 12 pg/ml and 17 μg/dl, respectively, whereas stimulated cortisol was 23 ± 12 μg/dl. Nine patients (28%) had relative adrenal insufficiency (stimulated cortisol ranged from 12 to 17 μg/dl).
Conclusions Relative adrenal insufficiency occurs in a substantial proportion of patients following major abdominal surgery. Preoperative adrenal function does not seem to determine postoperative adrenal responses.

P264

Clinical study on the relationship of adrenal function and prognosis in patients with severe sepsis

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Objective To explore the relationship of adrenal function and prognosis in patients with severe sepsis.
Methods A prospective study between July and December 2004 in six teaching hospitals. Two hundred and forty patients with severe sepsis were enrolled in this study. A short corticotropin stimulation test was performed in all patients by intravenously injecting 250 μg corticotropin. Blood samples were taken immediately before the test (T0) and 30 min (T30) and 60 min (T60) afterward, and the plasma cortisol concentration was measured by radioimmunoassay. At the onset of severe sepsis, the following parameters were recorded: age, sex, APACHE II, heart rate, mean arterial pressure, PaO_2/FiO_2, arterial pH, peripheral blood of hemoglobin, platelets and leukocyte concentration, and the number of organ failures. Patients were divided into two groups (survival and nonsurvival group) according to the 28-day mortality. Relative adrenal insufficiency was defined as the difference between T0 and the higher value between T30 or T60 (DTmax) < 9 μg/dl.
Results The 28-day mortality was 44.17%, and the rate of relative adrenal insufficiency was 38.33%. Between the survival group and nonsurvival group, the age, APACHE II, arterial pH, peripheral blood of platelets, the number of organ failures, and T0 and DTmax showed a significant difference. The mean T0 was 29.22 μg/dl, a value of T0 lower than 29.22 μg/dl showed good outcome, and the area under the ROC curve was 0.72. Using the reference value of DTmax < 9 μg/dl, DTmax higher than 9 μg/dl was significantly associated with death rates, and the area under the ROC curve was 0.72. Three groups of patient prognoses were identified: good (cortisol level at T0 < 29.22 μg/dl and DTmax > 9 μg/dl, 28-day mortality rate 18.37%); intermediate (T0 > 29.22 μg/dl and DTmax > 9 μg/dl or T0 < 29.22 μg/dl and DTmax < 9 μg/dl, 28-day mortality rate 45.24%); and poor (T0 > 29.22 μg/dl and DTmax < 9 μg/dl, 28-day mortality rate 86.21%).
Conclusion The base cortisol level and a short corticotropin stimulation test had a good prognostic value for severe sepsis.

P265

Thyroid hormone levels and their relations to survival in children with bacterial sepsis and septic shock

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Objectives Reported studies showed alternations of thyroid hormones in critical illness, mostly in adults and some in children. In this study, we aimed to measure thyroid hormone levels in children with sepsis and septic shock and to investigate the relation of these hormones with clinical state and survival.
Patients and methods Thyroid hormone levels of children with sepsis, with septic shock, and age-matched and sex-matched controls were measured.
Results There were 51 children in the sepsis group (Group S), 21 children in the septic shock group (Group SS) and 30 in the control group (Group C). Total tri-iodothyronin (TT3) levels were

(nmol/l): 0.91 ± 0.22, 0.64 ± 0.23, 2.11 ± 0.59; free tri-iodothyronin (FT3) levels were (pmol/l): 0.027 ± 0.006, 0.018 ± 0.007, 0.049 ± 0.010; total thyroxin (TT4) levels were (nmol/l): 100.62 ± 21.93, 65.79 ± 19.35, 109.65 ± 19.35; free thyroxin (FT4) levels were (pmol/l): 18.06 ± 3.87, 10.32 ± 1.29, 19.35 ± 3.87; and thyroid stimulating hormone (TSH) levels were (mIU/ml): 5.0 ± 2.0, 4.8 ± 2.4 and 5.2 ± 3.0, respectively, in children with sepsis, with septic shock, and controls. The TT3, FT3, TT4, and FT4 levels of group SS were significantly lower than those of groups S and C. The TT3 and FT3 levels of group S were lower than the levels of group C, but there was no significant difference between TT4, FT4 levels of groups S and C. TSH levels were slightly decreased both in sepsis and septic shock, but the difference was not significant ($P > 0.05$). Eleven (21.6%) children with sepsis and 15 (71.4%) children with septic shock died ($P < 0.001$). The levels of TT3, FT3, TT4, and FT4 were impressively lower in nonsurvivors of groups S and SS compared with survivors ($P < 0.001$).

Conclusions These changes in the hypothalamo-pituitary thyroidal axis may suggest a possible prognostic value of thyroid hormone levels in children with sepsis and septic shock. In addition, to the best of our knowledge, this report is the first study to compare the thyroid hormone levels in sepsis and septic shock in a large number of patients with healthy controls in childhood.

P266

Regulation of type 1 deiodinase activity in prolonged critical illness

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Introduction The low T3 syndrome invariably observed in prolonged critically ill patients can be explained at least in part by reduced hepatic type 1 deiodinase (D1) activity, whereby the T4 metabolism is shunted away from T3 production into inactive rT3. Infusion of TRH, however, restores the catalytic activity of D1 and concomitantly increases T3 to within the physiological range, indicating that D1 activity during critical illness is regulated via alterations within the thyroid axis [1].

It remains unknown, however, whether this observed reactivation of D1 activity is due to either a direct effect of TRH or the induced rise in circulating T4 and T3 concentrations.

Methods Burn-injured, parenterally fed, New Zealand White rabbits were randomized to receive a 4-day infusion of saline, T4 (9 μg/kg/day), T3 (5 μg/kg/day), T4 + T3 or TRH (60 μg/kg/hour). The doses of T4 and T3 aimed at, respectively, bringing plasma T4 and T3 levels into the range obtained by TRH infusion. Endocrine and biochemical organ system markers were studied. Animals were sacrificed for the assay of deiodinase activity in snap-frozen liver.

Results Compared with infusion of saline, rabbits receiving T4, T3 and TRH exhibited higher hepatic D1 activities and subsequent elevated T3 levels. Coinfusion of T3 with T4, however, evoked an additional increase in hepatic D1 activity ($P = 0.07$) with increased T4 to T3 conversion as demonstrated by significantly lower T4 ($P = 0.002$, T4 + T3 vs T4), higher T3 ($P = 0.004$, T4 + T3 vs T3) and lower rT3 levels ($P = 0.001$, T4 + T3 vs T4). Hepatic D1 activity was strongly correlated with plasma T3 ($R = 0.871$, $P < 0.0001$) but not with T4, rT3 and TSH concentrations.

Conclusion D1 activity during prolonged critical illness is most probably regulated via alterations in plasma T3.

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Reference

1. Debaveye Y, *et al.*: *Endocrinology* 2005, **146:**5604-5611.

P267

Predictive factors of the development of acute renal failure in the immediate post-hepatic transplant period

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Introduction The incidence of acute renal failure (ARF) in the immediate post-hepatic transplant period is around 12–51%. The aetiology is multiple. The ARF raises mortality of the hepatic transplant up to 50% according to some series. That is why it is so important to determine the factors that contribute to the development of ARF and to try to correct these as quickly as possible.

Materials and methods We studied 102 patients who had received an orthopic liver transplant (OLT) from a donor subject during the past 5 years. We performed a follow-up of 6 months with the aim of determining which factors are implicated in the development of renal dysfunction in the immediate post-transplant period. We analyzed characteristics of the donor, reasons for transplantation, Child–Pugh stage, and cold ischemic time, number of blood concentrates transfused during surgery, serology and biochemical parameters of renal and liver function before transplantation and at time of admittance to the ICU. We used univariable and multivariable studies.

Results We studied 102 patients that had received an OLT, of which 67.6% were male. The mean age was 52.58 years, and 52.08 years for the donors. The most frequent cause of brain death was due to CVA. The most frequent aetiology of OLT was alcoholic cirrhosis. Of the serologies, 33.3% were positive for HCV and 72.3% for CMV. We found series of factors that influence the development of ARF in the immediate post-transplant period: patients with a negative serology for CMV ($P = 0.005$), patients with hepatorenal syndrome before the transplantation ($P = 0.001$), blood concentrates transfused during surgery (3.98 ± 3.84 in the patients who did not develop ARF and 10.23 ± 8.28 in those who did develop ARF) ($P = 0.000$), Child–Pugh stage ($P = 0.000$), levels of urea and creatinine at the moment of admittance to the ICU ($P = 0.000$ and $P = 0.05$, respectively), albumin level ($P = 0.002$), total bilirubin level ($P = 0.001$), conjugated bilirubin ($P = 0.000$) and the level of total proteins ($P = 0.000$)

Conclusions The development of ARF in the immediate post-transplant period is more frequent in those patients with hepatorenal syndrome before transplantation, with stage C of Child–Pugh, with complications during surgery with the need for blood transfusions and in those with low serum albumin and high levels of bilirubin in the immediate post-transplant period.

P268

Predictive factors of mortality in liver transplantation

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Introduction The inclusion criteria for liver transplantation are wider every time and that makes the waiting list longer and longer; on the contrary, the organs from the donor subjects are limited. That is why it is so important to select the candidates and to know the predictive factors for success.

Materials and methods We studied 102 patients that had received an orthopic liver transplant (OLT) from a donor subject during the past 5 years. We studied the mortality during the 6-

month period post-transplantation. We analyzed variables of the donor: age, gender, cold ischemic time and cause of death. We evaluated the number of blood concentrates transfused during surgery, age, gender, serology of the receptor, reason for transplantation, stage according to the Child–Pugh classification and biochemistry parameters of liver and renal function in the pre-transplantation and immediate post-transplantation period. We made a descriptive study and a statistical study, univariable and multivariable, using Student's *t* test and the chi-quadrate.

Results We present 102 patients that had received an OLT, 67.6% male and 32.4% female. The mean age of the receptors was 52.58 years, and of the donors was 52.08 years. The most frequent cause of brain death of the donor subject was due to CVA (58.9%). The aetiology of liver failure was 50% due to alcoholic cirrhosis, 20.6% due to HCV, 3.9% due to fulminate failure and 6.9% due to hepatocelullar carcinoma. According to the Child–Pugh classification, 13.7% was in stage A, 43.1% in stage B and 33.3% in stage C. The HCV-positive percentage was 22.5%, and 13.7% was diagnosed with diabetes mellitus pre transplantation, 6.9% suffered from ischemic heart disease and 18.6% presented a hepatorenal syndrome. During the immediate postsurgery period, 51% presented renal dysfunction.

We identified the following as prognostic factors of mortality: renal dysfunction in the immediate postsurgery period ($P = 0.001$), cause of death of the donor ($P = 0.049$) and aetiology of liver failure ($P = 0.028$), with fulminant hepatic failure as the worse predictive factor, followed by cirrhosis due to HCV. Also, the parameters of liver function at the moment of admittance to the ICU: ASAT ($P = 0.006$), ALAT ($P = 0.002$), albumin ($P = 0.047$), and total proteins ($P = 0.039$).

Conclusions The hepatic and renal dysfunction at the moment of admittance to the ICU are good predictors of mortality. Other factors such as cause of brain death of the donor and the aetiology of the liver disease are also to be taken into account in the initial valuation and evaluation of the receptor.

P269

Biliary complications after cardiovascular procedures

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Objective Biliary complications after cardiopulmonary bypass procedures are infrequent but they carry a significant incidence of morbidity and mortality. The aim of this study was to ascertain the frequency of biliary complications following open heart surgery, to determine possible preoperative risk factors and to identify that early diagnosis and prompt institution of therapy are the most important factors to improve the outcome.

Materials and methods Within 3 years, all patients ($n = 4588$) who had undergone open heart surgery for a variety of cardiac lesions were attended at the ICU of our institution and were examined retrospectively for complications involving the gall bladder and biliary tract. All case histories of the patients were subjected to meticulous analysis. Patients with an indication of hepatic dysfunction, jaundice or biliary disorders were excluded from this study.

Results Biliary complications occurred in 14 patients, 12 of whom had to undergo subsequent abdominal surgery. Gangrene and perforation of gallbladder was the most common complication ($n = 5$), followed by acute acalculous cholecystitis ($n = 4$), distension of common bile duct without indications of biliary stasis and presence of sludge ($n = 3$), cholelithiasis ($n = 1$) and empyema ($n = 1$). The majority of patients presented within the third postoperative week (21 ± 11 postoperative days). Clinical and laboratory findings included a distended abdomen, elevated white blood cells, elevated C-reactive protein and lactate levels, nonspecific changes in the liver function chemistries and unexplained sepsis. A specific preoperative diagnosis was established in 13 patients (93%). Cholecystectomy was performed in five patients and percutaneous drainage of gallbladder in seven patients. Two patients responded well to conservative measures and diagnostic laparotomy was avoided. Five patients had gangrenous gallbladders, with frank perforation in two. The mortality rate was 43%. Biliary complications correlated significantly with advanced age (66 vs 63.5 years), the male sex (men/women: 10/4), combined cardiac surgical procedures (CABG ± valve replacement), preoperative low cardiac output syndrome (EF < 45%), prolonged bypass time (170 vs 107 min), aortic cross-clamp time (129 vs 68 min) and mechanical ventilation (>48 hours), the usage of IABP, multiple transfusions, systemic inflammatory response syndrome, visceral hypoperfusion and ischemia, and the administration of inotropes and other medications.

Conclusion Biliary complications after cardiac surgery are uncommon but life-threatening and may result from hypoperfusion of the gallbladder due to various factors. Clinical features are often subtle, and a high index of suspicion is necessary for an early diagnosis and for the institution of appropriate treatment. Delay of operative management on the grounds of recent cardiac surgery is not justified and is accompanied by an unacceptable mortality rate.

P270

Complications and outcome in conservative management of acute pancreatitis

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Objective Acute pancreatitis (AP) remains a potentially life-threatening disease and, despite international accepted treatment guidelines, the management of AP differs among hospitals.

Methods This retrospective study analyzes all the complications for 254 patients hospitalized in our department for AP in the past 10 years (1995–2004).

Results The analysis included 245 patients (55% men, age 57 ± 10 years). The aetiology of AP was alcoholic in 19.5% and biliary in 58.9% of patients (other causes, 21.6%). Ten patients died of septic multiorgan failure (mortality, 10/245; 4.1%). Severe complications occurred in 53 patients (21.6%), including acute renal failure in four, ileus in 19, and respiratory or cardiac failure in 13 patients. Eight patients needed emergency surgery. Sepsis occurred in nine patients. Other complications were: pneumonia, delirium, cholecystitis, diabetes mellitus, gastric or duodenal ulcers, and pericardial effusion. Of 245 patients, 156 (63.7%) had at least one complication. Mechanical ventilation, hemoperfusion, or hemodialysis was rarely necessary. Computed tomography (CT) was performed in 206 of 245 patients (84.1%) and showed pancreatic necrosis in 47 patients (22.8%). C-reactive protein during the first 48–72 hours and CT findings proved useful in predicting the outcome in multivariate statistical analyses. By logistic regression, however, complication rates were associated with Ranson score, but not with CT findings, C-reactive protein, sex, age, etiology, or serum enzymes.

Conclusions A conservative management of AP results in a low rate of complications and mortality. Clinical assessment (Ranson score) is sufficient to predict the severity of pancreatitis in most patients. None of our patients with AP need any special treatment and the cost-effective care is sufficient.

P271

Predictors of serious local complications in patients with severe acute pancreatitis

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Objective Serious local complications that can develop following the acute phase of severe pancreatitis include abscess formation, vascular injuries, and gastrointestinal (GI) perforations. These complications are caused by extensive necrosis of fat in the peripancreatic retroperitoneum that extends into the intraperitoneum/retroperitoneum. The purpose of this study was to determine the predictors of such local complications.
Materials and methods Forty-five consecutive patients who were admitted to our ICU for acute pancreatitis were the subjects of this study (male: 32, female: 13, age 51.4 ± 18.9 years). The following parameters were assessed: Ranson score; APACHE II scores, SOFA scores, and CRP levels on admission and day 7; and enhancement CT findings on admission (first CT) and days 7–10 (second CT). CT findings were assessed using the CT severity index of Balthazar and colleagues. $P < 0.05$ was considered statistically significant.
Results Twelve patients with acute pancreatitis developed local complications. Five patients have GI perforations that accompanied abscess formations in three cases. Six patients have vascular injuries (arterial rupture: five cases, venous rupture: one case, venous occlusion: one case). The other patient developed intraperitoneum abscess and sepsis. A laparotomy was performed on two patients with colon perforations and one patient with an intraperitoneum abscess. Transarterial embolization was performed on five patients with arterial ruptures. Stomach and duodenum perforations were treated with percutaneous drainage. Three patients died during the study period: one from bleeding associated with arterial rupture (day 51) and two from colon perforations (days 17 and 162).
Ranson scores, APACHE II scores, SOFA scores, and CRP levels of patients who had complications on admission (C group) were 5.2 ± 2.1, 12.7 ± 8.3, 5.4 ± 3.8, and 13.4 ± 10.6 mg/dl, respectively, and those of patients who did not have complications on admission (non-C group) were 3.0 ± 1.7, 7.6 ± 5.6, 2.8 ± 3.0, and 6.6 ± 7.0 mg/dl, respectively. The Ranson, APACHE II, and SOFA scores of the C group were significantly higher than those of the non-C group. On day 7, APACH II scores, SOFA scores, and CRP levels in the C group were 11.1 ± 6.7, 5.8 ± 3.8, and 20.3 ± 6.3 mg/dl, respectively, and for the non-C group were 4.5 ± 4.3, 1.7 ± 2.5, and 5.7 ± 5.1 mg/dl, respectively. The C group had significantly higher scores and CRP levels than the non-C group. Severity indices of the first and second CT observations were 8.1 ± 1.8 and 8.2 ± 1.7, respectively, for the C group and 2.9 ± 1.3 and 2.6 ± 1.3, respectively, for the non-C group. Severity indices were significantly higher in the C group.
A multivariate logistic regression analysis using a stepwise method was performed to identify significantly independent factors associated with the development of complications. As strong correlations were observed among Ranson, APACHE II, SOFA scores, CRP levels, and CT severity indices, we selected the day 7 APACHE II scores, the day 7 CRP levels, and the CT severity indices on the second CT as variables. CT severity indices and CRP levels were significantly independent factors ($P = 0.03$ and 0.41, respectively). An OR for developing complications was 3.6 when a CRP level increased by 5 mg/dl (95% CI: 1.1–10.7). Similarly, the OR was 5.0 when a CT index increased by 2 points (95% CI: 1.2–21.4).
Conclusion Persistent inflammatory reactions and high severity indices on the second CT are considered significant predictors of serious local complications associated with acute pancreatitis.

P272

Severe acute pancreatitis in the ICU

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Objective To study the clinical characteristics and prognostic factors of patients with severe acute pancreatitis (SAP) admitted to a general purpose ICU of a tertiary care teaching hospital.
Materials and methods Case records of consecutive patients with SAP admitted to the ICU from July 2002 to November 2005 were retrospectively reviewed. Collected data included the demography, etiology, co-morbid illnesses, SOFA and APACHE II scores at admission and after 24 hours, necrosis on CT scan, organ failures and their management, infections, nutrition given, specific interventions done and outcome. The patients were distributed into survivor and nonsurvivor groups and the factors determining outcome were analysed.
Statistical analysis was performed with SPSS 13 software; tests used include ANOVA, the *t* test and the chi-square test.
Results Thirty-seven patients with SAP were identified; 13 of them survived ('survivor' group) and 24 died ('nonsurvivor' group). Age, sex, co-morbid illnesses and etiology of pancreatitis did not affect the outcome. Patients with weight >70 kg had a poorer outcome. The mean APACHE II scores at admission were 11.2 ± 5.4 and 20.1 ± 6.6, respectively, in the survivor and nonsurvivor groups ($P = 0.01$) and SOFA scores were 4.6 ± 3.2 and 8.5 ± 4.3, respectively ($P = 0.004$). The net change in the APACHE II scores in 24 hours was −11 in the survivor group compared with −1 in the nonsurvivor group ($P < 0.001$). The organ failures were significantly higher in the nonsurvivor group as against the survivor group. Severe pulmonary failure (lung injury score >2.5), renal failure at admission and need for vasopressors/inotropes were present in 15.4% vs 70.8%, 7.7% vs 62.5% and 23% vs 100% in the survivor and nonsurvivor groups, respectively ($P = 0.05$, <0.001 and 0.001, respectively). The mean number of days patients required vasopressor/inotrope therapy, mechanical ventilation and renal replacement therapy were significantly higher in the nonsurvivor group. Also, the number of transfusions required was higher. Nasogastric feeding was successful for a longer duration in the survivor group.
The CT scan performed in 25 patients showed necrosis present in 24 patients (eight survivors and 16 nonsurvivors) while one nonsurvivor had no necrosis. Necrosis >50% was associated with a poor outcome (present in 1/8 survivors and 15/17 nonsurvivors, $P < 0.001$). Drainage of necrosis was by percutaneous route or surgically (open); three survivors and 13 nonsurvivors underwent drainage. Five out of 8 survivors (62.5%) and 4/16 nonsurvivors (25%) had sterile necrosis. Gram-negative enteric bacilli were the common organisms encountered.
Conclusion SAP has a mortality of 64.8% even with ICU management. Body weight >70 kg, high APACHE II score, organ failures, especially pulmonary, cardiovascular and renal, and pancreatic necrosis >50% are independent predictors of mortality. A decrease in the APACHE II score in 24 hours identifies patients with a good prognosis.

P273

Acute liver failure in children in Istanbul University: retrospective analysis of 30 cases

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Objective Acute liver failure (ALF) can show different demographical characteristics in different countries. Liver transplantation is still the life-saving treatment modality if performed in a timely manner in patients who will not recover with supportive measures. Prognostic criteria for pediatric ALF to discriminate children who will require liver transplantation has not yet been established. We aimed to evaluate the case for pediatric patients in Istanbul retrospectively.
Materials and methods The files of children with ALF diagnosed during a 15-year period between 1991 and 2005 were reviewed retrospectively. All the patients were re-evaluated to confirm the diagnosis according to the current definition of ALF by an INR ratio >2 and/or prothrombin time of 24 s or above and evidence of acute liver disease (without any clinical stigmata of cirrhosis) irrespective of the presence of encepalopathy. Thirty patients (17 boys, mean age 7.1 ± 4.9 years) with the diagnosis of ALF were entered into comprehensive analysis. Clinical and laboratory data were analysed as suggested in a previous European pediatric ALF meeting held in Hamburg, October 2003. Possible prognostic factors to determine the outcome, initial and worst laboratory values were entered into relevant statistical analyses (SPSS version 10.0, Chicago, IL, USA). The chi-square test, Fisher's exact test and Mann–Whitney U test were used to compare survivors and nonsurvivors where appropriate. Pearson or Spearman tests were used to investigate the correlations.
Results Jaundice was observed in 90% of the children. Hepatomegaly existed in 40%, splenomegaly in 30% and ascites in 40%. Fifty-three percent had grade I or grade II encephalopathy, whereas 20% already had grade IV encephalopathy on admission. The degree of encephalopathy correlated with initial hematocrit, platelet counts and prothrombin time as well as with the presence of splenomegaly ($P < 0.05$ for all). Encephalopathy did not exist in 20% initially at all. None of these clinical findings influenced the outcome statistically. Mortality seemed higher in girls (69.2% vs 52.9%) and those diagnosed before the year 2000 (67% vs 50%), although the difference was not statistically significant. Survival rates seemed higher in cases of hepatitis A, hepatitis B and toxic hepatitis, whereas mortality was highest in mushroom poisoning and fulminant Wilson's disease.
The initial leucocyte count was higher (14,474 ± 7368 vs 10,390 ± 6208/mm^3, P = NS); total and conjugated bilirubin were increased (26.9 ± 14.9 vs 19.3 ± 19.3 mg/dl and 18.6 ± 12.1 vs 12.9 ± 14.0 mg/dl, P = NS) as well as BUN (16.1 ± 13.3 vs 10.3 ± 7.1 mg/dl, P = NS) among nonsurvivors. The INR was significantly lower in the survivor group (4.4 ± 1.1 vs 3.1 ± 0.9, $P < 0.05$). The maximal leucocyte count and maximal INR levels were significantly higher among the nonsurvivors (19,623 ± 14,917 vs 11,680 ± 4483/mm^3 and 4.9 ± 0.7 vs 3.8 ± 0.9, $P < 0.05$) whereas minimal serum glucose levels were significantly lower (45.1 ± 28.2 vs 60.9 ± 14.5 mg/dl, $P < 0.05$).
Conclusion Hepatitis A, toxic hepatitis and fulminant Wilson's disease are the leading etiological factors in Turkish children with ALF in Istanbul. The initial INR level seems to be the only prognostic factor on admission. However, the maximal leucocyte count and INR levels as well as minimal serum glucose levels during the hospital stay may also have a role in determining the outcome. The outcome of ALF seems to be improved after the year 2000 in our series, possibly due to the improvement of intensive care facilities.

P274

Hemolysis Elevated Liver Low Platelet Acute Renal Dysfunction syndrome: evidence for a new entity in the critically ill obstetric patient

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Introduction The incidence of HELLP syndrome complicated with acute renal failure (ARF) is unknown because of a paucity of large series dealing with this subject. Recent experimental and clinical investigations indicate that ARF presents a condition that exerts a fundamental impact on the course of disease, the evolution of associated complications and on prognosis independently from the type and severity of the underlying disease.
Objective To test the pertinence of a new classification of HELLP syndrome derived from the Tennessee Classification [1] and containing renal dysfunction as a prognostic factor.
Patients and methods A retrospective analysis of the prospectively collected data part of the APRiMo study [2]. Critically ill obstetric patients first managed in tertiary referral maternity care for high-risk pregnancies, then transferred to our independent multidisciplinary ICU. Inclusion criteria: patients that developed HELLP syndrome in prepartum or postpartum. The main outcome of interest was vital status at ICU discharge. Demographic data, obstetric management modalities, diagnosis of ICU admission, SAPS-Obst, APACHE III-J, daily MODS and SOFA scores, and ICU complications were collected. We used the following classification. Complete HELLP syndrome (Class 1): platelets < 100,000/mm^3, LDH ≥ 600 UI/l, ASAT ≥ 70 IU/l. Incomplete HELLP syndrome (Class 2): only one or two factors of the aforementioned criteria. B: acute renal dysfunction, with a maximum serum creatinine level between 100 and 200 µmol/l at day 1 of ICU admission. C: ARF, with a maximum serum creatinine level ≥ 200 µmol/l at day 1 of ICU admission. A: no renal dysfunction. Patients presenting with HELLP syndrome could therefore be classified into six different categories.
Results During the study period January 1996–December 2004, 261 patients developed HELLP syndrome (21.1% mortality) from a database of 640 patients (13.3% overall mortality) (Table 1). In a logistic regression model with renal function represented by three dichotomous variables and HELLP syndrome expressed in a dichotomous manner as follows (Class 1 = 2, Class 2 = 1), B and C are associated with a respective OR concerning mortality of 2.8 and 8.7.

Table 1 (abstract P274)

	A	B	C
D/Cl1 (n = 30/80)	n = 1/26*,†	n = 7/17‡	n = 22/37§
D/Cl2 (n = 25/181	n = 9/105*,†	n = 5/44	n = 11/32

D/Cl1, dead patients among the Class 1 HELLP syndrome patients/total number of patients with Class1 HELLP syndrome; D/Cl2, dead patients among the Class 2 HELLP syndrome patients/total number of the patients with Class 2 HELLP syndrome. *$P < 0.001$ A vs C; †$P < 0.001$ A vs B; ‡$P = 0.009$ vs 2B; §$P = 0.039$ vs 2C.

Discussion and conclusion Adding renal dysfunction to the HELLP syndrome classification refined the prognosis of patients. Acute renal dysfunction is a strong independent denominator of survival in the critically ill obstetric patient.
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Critically ill obstetric patients with partial HELLP syndrome: still need HELP?

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Introduction HELLP syndrome is a specific complication of pregnancy characterized by hemolysis, elevated liver enzymes and low platelet count. Frequently, the pregnant patient presents with part of the biological disturbances that define HELLP syndrome, which is commonly known as partial HELLP. Few studies have focused on the specific prognosis of this condition.
Objective To compare morbidity and mortality related to partial and complete HELLP syndrome [1].
Patients and methods Retrospective analysis of data collected prospectively from an observational study (APRiMo study [2]). Patients included were critically ill obstetric patients admitted to an independent general ICU and that developed some or all of the biological disturbances characteristic of HELLP syndrome. Study period: January 1996–September 2004. The analysed data involved: acute physiology score at day 1 of hospitalization in the ICU, organ dysfunction, obstetric history and management (transfusion, delivery mode, etc.), and major morbid events in the ICU. The main outcome of interest was survival status at ICU discharge. Patients were divided into three groups: partial HELLP (P), complete HELLP (C) and patients without any criteria of HELLP syndrome (NoH). Significance between groups was assessed by two-tailed Pearson correlation, with $P < 0.05$ considered significant. Results are expressed as means ± SD. Data were computed using R version 2.1.
Results See Table 1.

Table 1 (abstract P275)

	Partial HELLP ($n = 183$)	Complete HELLP ($n = 62$)	No HELLP ($n = 353$)
SAPS – obstetric	22 ± 7*	29 ± 7‡	15 ± 6†
SAPS II	29 ± 19	40 ± 25	20 ± 10‡
SOFA day 1	6 ± 4‡	10.5 ± 4†	3 ± 2*
Mass transfusion	13	15†	13
ARF	29*	25†	26
Death (*n*)	28*	22†	26
Length of stay	5 ± 4	7 ± 8†	4.3 ± 4

*$P < 0.001$, partial HELLP vs no HELLP; †$P < 0.0001$, complete HELLP vs no HELLP; ‡$P < 0.001$, complete HELLP vs partial HELLP.

Discussion and conclusion Complete HELLP showed a significantly worse outcome than partial HELLP. But partial HELLP was associated with a high rate of maternal mortality (15%) and a significant increase in major morbid events during ICU hospitalization. It is relevant to distinguish between partial and complete HELLP syndrome (15% vs 40% mortality). Mortality in the case of partial HELLP is still very elevated, sustaining aggressive management as for complete HELLP.
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Assessment of kidney function in ICU patients

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Introduction Kidney function assessed by serum creatinine levels has low sensitivity for detection of decreased kidney function because of false-negative results. The aim of the study was to evaluate other methods of assessment of kidney function and compare these with the golden standard, the measured inulin clearance (GFR).
Methods The GFR and other kidney function assessments were measured during a 24-hour period. The GFR was compared with 1-hour and 24-hour measured urinary creatinine clearance (Ccr1 and Ccr24), levels of cystatine C and β-trace protein, using five equations for glomerular filtration rate (GFR) based on cystatine C (Hoek, Larsson, Le Bricon, Filler, Sjöström), and equations for GFR based on the creatinine level (Cockcroft Gault, MDRD, MDRDs, Jelliffe). Bias was assessed by the mean difference between GFR and different methods, precision by SD of the bias, and accuracy by the proportion of patients for whom the difference in the GFR was within 10% or 30% of the GFR (Acc10–30%).
Results Fifty patients were included, 64% were male, age was 56 ± 18 years, and APACHE II score was 19 ± 6. Creatinine was 0.66 mg/dl (0.45–1.58), cystatin C was 1.26 mg/dl (1.00–2.63) and β-trace protein was 0.92 mg/dl (0.67–1.85). The GFR was 64 (20–98) (ml/min/1.73 m^2); 72% of patients had GFR <90 and 48% had GFR <60. Bias was lowest for cystatin C-based equations (range: 3–9), was intermediate for Ccr1 and Ccr24 (27 vs 17) and great for the four creatinine-based equations (range 33–196). Precision was low for all methods of GFR assessment (range 28–141). Also, accuracy was low: Acc10% for all methods ranged from 0% to 20%, and Acc30% from 2% to 50%. Cystatin C and β-trace protein were better than creatinine levels for detection of GFR <60 (ROC analysis: AUC = 0.95 vs 0.91 vs 0.87).
Conclusions Cystatin C and β-trace protein hold promise for assessment of kidney function in ICU patients. Cystatin C and β-trace protein performed better than creatinine for the detection of kidney insufficiency. Also, GFR assessed on cystatin C-based equations were better than Ccr (low bias); however, they also lacked precision and accuracy.

P277

Validation of the Cockroft–Gault formula for estimation of creatinine clearance in the critically ill population

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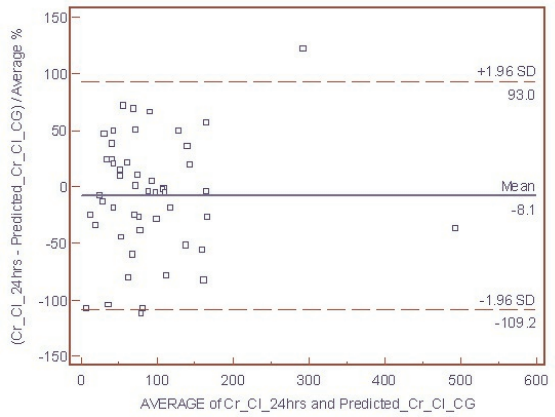
Background Estimation of creatinine clearance by the Cockroft–Gault (CG) formula is used in daily practice to calculate the glomerular filtration rate (GFR) in critically ill patients. This formula was derived from a cohort of noncritically ill patients and has not been validated against a standard measurement of the GFR such as 24-hour urine creatinine clearance in the critically ill patient.
Objective To quantify the discrepancy in GFR estimated by the CG formula and 24-hour urine creatinine clearance.
Method A prospective cohort study was conducted in 50 adult patients in a mixed medical–surgical ICU. Inclusion criteria were ITU stay >48 hours and indwelling urinary catheter. Exclusion criteria were age <18 years, pregnancy, hemodialysis or peritoneal dialysis, urine output <400 ml/day and patients receiving

Figure 1 (abstract P277)



cimetidine, ranitidine, cefoxitin, trimethoprim or diuretics. We estimated the GFR by the CG formula and measured the GFR by the 24-hour urine creatinine clearance. A Bland and Altman plot was used to find the percentage difference between the paired observations. The association between the two methods was measured by the product moment correlation coefficient.

Results The mean GFR estimated by the CG formula was 95.19 (Cl) and that by 24-hour urine creatinine clearance was 90.69 (Cl). The bias as measured by the mean percentage of error (MPE) and the precision as measured by the mean absolute percentage of error (MAPE) between these two methods were −8.07 and 103.18, respectively. The correlation coefficient of the CG formula as a measure of the GFR was 0.65 ($P < 0.0001$).

Conclusion We conclude that CG formula has a strong correlation with the measured GFR but is not a reliable measure and overestimates the GFR in the critically ill population.

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Acute renal failure prolongs weaning from mechanical ventilation in critically ill patients

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Acute renal failure (ARF) determines a worse prognosis in various medical scenarios. Since the syndrome of ARF can potentially interfere with the weaning from mechanical ventilation (MV), we sought to investigate whether the presence of ARF has any impact on weaning from MV. We studied 140 patients who received invasive MV for at least 48 hours in an oncologic ICU. Exclusion criteria: neurosurgical patients, pulmonary resections or strict end-of-life care. ARF definition: at least one value of serum creatinine (SCr) ≥1.5 mg/dl during the ICU stay. Patients were divided into ARF ($n = 93$) and non-ARF groups (NRF, $n = 47$). Criteria for weaning: PEEP ≤8 cmH_2O, pressure support ≤10 cmH_2O, FiO_2 ≤0.4 and spontaneous respiration. Primary endpoint: length of weaning. Secondary endpoints: length of MV, length of stay in ICU, and mortality. Groups were similar regarding age and gender. A higher number of ARF patients had hematological tumors (19.3 vs 6.4%, $P = 0.04$). The diagnosis of acute respiratory insufficiency (45 vs 44%) during the ICU stay and the diagnosis of ALI/ARDS as a cause for MV (18.2 vs 10.6%) did not differ between groups. SAPS at entry was not different (48.1 ± 1.4 vs 43.5 ± 15.1) but ARF patients had markers of more severe disease in the long term: severe sepsis or septic shock ($P < 0.0001$); higher number of antibiotics ($P = 0.0018$); longer time of vasoactive drug (VAD) usage ($P = 0.0005$). Oliguria (urine output <500 ml/day, for at least 24 hours) was found in 47% of ARF patients, with the median time of 72 hours. SCr at ICU admission in the ARF group was 1.6 ± 0.1 mg/dl vs 0.7 ± 0.03 mg/dl in NRF. The total length of MV was higher in ARF patients (13 ± 11 vs 9 ± 6 days, $P = 0.017$). Moreover, ARF patients used higher levels of FiO_2 (highest FiO_2 80, IQ 50–100 vs 65, IQ 50–100, $P = 0.024$). Less ARF patients reached criteria for weaning (42 vs 60%, $P < 0.05$), and had longer length for weaning from MV (83 ± 105 vs 33 ± 45 hours, $P = 0.012$). Cox regression analysis showed that an 85% increase in SCr (HR 2.30, CI 1.3–4.08), the presence of oliguria (HR 2.51, CI 1.24–5.08) and number of antibiotics greater than four (HR 2.64, CI 1.51–4.63) independently predicted weaning failure. The length of ICU stay (15 ± 12 vs 11 ± 7 days) and ICU mortality (67 vs 43%) were significantly higher in ARF patients. Multivariate analysis showed that oliguria (OR 27.3, 7.42–100.5), ARF (OR 2.43, 1.16–4.74) and prolonged use of VAD (OR 4.42, 1.28–15.2) were independent risk factors for mortality.

Increases in SCr, and particularly oliguria, during the ICU stay seriously impact on the duration of MV, weaning from MV and mortality in ICU patients. Although the presence of ARF appears to be a marker of a more severe condition, it is an independent negative factor for mechanically ventilated cancer patients.

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Three-year outcome of severe acute tubular necrosis: a prospective study of critically ill patients

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Introduction Severe acute tubular necrosis (ATN) in critically ill patients is associated with considerable morbidity, mortality and use of health resources. Its precise long-term outcomes, however, have not been well described. The objectives of this observational study were to establish long-term survival and renal recovery for severe ATN in a well-defined population.

Methods Four hundred and twenty-five critically ill patients with hospital-acquired ATN necessitating renal replacement therapy (RRT) during 1992 and 2001 were followed up for 3 years. RRT was either intermittent hemodialysis or continuous RRT. No patient had chronic renal dysfunction prior to ARF. Patients were classified according to the cause of ATN as surgical or medical. ATN was categorized as ischemic, septic or nephrotoxic. Patient characteristics were documented at commencement of RRT. Major outcomes (survival and renal status) were determined at discharge and after 1 and 3 years of follow-up.

Results The study population was characterized by high age (mean 65 years), excess comorbidity and by extensive organ failure (mean 2.4 failed organs). The overall inhospital, 1-year and 3-year case fatality rates were 47%, 65% and 71%, respectively. All survivors had renal functional recovery without further need of RRT at discharge and only 0.6% progressed to end-stage renal disease after 1 year. After 3 years, 2% of the survivors needed chronic RRT.

Conclusions In contrast to the poor inhospital prognosis of critically ill patients with severe ATN, the overwhelming majority of surviving patients become independent from renal replacement therapy. In patients without pre-existing renal dysfunction, severe chronic renal failure is unusual and the persistent need for maintenance hemodialysis is rare.

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Renal replacement therapy and bloodstream infections in cardiovascular intensive care patients

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Objective To describe bloodstream infection epidemiology in cardiac patients undergoing hemodialysis admitted to ICUs.
Methods We analyzed epidemiological data of laboratorial-confirmed bloodstream infection (BSI) episodes occurring in patients undergoing hemodialysis from October 2004 to March 2005. BSI criteria were defined by the Centers for Disease Control and Prevention. The presence of uncuffed, nontunneled, temporary central catheters for hemodialysis and other central venous catheters was daily monitored. BSI episodes were classified as dialysis-related when they occurred within 48 hours after this procedure.
Results There were 20 BSI episodes in 16 patients among the 168 (9.5%) who underwent hemodialysis in that period. The mean age was 73.5 ± 9.8 years and the mean ICU length of stay before BSI was 31.5 days. Eight patients (50%) were in the postoperative period. At hospital admission five (31%) patients had normal renal function, nine (56%) presented acute nondialytic chronic renal failure and only one had dialytic chronic renal failure. Sixteen episodes (80%) were hemodialysis related: 10 (62.5%) after continuous vein–venous hemodialysis (low-flux hemodialysis) and six (37.5%) after classic hemodialysis (high-flux hemodialysis). There was no statistically significant difference between these two procedures ($P = 0.51$). The most common pathogen was methicillin-resistant *Staphylococcus aureus* in seven cases. Three blood cultures had two agents and only one had *Candida tropicalis*. Nine catheters (45%) were inserted in the femoral vein, eight (40%) in the subclavian vein and three in the jugular (15%). Nine patients (56.3%) died within 15 days after BSI episodes.
Conclusions BSI incidence was higher in old patients and those with a long ICU length of stay. It was lower in patients who underwent classic hemodialysis, which is carried out by skilled nurses from the Dialysis Program. Clinical patients' conditions and technical aspects of this approach influenced the data.

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How continuous is continuous veno-venous haemofiltration?

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Introduction Data exist from centres in the United States and Australia demonstrating that only 67–85% of the planned cycle time of CVVH could be delivered due to unplanned interruptions. As there is some evidence that higher CVVH doses may improve outcome, interruptions may adversely affect the outcome of critically ill patients with acute renal failure.
Methods We undertook an audit of CVVH in two tertiary adult ICUs (total of 15 beds) in the United Kingdom. Patients requiring CVVH were audited, and data on length and causes of any interruptions were collected.
Results Over a 4-month period 34 patients received CVVH, ranging from a total of 10 hours to 40 days. Two hundred and thirty CVVH cycles were run, comprising 4511 hours (~75 days) of CVVH. Only six out of 34 patients (17.6%) received CVVH without any interruptions, seven patients had one interruption, but two patients had at least one interruption during each cycle of their CVVH treatment. A total 351 hours (7.7%) of CVVH time were lost due to interruptions. The length of interruptions for individual patients, however, varied from 0% to 34% of their total CVVH time. The longest period of continuous CVVH lasted 17 cycles (each 24 hours), and the shortest period was 50 min until the first interruption. Table 1 presents the causes of interruptions and their duration.

Table 1 (abstract P281)

Causes	Events (%)	Time lost	% of lost time
Filter clotting	70 (70)	248.5	70.7
Catheter problems	6 (6)	16.5	4.7
Air in circuit	2 (2)	3	1.1
Machine faulty	5 (5)	9.3	2.6
Planned	10 (10)	52.8	15
Unspecified	7 (7)	20.9	5.9

Discussion This audit demonstrates that filter clotting is by far the most common cause for interruption of CVVH and is responsible for 70.7% of lost CVVH time. Planned interruptions represent a small minority (10%). The total time lost from CVVH was only 7.7%, considerably less than previously reported. This may well be due to the closed organisation of our units and increased awareness of the important role of CVVH among staff. However, time lost from CVVH varied widely (0–34%) and one patient illustrates the persisting problem: repeated prescription of an erroneously low CVVH dose of 28 ml/kg/hour (instead of 35 ml/kg/hour) and multiple unplanned interruptions led to an average dose of only 18 ml/kg/hour, approximately one-half of the intended dose.
Conclusion Multiple unplanned interruptions occur frequently during CVVH treatment in intensive care and can have considerable negative impact on the total delivered dose of CVVH.

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Impact of continuous veno-venous hemodiafiltration with regional citrate anticoagulation on the acid–base balance of critically ill patients

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Background Continuous veno-venous hemodiafiltration (CVVHDF) with regional citrate anticoagulation (RCA) has been applied to the treatment of critically ill acute renal failure (ARF) patients for years. It has a substantial effect on acid–base homeostasis. Accordingly, we investigated a cohort of patients requiring CVVHDF and assessed their acid–base changes by quantitative biophysical principles (Stewart–Figge approach).
Methods We studied 32 consecutive critical care ARF patients on CVVHDF with RCA. All relevant variables for acid–base analysis were measured according to the Stewart–Figge methodology.
Results Before CVVHDF treatment, the patients had metabolic acidosis with mild increase of the anion gap. The excess of unmeasured anions was the most important component of acidosis. Median lactate, phosphate and chloride levels were in the normal range. The median albumin was 2.3 mg/dl and had an alkalinizing effect.
On the third CVVHDF day, the median pH, bicarbonate, anion gap, BE and SIG had significantly decreased. The median value of the total calcium–ionic calcium ratio, a surrogate marker of citrate accumulation, did not change significantly over treatment, and was maintained below 2.5 mg/dl.

Table 1 (abstract P282)

	Pre	25th/75th	D1	25th/75th	D2	25th/75th	D3	25th/75th	Friedman
pH	7.35	7.25/7.41	7.37	7.33/7.4	7.42	7.38/7.45	7.42	7.38/7.46	$P < 0.0001$
pCO_2	34.9	30.7/42.6	37.9	33.9/42.3	38.7	34.3/42.9	38	34.5/41.5	$P = 0.3773$
HCO_3	19.3	17.3/21	21.6	19.5/23.5	24.6	21.6/25.9	25.5	21.4/26.6	$P < 0.0001$
BE	−5.9	−8.7/−3.3	−2.9	−5.1/−1.3	0.2	−3.2/2.3	0.8	−2.6/2.6	$P < 0.001$
SIDa	40	36/43.6	39.1	36.2/40.8	39	36.6/40.5	39.2	36.5/41.8	$P = 0.9189$
SIDe	29.1	26.4/30.7	31	28.2/33	33	31.2/34.6	33.6	32/36	$P < 0.0001$
SIG	10.4	7.2/14.5	7.21	5.8/10.8	5.5	3.7/7.2	5.1	4/7	$P < 0.001$
AG	17.6	15.7/22.8	16.6	14.5/18.5	13.8	11.7/16	14.1	13/15.7	$P < 0.0001$
A−	8.6	7.7/10.5	8.9	8.8/10.5	8.6	7.8/10.6	8.7	7.9/10.3	$P = 0.7704$

Conclusions In critically ill ARF patients, CVVHDF with RCA is a safe RRT modality and it corrected metabolic acidosis through its effects on unmeasured anions.

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Metabolic disturbances encountered during pediatric continuous renal replacement therapy

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Objective Continuous renal replacement therapy (CRRT) has become an important supportive therapy for critically ill children with acute renal failure. In Turkey commercially available diafiltration and replacement fluids cannot be found on the market. Instead, peritoneal dialysis fluids for dialysis and normal saline as replacement fluid are used. The first objective of this study is to examine the metabolic complications due to CRRT treatments. The second objective is to determine demographic characteristics and outcomes of the patients that receive CRRT.
Methods A retrospective chart review in a university hospital.
Patients All pediatric patients treated with CRRT between February 2004 and December 2004.
Measurements and results Thirteen patients received CRRT; seven survived (53.8%). All patients were treated with continuous veno-venous hemodiafiltration. The median patient age was 71.8 ± 78.8 (1.5–180) months. Blood flow rates varied from 20 to 150 ml/min. Ultrafiltration and dialysis rate ranges were 90–130 ml/1.73 m^2/hour and 200–1085 ml/1.73 m^2/hour, respectively. The replacement fluid dose was 17.1 ± 13.5 ml/kg/hour (5–37). Hyperglycemia occurred in 76.9% ($n = 10$) and metabolic acidosis occurred in 53.8% ($n = 7$) of the patients. The median age was lower (48.8 vs 106.2 months), the median urea level (106.2 vs 71 mg/dl) and %FO (17.2% vs 7.6%) were higher, and the CRRT initiation time was longer (8.6 vs 5.6 days) in nonsurvivors vs survivors for all patients, although not statistically significant. CRRT was stopped all of the survivors, and four of the nonsurvivors (67%) were on renal replacement therapy at the time of death.
Conclusions Hyperglycemia and metabolic acidosis was frequently seen in CRRT patients when commercially available diafiltration fluids were not available. Early initiation of CRRT offered survival benefit to critically ill pediatric patients. The mortality is associated with the primary disease diagnosis.

P284

Hybrid renal replacement techniques vs continuous haemodiafiltration in haemodynamically unstable patients

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Introduction Acute renal failure in the critical care setting is a frequent and troublesome condition that can lead to significant morbidity and mortality. It is usually part of multiorgan failure with an expressive burden in the ICU.
Objectives The authors present a retrospective study comparing a hybrid renal replacement technique (HRRT) vs a continuous renal replacement technique (CRRT) in two groups of haemodynamically unstable patients admitted to the medical/surgical ICU.
Materials and methods One group ($n = 26$) received HRRT during 2003 and the other ($n = 27$) received CRRT during 2004, the year of implementation of HRRT in our ICU. Severity scores (SAPS II, APACHE II, SOFA and MODS), underlying disease and haemodynamic parameters were considered. Descriptive statistical analysis was performed by the mean and standard deviation for each parameter. Differences between numerical variables were analysed by Student's *t* test or using the Mann–Whitney test. Multiple regression analysis was performed to evaluated differences in mortality.
Results Both groups of patients had similar severity scores, underlying diseases and haemodynamic profile (Table 1). The urea and creatinine reduction rates (UUR and CRR) were also evaluated. Patients treated with HRRT showed a lower mortality (62% vs 84%), less heparin need, and a higher URR and CRR. Odds for mortality in the CRRT group were about three times higher (95% CI, 0.86–12.11), but not statistically significant ($P = 0.074$) (Table 2).
Conclusion HRRT is a valid alternative to CRRT in haemodynamically unstable critically ill patients. Further studies are

Table 1 (abstract P284)

Parameter	CRRT (group 1)	HRRT (group 2)	*P* value
Patients (*n*)	26	27	
Age (mean ± SD)	56.3 ± 15.6.2	61.7 ± 16.5	0.222
ICU stay (mean ± SD)	11.9 ± 13.5	19.3 ± 18.6	0.071
Ventilation (days)	8.2 ± 4.1	13.1 ± 6.6	0.172
Mortality [*n* (%)]	22 (84%)	17 (62%)	0.074
APACHE II (mean ± SD)	32.5 ± 7.4	30.8 ± 9.2	0.466
SAPS II (mean ± SD)	65 ± 17.7	73.4 ± 18.3	0.071
SOFA (mean ± SD)	13.7 ± 2.4	13.4 ± 2.1	0.6
MODS (mean ± SD)	11.1 ± 1.6	11.1 ± 1.7	0.669

Table 2 (abstract P284)

Parameter	CRRT group	HRRT group
Number of dialytic procedures	44	67
Dialytic procedures with amine support	14 (31.8%)	23 (39.7%)
Delivered dialysis (hours, mean/patient ± SD)	55 ± 22	16.4 ± 4.3
URR (%)	21.1	42.6
CRR (%)	26.7	36.5
Blood pump velocity (ml/min) (mean ± SD)	166.5 ± 35.6	156.5 ± 33.2
Heparin consumption per patient (units)	44,650	11,130

needed to establish a difference in outcome related to the use of a particular renal replacement technique.

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Citrate anticoagulation realized as CVVHD using a newly designed dialysate solution

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Background Citrate anticoagulation is an excellent alternative to heparin anticoagulation for patients at high risk of bleeding requiring continuous renal replacement therapy. However, citrate anticoagulation has some potential adverse effects such as metabolic alkalosis and acidosis, hypernatremia, hypocalcemia and hypercalcemia. Thus, most citrate anticoagulation protocols use specially designed dialysis fluids to compensate for most of these disarrangements. We present a newly designed dialysate for citrate anticoagulation and looked at the filter life time, acid–base and electrolyte disarrangements.
Methods Based on theoretical considerations we composed a dialysis fluid suitable for a 2 l/hour dialysis flow rate. The dialysate contained 133 mmol/l sodium, 2 mmol/l potassium, 1.1 mmol/l magnesium, 20 mmol/l bicarbonate and 112.2 mmol/l chloride. All treatments were performed as CVVHD. Routine filter changes were performed after 72 hours of treatment.
Results Forty-five patients were included in the study. Treatments were well tolerated. The filter life was appropriate (57.4 ± 17 hours). In a few patients mild metabolic alkalosis (pH > 7.45 plus BE > +3) was easily counteracted by increasing the dialysis fluid flow. Acid–base values returned to normal within 24 hours after increasing the dialysate flow. The maximum dialysate flow was 3000 ml/hour. Hypernatremia and hypocalcemia were not observed. The systemic ionized calcium concentration was successfully controlled by adjustments of a continuous calcium infusion made with respect to the results of 6 hourly measurements.
Conclusion The analyzed citrate anticoagulation protocol was well tolerated and the filter life time was appropriate. Regional anticoagulation with trisodium citrate in combination with a customized calcium-free dialysate is a safe and effective alternative to a heparin-based anticoagulation regimen.

P286

High dose hemofiltration in the intensive care of sepsis in cancer patients

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Surgical operations, chemotherapy or/and radiotherapy often cause critical forms of organ failure in cancer patients. Mortality in multiorgan failure cancer patients inducted by sepsis is about 97–100%. High-dose haemofiltration (CHDHF) or haemodiafiltration (CHDHDF) early application in sepsis treatment promotes the organ failure recovery and reduces lethality in cancer patients.
One hundred and fifty-six patients (APACHE II = 32.3 ± 3.6) with multiorgan failure were studied in the Cancer Research Center in Moscow. All patients received CHDHF or CHDHDF as well as standard intensive care. Seventy-six of these patients suffered from acute sepsis. The expected and real mortality were compared within the groups of patients with and without sepsis. The cytokine and medium molecular substances concentrations were measured in the blood, urine and in the filtrate.
CHDHF and CHDHDF were performed with Fresenius and Edwards equipment with the substrate flow up to 10000 ml/hour in the 42% predilution and 58% postdilution mode. The treatment duration varied from 2 to 25 days. The average substitution volume in all patients was 4–9 l/hour. The filtration fraction equal to 33% of blood flow can be safely reached at Hct = 20–25%. The membrane was replaced every 36 hours in spite of the absence of polyestersulphone membrane thrombosis. MALDI analysis and electrophoresis were used for protein detection in filtrate. It was found that during CHDHDF the proteins with molecular weight up to 77 kDa are eliminated. This fraction contains 29–31% of albumin and 11–17% of transferrin. The excess of associated proinflammatory cytokines are also eliminated with high efficiency. The C3 component of complement system, leukotriene B4, and thromboxane are not eliminated.
CHDHF and CHDHDF were hemodynamically tolerant in all patients. In nonseptic patients ($n = 74$) with MOF the mortality was 52%, which is statistically significant in retrospective comparison with patients without HDF ($P < 0.01$). In septic patients with MOF the mortality was 82% ($P < 0.01$ in retrospective comparison with patients without HDF). The application of CHDHF and CHDHDF immediately after the diagnosis 'septic shock' was made ($n = 16$) permitted one to stop the shock development within 8–20 hours in all patients. The organ failure recovery in CHDHF and CHDHDF patients varied from 7 to 93 days. The further quality of life was determined by the treatment efficiency and by the recovery degree of organ function.
In conclusion, CHDHF and CHDHDF are safe and efficient in early application in cancer patients with MOF intensive care. Vitally important proteins losses must be calculated and compensated.

P287

Physiological response to superantigen-adsorbing hemoperfusion in toxin-concentration-controlled septic swine

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Introduction Superantigens are suspected of being potent initiators of Gram-positive sepsis, and new therapies for superantigen elimination are required. The effects of hemoadsorption with a superantigen-adsorbing device (SAAD) should be evaluated in septic swine. The aim of this study was to examine the efficacy of SAAD by sequential monitoring of physiological and serological parameters.
Methods Twelve landrace male pigs (25–38 kg) were mechanically ventilated and anesthetized with isofluorane. A Swan–Ganz catheter was inserted into the right jugular vein and the right carotid artery was used for the monitoring of blood pressure. The anti-toxic shock syndrome toxin-1 (anti-TSST-1) IgG antibody and anti-TSST-1 IgM antibody were under detection the level, as judged by ELISA. The LPS in the blood stream was also

under the detection level (<5 pg/ml). TSST-1 was infused at 2 μg/kg/hour, and the blood concentration was maintained at the clinical level for 6 hours, LPS (10 μg/kg/hours) was then infused to induce lethal shock. Heparin (200 U/kg/hour) was used as the anticoagulant. All animals were hemoperfused with SAAD or a control column for 8 hours and changes in pathological parameters and mortality were examined.

Results Animals perfused with SAAD had a highly significant ($P < 0.01$) survival advantage compared with control groups at 24 hours after initiation of TSST-1 infusion. SAAD also suppressed the increase in the arterio-venous shunt ratio and decrease of partial arterial oxygen pressure at 6 hours after TSST-1 infusion initiation.

Conclusion We suggest that there is a potential application of SAAD in treating superantigen-induced respiratory dysfunction and sepsis.

P288

Immunoadsorption of lipopolysaccharides, IL-6 and complement-activation product 5a in severe sepsis and septic shock

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Background In severe sepsis and septic shock, endotoxin (lipopolysaccharides [LPS]), IL-6 and complement-activation product 5a (C5a) trigger inflammatory cascades resulting in multiple organ dysfunction and failure of the cell-mediated immune system (immunoparalysis). This correlates with uncontrolled infection and fatal outcome. We therefore determined whether simultaneous removal of systemic LPS, IL-6 and C5a by selective immunoadsorption (IA) reduces hyperinflammation, reverses immunoparalysis and improves organ functions in patients with severe sepsis and septic shock.

Design In a prospective, controlled, open-label fashion, 29 patients with severe sepsis or septic shock hospitalized in the ICUs of a university hospital were included in a proof-of-concept trial (ISASS-1). Patients were enrolled between 2002 and 2004 and followed-up for 28 days, until hospital discharge or death.

Methods In addition to the best supportive ICU care, 11 patients (age 57.8 ± 2.2 years, Acute Physiology and Chronic Health Evaluation II [APACHE-II] score 23.7 ± 1.6) received extracorporeal LPS-IA, IL-6-IA and C5a-IA on 5 consecutive days for 7.5 hours each. As control, prognostically relevant parameters of 18 contemporary patients (age 55.2 ± 2.6, APACHE II score 22.9 ± 1.2) were followed up.

Results There was no difference between the study groups at baseline. Target molecules were reduced under IA: IL-6 (361.7 ± 116.0 to 38.2 ± 15.2 pg/ml, $P = 0.003$), C5a (297.6 ± 43.1 to 79.2 ± 14.5 ng/ml, $P < 0.001$) and markers of endotoxemia. In IA-treated individuals, IL-6 ($P < 0.001$), CRP ($P = 0.001$) and APACHE II score ($P = 0.002$) was significantly lower at day 7. Monocytic HLA-DR improved in IA patients ($P < 0.001$) and was unchanged in controls. HLA-DR recovered in all immunoparalytic patients under IA (4993.6 ± 1162 to 15,295.3 ± 2197 molecules/cell, $P = 0.002$).

Conclusions Immunoadsorption is a new, selective approach to target key inflammatory mediators in septic patients. Simultaneous targeting of LPS, IL-6 and C5a reduced major inflammatory mediators, reversed immunoparalysis and improved major disease severity scores.

P289

Hemoperfusion with an immobilized polymyxin B fiber column improves gastric mucosal pH with sepsis patients

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Objective A favorable prognosis has been reported for critically ill patients when the gastric mucosal pH (pHi) is improved at an early stage even if the pHi is low, but reports about the pHi in patients with sepsis are limited. We therefore studied the value of the pHi of sepsis patients whose global oxygen metabolism has been stabilized. In addition, we studied whether it would be able to improve the pHi of sepsis patients by using the direct hemoperfusion with an immobilized polymyxin B fiber column (DHP-PMX).

Materials and methods Before the start of DHP-PMX, the global oxygen metabolism and tissue oxygen metabolism were measured. A thermodilution catheter was used to determine the oxygen delivery index (DO_2I), oxygen consumption index (VO_2I), and oxygen extraction ratio (O_2ER) as parameters of global oxygen metabolism. A thermodilution catheter was also used to monitor hemodynamics and the fluid balance was managed to maintain the central venous pressure in the range of 7–10 mmHg. A gastric tonometer was used for measurement of pHi. Thirty-two patients with sepsis satisfying the following criteria were enrolled in the study: signs of systemic inflammatory response syndrome due to infection; mean arterial blood pressure >60 mmHg (irrespective of the use of catecholamines); and stable global oxygen metabolism ($DO_2I > 500$ ml/min/m^2 and $VO_2I > 120$ ml/min/m^2). DHP-PMX was performed twice within 24 hours (for 3 hours each time). The pHi and arterial blood gases were measured four times (before DHP-PMX as well as 24, 48, and 72 hours afterward). The Sequential Organ Failure Assessment (SOFA) score was calculated before DHP-PMX. The APACHE II score was also calculated to assess the severity of each patient's condition before DHP-PMX.

Results Twenty-six patients survived and were discharged from hospital, whereas the other six patients died. The cause of death was hepatic failure in two patients and cardiac failure in four patients. Forty-five bacterial strains were detected in 32 subjects and the most commonly isolated microorganisms were Gram-negative bacteria. DHP-PMX was performed in patients with Gram-negative or mixed Gram-negative and Gram-positive infections. Antibiotic therapy was judged to be adequate when the patient received antibiotics to which each isolated microorganism was sensitive. Although it was not possible to identify bacteria in four patients, cultures were positive in 28 patients and adequate antibiotic treatment was given to them. The SOFA score was 9.1 ± 1.0 and the APACHE II score was 20 ± 1.0 before DHP-PMX. All of the patients were on mechanical ventilation. The pHi was 7.22 ± 0.04 immediately before the start of DHP-PMX, 7.28 ± 0.03 ($P = 0.036$) at 24 hours afterward, 7.32 ± 0.03 ($P = 0.006$) at 48 hours afterward, and 7.34 ± 0.02 ($P = 0.0034$) at 72 hours afterward, showing a significant increase from 24 hours onward compared with the pretreatment value.

Conclusion These findings suggest that DHP-PMX improves the pHi. This was a prospective uncontrolled observational study including a limited number of patients. The results of larger, better powered, multicenter clinical trails are necessary if we are to assess accurately the benefit of DHP-PMX.

P290

The effect of polymixin B immobilized on fibers and continuous veno-venous hemodiafiltration on tetrahydrobiopterine and NO metabolites in septic patients

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Introduction Hemoperfusion with a column of polymixin B immobilized on fibers (PMX) increases the blood pressure too rapidly for the effect to be attributable to endotoxin removal. On the other hand, continuous veno-venous hemodiafiltration (CVVHDF) also has effects of increasing blood pressure in septic patients. Since inducible NO synthase (iNOS) is known to be involved in the profound hypotension, we hypothesized that a decrease of tetrahydrobiopterine (BH4), an essential cofactor of iNOS, might account for the rapid effect of PMX and CVVHDF on blood pressure, if PMX and CVVHDF can decrease BH4. In this study we therefore measured the plasma level of BH4 and NO metabolites (NOx) in septic patients, and evaluated whether PMX and CVVHDF can decrease them.
Methods With institutional approval and informed consent, we studied 14 septic patients (aged 67.1 ± 13.2 years). Fourteen healthy volunteers (aged 38.4 ± 10.3 years) served as controls for BH4 and NOx. Plasma BH4 was quantified by HPLC with fluorimetric detection.
Analysis All results are expressed as the mean ± SD, with statistical evaluation by a paired *t* test and unpaired *t* test and repeated-measures one-way ANOVA followed by Fisher's PLSD for multicomparisons.
Results The plasma level of BH4 in septic patients was indeed markedly elevated compared with that in volunteers (140.0 ± 148.1 vs 24.1 ± 4.8 pmol/ml, $P < 0.01$). Level of NOx was 140.3 ± 70 vs 28.7 ± 11.6 nmol/ml, $P < 0.01$). Comparison of BH4 and NOx concentrations at inflow and outflow of the PMX column or CVVHDF dialyzer confirmed significantly low values at the outflow.
Discussion and conclusion Several lines of experimental and clinical evidence indicate that hyperproduction of NO by iNOS contributes to the hypotension, cardiac depression and vascular hyporeactivity. However, the efficacy of NOS inhibitor in patients with septic shock failed to find any beneficial effect in terms of the incidence of noncardiovascular organ dysfunction. A possible explanation for these puzzling results may be the use of a nonspecific NOS inhibitor, which blocks both endothelial NO synthase (eNOS) and iNOS, since eNOS is necessary to inhibit adhesion of platelets and leukocytes to the endothelium and plays a protective role against inflammation. We hypothesized that removal of BH4 might decrease iNOS activity without greatly affecting the activity of eNOS, since eNOS has access to tissue stores of BH4, but NO generation from iNOS is critically dependent on BH4 availability. The marked increase in BH4 concomitantly with NOx in septic shock patients and its reduction by PMX or CVVHDF are consistent with our hypothesis, and appear to justify further research on BH4 removal as a potential therapeutic target. In conclusion, BH4 plays the greater role in inducing excessive vasodilatation in septic shock, and PMX or CVVHDF can decrease BH4 and NOx.

P291

Relationship between effect of polymyxin B-immobilized fiber and high-mobility group box-1 protein in septic shock patients

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Introduction Septic shock remains a major cause of multiple organ failure with a high mortality rate. A relationship between high-mobility group box-1 protein (HMGB-1) and septic shock was recently reported. On the other hand, treatment of direct hemoperfusion with polymyxin B-immobilized fiber column (PMX; Toray Industries Inc., Tokyo Japan) was developed in Japan in 1994 and has been used for treatment of septic shock of endotoxemia. Reduction of the serum endotoxin level by PMX has been recognized. Clinical effectiveness data of this column have also been reported, for example increasing the systolic blood pressure and improvement of the systemic vascular resistance index. Although a decrease of inflammatory cytokine after direct hemoperfusion with PMX has been reported, the detailed mechanism of PMX is not known.
Patients and methods We treated 10 septic shock cases by direct hemoperfusion with PMX. All patients were diagnosed with sepsis according to the criteria of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference and required intensive care for unstable circulation state. We measured the HMGB-1 level at three points; before direct hemoperfusion with PMX, after direct hemoperfusion with PMX and 12 hours afterward. We also examined clinical data; systolic blood pressure and Sepsis-related Organ Failure Assessment (SOFA) score.
Results There were five peritonitis cases and five severe pneumonia cases. Five cases admitted the decrease of the HMGB-1 value immediately before and after direct hemoperfusion with PMX implementation. Especially in five peritonitis cases, the HMGB-1 value at 12 hours compared with that before direct hemoperfusion with PMX implementation had decreased in all cases. Increasing systolic blood pressure was confirmed in three cases and a decrease of HMGB-1 was admitted in five cases. Before and after direct hemoperfusion with PMX, there was significant correlation ($P = 0.0384$) of systolic blood pressure reaction and HMGB-1 decrease.
Discussion The possibility of the adsorption of HMGB-1 by direct hemoperfusion with PMX has been shown. Also, the possibility that the adsorption of HMGB-1 was the factor of the morbid state improvement by direct hemoperfusion with PMX was suggested.

P292

Extracorporeal albumin dialysis in paediatric patients with sepsis and multiorgan dysfunction

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Introduction Extracorporeal membrane oxygenation (ECMO) is used in managing paediatric patients with severe cardiorespiratory dysfunction refractory to conventional treatments. The survival in such patients is reported to be between 45% and 70%. However, the survival of paediatric patients on ECMO with multiorgan

dysfunction in the setting of sepsis is very low, with a reported mortality of 100%. We report a series of five paediatric patients with sepsis and multiorgan dysfunction who were managed by extracorporeal albumin dialysis (EAD) during their course on ECMO.

Patients and methods All paediatric patients with sepsis-induced multiorgan dysfunction who were treated in our unit with ECMO and EAD were included. Patients who were treated with EAD mainly for high bilirubin in the absence of evidence of severe sepsis were excluded. All patients fulfilled the criteria for severe sepsis as suggested by the ACCP/SCCM Consensus Conference Committee. EAD was performed using a molecular adsorbent recirculating system (Gambro AB, Stockholm, Sweden).

Results The age of the patients ranged between 1 month and 17 years. The primary diagnosis was pneumonia in four patients (bacterial in three patients and viral in one patient) and meningococcal septicaemia in one patient. All patients had positive bacterial cultures and two patients also had positive viral serology at the time of admission for ECMO. All patients had cardiac and respiratory dysfunction at the time of admission for ECMO. In addition two patients had renal dysfunction and one patient each had hepatic and haematological dysfunction at the time of admission for ECMO. All these patients deteriorated subsequently and EAD was used as rescue therapy. At the time of institution of EAD four patients had dysfunction of four organs (respiratory, cardiac, renal and liver) and one patient had dysfunction of five organs (respiratory, cardiac, renal, liver and haematological dysfunction). All patients received between one and three EAD treatments. Two out of the five patients (40%) survived to hospital discharge. All these patients would have been expected to die according to our previous experience as well as the published results in such a group of patients.

Conclusion EAD may prove to be an effective treatment in paediatric patients with sepsis-induced multiorgan dysfunction. Further research is required to identify the group of patients who would benefit most from the use of EAD in the setting of sepsis-induced multiorgan dysfunction.

P293

Dialytic techniques in critical patients: slow low-efficient daily dialysis or CVVHDF?

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Introduction In critically unstable patients, conventional dialysis is difficult to perform and continuous methods have been the treatment of choice. The use of mixed dialytic techniques such as slow low-efficient daily dialysis (SLEDD) offers the combined advantages of conventional haemodialysis and continuous dialytic techniques.

Objectives To compare the costs/efficacy/efficiency as well as nurse care between SLEDD and continuous techniques (CVVHDF).

Materials and methods A retrospective and comparative study was performed considering both methods from 1 October 2003 to 31 March 2004. The study evaluated the following parameters: number of patients enrolled, age, gender, number of procedures, APACHE II score, SAPS II score, heparin consumption, volume extracted, duration of procedures, blood pumping speed, BUN clearance and costs.

Results The authors compared SLEDD with 24-hour CVVHDF. The urea clarification rate with SLEDD was 48.3% compared with 37% with CVVHDF; creatinine clearance in SLEDD was 43% compared with 31.7% with CVVHDF; economic advantages were also compared per technique (€37.50 vs €235 in SLEDD and CVVHDF, respectively). Heparin used in SLEDD was 4400 IU compared with 12,000 in CVVHDF.

Conclusion SLEDD was more efficient in removing urea and creatinine and was well tolerated in haemodynamically unstable patients. Each SLEDD session was six times less expensive than each 24-hour session of CVVHDF. SLEDD also permitted access to daily dialysis in more patients, a lower nurse workload and better time management in patient care.

P294

Infection in ICU patients with acute kidney injury treated with renal replacement therapy

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Introduction Patients with chronic kidney disease have decreased immunity and increased risk for infection. We evaluated the occurrence rate of infection in ICU patients with acute kidney injury, and its impact on hospital mortality.

Methods Retrospective evaluation of all ICU patients with acute kidney injury treated with renal replacement therapy (RRT) during a 5-year period (2000–2004) in the 22-bed SICU, eight-bed CSICU, and six-bed Burn Unit of a Belgian tertiary care hospital. Infection was scored based on chart review, and the pharmacy database on antibiotic prescription.

Results During the study period 406 patients were included. The median (IQR) age was 64 (53–73) years, 68% of patients were male, and the APACHE II score was 24 (17–30). At the start of renal replacement therapy, 69% of patients were treated with vasoactive therapy, and 73% were ventilated. Infection occurred in 87% of patients; 38% had more than one infection. The start of infection was during the treatment period with RRT in 41.4% of all infections, and in 58.6% before or after the treatment period with RRT. The incidence rate of infection was 5.92 per 100 patient-days. Patients who developed infection had a longer length of stay in the ICU (7 [15–31] days vs 5 [3–7] days; $P < 0.001$). There was no difference in mortality between patients with and without infection (62.5% respectively 54.9%, $P = 0.295$). Infection was not associated with inhospital mortality, even after adjustment for age, type of ICU admitted to, APACHE II score, and severity of illness at start of RRT (i.e. treatment with vasoactive therapy) or mechanical ventilation (odds ratio for inhospital death: 0.52 [0.21–1.28], $P = 0.152$) (logistic regression analysis).

Conclusions In this cohort of ICU patients with acute kidney injury and treated with RRT, infection had a high occurrence rate of almost 90%. Also, more than one-third of these patients had more than one infection episode. Infection was not associated with increased inhospital mortality.

P295

Long-term mortality of critically ill patients with acute renal failure requiring renal replacement therapy: a 5-year population-based cohort study

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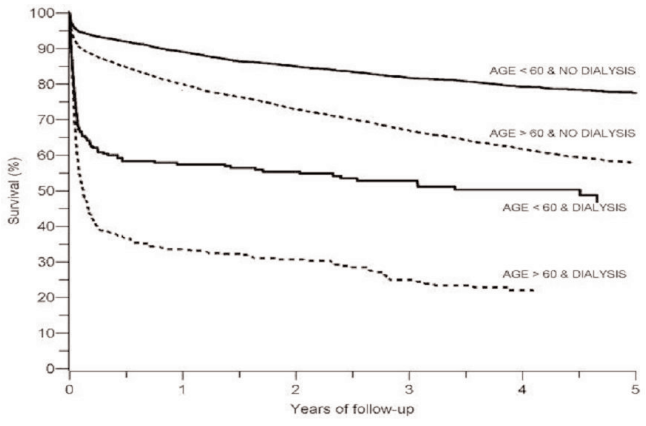
Background Despite evidence of a notoriously high short-term mortality of critically ill patients with acute renal failure (ARF), requiring renal replacement therapy (RRT), limited data exist on medium-term and long-term mortality of these patients.

Objective To examine 90-day and 5-year mortality of critically ill patients with ARF, requiring RRT, compared with critically ill patients without ARF, requiring RRT.
Design A population-based cohort study.
Methods Aarhus University Intensive Care Study Cohort enabled us to identify all patients, aged 15 years or more, with first-time admission to three multidisciplinary ICUs within Aarhus University Hospital from 1999 to 2003. We obtained information on the presence of ARF requiring RRT through the study cohort. Complete follow-up on mortality was obtained from the Danish Civil Registration System. We constructed Kaplan–Meier survival curves, based on the date of ICU admission, for the main study variables (RRT: yes/no and age groups: 15–59, 60+ years) and computed contingency tables for 90-day and 5-year mortality. We computed 90-day mortality rate ratios (MRR) and 5-year MRR for patients surviving 90 days, stratified on age group.
Results We identified 16,038 patients with a first-time ICU admission; 685 (4.3%) of those had ARF requiring RRT. The median age was 66.2 years (range 17.7–89.7) among patients with ARF requiring RRT, and 63.8 years (range 15.1–101.7) among those without ARF. Ninety-day and 5-year mortality among patients with ARF requiring RRT, aged 60+ years, was 60% and 79%, compared with 39% and 53% among those younger than 60 years (see Fig. 1). The 90-day MRR for patients with ARF requiring RRT aged 15–59 and 60+ years was 6.8 (95% CI: 5.5–8.5) and 6.2 (95% CI: 5.4–7.1) when compared with patients without ARF requiring RRT. In comparison, the corresponding 5-year MRR for patients surviving the first 90 days after ICU admission was 1.3 (95% CI: 0.8–2.0) and 1.6 (95% CI: 1.2–2.1), respectively.
Conclusion ARF requiring RRT in critically ill patients is associated with a substantial increase in medium-term mortality, most markedly among elderly patients. However, among critically ill patients with ARF requiring RRT who survive the first 90 days after ICU admission, the 5-year mortality seems to be only slightly increased.

Figure 1 (abstract P295)



P296

Outcome of patients treated with renal replacement therapy for acute kidney injury

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Background Despite improvement of therapy, mortality remains constant for patients with acute kidney injury (AKI) treated with renal replacement therapy (RRT). The aim was to evaluate the mortality of AKI-RRT patients over a 10-year period.
Methods A retrospective study on all ICU patients with AKI-RRT in a tertiary-care ICU. Data are presented as the number (interquartile range) or proportion.
Results Over a 10-year period, 1330 ICU patients had AKI-RRT. Results per year are presented in Table 1. Outcome improved (hazard ratio [HR] [/year] = 0.95 [0.93–0.98], $P < 0.001$). This trend to improved outcome remained, even after adjustment for age, APACHE II score, vasopressor use or mechanical ventilation at the start of RRT: HR (/year) = 0. 96 [0.94–0.99], $P = 0.002$).

Table 1 (abstract P296)

Year	*n*	Age (years)	APACHE II score ($P < 0.01$)	Mechanical ventilation (%)	Vaso-pressors (%)	Dead (%) ($P < 0.01$)
1995	122	62 (19)	26 (16)	67.2	63.9	72.1
1996	125	63 (17)	24 (12)	66.4	68.0	74.4
1997	126	61 (19)	25 (13)	70.6	73.8	77.0
1998	123	64 (20)	25 (13)	65.9	68.3	65.9
1999	106	66 (17)	26 (12)	56.6	66.0	62.3
2000	101	63 (21)	29 (13)	75.2	69.3	68.3
2001	149	66 (21)	21 (11)	71.8	70.5	57.4
2002	149	63 (22)	29 (10)	67.8	75.2	65.1
2003	173	64 (22)	26 (11)	70.5	76.3	64.7
2004	156	64 (20)	19 (9)	67.3	61.5	52.6

Conclusions Over a 10-year observation period we observed an improvement in survival for ICU patients with AKI-RRT.

P297

Prognostic value of early vs late acute renal dysfunction in the critically ill obstetric patient

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Introduction Acute renal dysfunction/failure (ARF) is newly considered as an independent mortality risk factor in the ICU [1]. The time of onset of ARF could have a prognostic impact.
Objective To determine prognosis of acquired vs not acquired renal dysfunction.
Methods Retrospective analysis of prospectively collected data as part of the APRiMo study [2]. We defined ARF as serum creatinine level >100 µmol/l. We defined the early ARF group (E) as renal dysfunction that occurred during maternity management (less than 24 hours before transfer to the ICU) or at day 1 of ICU admission. The late ARF group (L) was defined as renal dysfunction occurring from day 2 of ICU admission. Inclusion criteria: critically ill obstetric patients presenting with one or more of the presenting conditions: severe pre-eclampsia/eclampsia, postpartum haemorrhage, stroke, HELLP syndrome, hemolytic uremic syndrome, and so on. Exclusion criteria: length of stay in the ICU <2 calendar days, chronic renal failure. Setting: patients first managed in a tertiary referral maternity for high-risk pregnancies, then transferred to our independent multidisciplinary ICU. Collected data: demographic, obstetric management, daily SOFA score. Main outcome of interest: vital status at ICU discharge. Adequate statistical tests were used (*t* test, chi-square test, etc.). $P < 0.05$ was considered significant.

Results Six hundred and forty patients, overall mortality 13.3%, included $n = 223$: 193 in group E and 30 in group L. There was no difference in demographic data, main admission diagnosis between E and L groups. Mean maximum creatinine level: group E = 270 μmol/l, group L = 220 μmol/l ($P = 0.15$). Renal replacement therapy: 30/193 and 7/30 ($P = 0.3$). Comparing group L vs group E: L had a higher mortality rate (73% vs 20.7%; $P < 0.001$), duration of mechanical ventilation (5.8 ± 1 vs 3.5 ± 0,26; $P = 0,001$), rate of massive transfusion in the ICU (13/30 vs 34/193; $P = 0.003$) and length of stay (8.9 vs 6.2, $P = 0.03$). Mean day 1 MOD score summing organ dysfunctions without renal dysfunction: 7.6 ± 3.3 vs 5.5 ± 4 ($P = 0.45$). Mean total maximum MOD score (TM_MODS):11 ± 6 vs 6 ± 5, $P = 0.001$. For group E, nonsurvivors (NS) showed significantly more unstable haemodynamic state with a lower diastolic arterial pressure ($P = 0.007$), uterine atonia ($P = 0.001$), transfusion rate in the labor ward/operating room and ICU stay than survivors (S). For group L, NS vs S: mean MODS at day 1 ICU admission 8.1 ± 3.7 vs 6.2 ± 2.7, $P = 0.15$), mean TM_MODS (16.2 ± 3.3 vs 7.8 ± 3.1, $P < 0.001$). NS were paradoxically younger than the S (29 years vs 35 years, $P < 0.01$). Duration of mechanical ventilation was higher among NS ($P = 0.001$). The main diagnosis of admission was postpartum hemorrhage complicating HELLP syndrome or sepsis. Three organ failures lasting >2 days (renal failure not counted) is associated with 100% mortality ($n = 17$).

Conclusion Acquired ARF is an important prognostic factor. It is more serious than early ARF for the same level of serum creatinine.

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P298

Effects of autotransfusion on sublingual microvascular perfusion in hemodialysis patients before and after ultrafiltration

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Critical Care 2006, **10(Suppl 1):**P298 (doi: 10.1186/cc4645)

Background Passive leg raising (PLR) can be used effectively to treat hypotension associated with hypovolemia by autotransfusion. We investigated the microvascular response to autotransfusion by PLR before and after ultrafiltration in patients on hemodialysis.

Patients and methods Patients who were on chronic intermittent hemodialysis were assessed for sublingual microvascular flow by sidestream darkfield (SDF) imaging before and 1 min after PLR (45° upward) before and after ultrafiltration (UF). Sublingual capillary flow was estimated using a semiquantitative microvascular flow index (MFI) in small (diameter 10–25 μm), medium (25–50 μm), and large-sized (50–100 μm) microvessels (0 = no flow; 1 = sludging [0–0.5 mm/s], 2 = moderate flow [0.5–1.0 mm/s], 3 = high flow [1.0–3.0 mm/s]). Changes were evaluated with nonparametric paired Wilcoxon test. Associations were determined with the sign test. $P < 0.05$ was judged to indicate a significant difference.

Results Sixteen patients took part in the study. The underlying disease causing renal insufficiency was predominantly hypertension (HT, $n = 6$) and diabetes mellitus ($n = 6$). At the start of ultrafiltration, PLR did not alter the microvascular flow (P = NS). After UF (median volume extraction 2.8 l) the capillary MFI increased in most patients after PLR ($P < 0.01$), whereas flow was not affected in large-sized microvessels (P = NS). The change in capillary MFI before and after UF was related to the UF volume in HT patients ($P = 0.01$), but not in the other patients.

Conclusion Autotransfusion by PLR improves sublingual capillary microvascular perfusion in hypovolemia after UF. SDF imaging and PLR may be a useful bedside tool to evaluate the patient's volume status. In this small dataset, the finding that derangement of microvascular perfusion after UF occurs predominantly in HT patients merits further studies.

P299

Recognition and management of intra-abdominal hypertension and abdominal compartment syndrome in Australasia

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Objective To determine ICU awareness regarding measurement of intra-abdominal pressure (IAP), features of intra-abdominal hypertension (IAH), and management of abdominal compartment syndrome (ACS).

Methods The survey explored experience, measurement methods and understanding of IAP, causes of IAH and management of ACS.

Results Ninety-two percent of the ICU Registrars used IAP but 52% only infrequently. While 90% understood that IAP can cause rises in intraperitoneal pathology, retroperitoneal causation of IAH was poorly understood. Ninety-two percent correctly said that ACS should be treated by abdominal decompression. Only 70% of our respondents would not perform CT of the abdomen predecompression. Thirty-three percent erroneously said that they would treat IAP >30 mmHg regardless of organ dysfunction and another 22% were unsure of the threshold of therapy for ACS.

Table 1 (abstract P299)

No.	Question	Yes (%)	No (%)	Unsure (%)
1	IAP is measured by instilling 50 ml saline into the Foley catheter and then transducing the pressure	50	16	34
2	IAP rises due to intraperitoneal pathology	95	0	5
3	IAP rises due to retroperitoneal pathology	56	22	22
4	IAH is an epiphenomenon and not a phenomenon	16	16	68
5	IAH + organ dysfunction defines ACS	69	9	22
6	ACS should be treated regardless of the IAP	63	13	24
7	ACS is an epiphenomenon and not a phenomenon	13	38	49
8	ACS should be treated only if there is lactic acidosis	3	83	14
9	Before treating ACS, a contrast-enhanced CT scan of the abdomen should always be done	9	71	20

Conclusions Australasian Fellows appreciate IAP measurements and manage ACS appropriately. Retroperitoneal causes of IAH and the threshold for treatment for ACS were poorly understood.

P300

Technique of temporary abdominal closure in abdominal compartment syndrome for preventing environmental contamination: seal and continuous high-pressure aspiration

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Critical Care 2006, **10(Suppl 1):**P300 (doi: 10.1186/cc4647)

Objective In abdominal compartment syndrome (ACS), which is known as a lethal complication with severe peritonitis or

intraperitoneal and retroperitoneal massive bleeding, we often cannot close the abdominal wound and have to adopt a strategy called open abdomen because of intestinal and retroperitoneal bulky edema. Exudate and blood in these cases is too massive to be completely absorbed by dressing gauze. Spilled exudate and blood from an abdominal open wound and dressing gauze easily causes contamination to the environment. We can prevent contamination by the exudate and bleeding with the 'seal and continuous high pressure aspiration method (S-CHPA)'. The aim of this study is to clarify the usefulness of SCHPA.

Patients and methods The procedure of S-CHPA was as follows; a sump tube wrapped in gauze was inserted in the abdominal open wound apart from the wound, and the wound was sealed by a surgical drape. We examined the spread of contamination of exudate and blood from the abdominal wound, the volume of exudate and blood from the abdominal wound, the frequency of dressing change, and complications due to S-CHPA or the open abdomen in seven patients with ACS.

Results Concerning the spread of contamination of exudate and blood from the abdominal wound, there was no contamination to the environment because of complete aspiration with a completely sealed negative-pressure system, and aspirated exudate and blood in the disposable bag was wasted as a closed system without spreading contamination. No exudate and blood spilled over beyond the sealed drape and closed system. Exudate and blood was completely aspirated into the disposable bag, whose weight was able to be accurately and easily measured (247 ± 269 g/hour). On the contrary, the volume of exudate and blood soaked into the gauze dressing the wound and the drain was only 6 ± 16 g/day.

The frequency of dressing change except for the daily routine one was 0 per day in this procedure. There are no complications concerning S-CHPA and infectious complications due to foreign bodies such as plastic infusion bag or massive sponge reaft in the peritoneal cavity.

Conclusion S-CHPA is a useful procedure for open abdomen patients to prevent contamination to the environment. This procedure is also useful for exact measuring of fluid loss and blood loss, exact evaluation of the total water balance, and the saving cost of dressing sponges and costs of labor for dressing changes.

P301

Abdominal compartment syndrome following rectus sheath hematoma: bladder-to-gastric pressure difference as a guide to treatment

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Introduction Rectus sheath hematoma (RSH) is a well-recognised complication of low molecular weight heparin (LMWH). In the past, surgeons were reluctant to operate on RSH. Increased intra-abdominal pressure (IAP) and abdominal compartment syndrome (ACS) have been reported in association with RSH. IAP is usually measured via the bladder (IBP) but can be increased compared with gastric pressure (IGP). We report two cases of ACS caused by LMWH-induced RSH where simultaneous IBP-IGP was recorded. We hypothesized that a high bladder-to-gastric-pressure difference was a marker of localised ACS, whereas a low bladder-to-gastric-pressure difference was a marker of systemic ACS.

Methods IGP was measured with the Spiegelberg IAP catheter (Spiegelberg, Hamburg, Germany) and IBP with the FoleyManometer (Holtech Medical, Copenhagen, Denmark).

Patients *First case* An 81-year-old woman was admitted with LMWH-induced RSH-related cardiorespiratory failure. The SAPS II score was 61, APACHE II score 28, and SOFA score 12. The IBP rose from 2 mmHg on day 1 to 40 mmHg on day 3 and IGP from 19 to 38, respectively; this together with organ failure lead to the diagnosis of ACS. The mean bladder-to-gastric-pressure difference was 1.1. She was intubated and ventilated, on high FiO_2 and vasopressors. On day 3 she deteriorated dramatically and a surgical 'rescue' evacuation of the hematoma (3 l) was performed. This resulted in a drop of IBP to 18 mmHg postoperative and 11 mmHg over the following days. She regained spontaneous diuresis a couple of hours after decompression, vasopressors were stopped the next day and she was weaned from the ventilator the day after. She was discharged on day 10.

Second case A 77-year-old man was admitted following respiratory distress, lactic acidosis and (pre)renal insufficiency related to LMWH-induced RSH. The SAPS II score was 49, APACHE II score 25, and SOFA score 4. The IBP was 24 mmHg on day 1 while the IGP was only 5.5 mmHg. He was intubated later that day. The high IBP together with cardiorespiratory failure lead to the diagnosis of localised ACS (normal IGP). The mean bladder-to-gastric-pressure difference was 6.1. He was treated conservatively with sedation + curarisation, resulting in normalisation of IBP. On day 14 he was extubated and regained diuresis. He was discharged on day 24.

Conclusion IBP can be increased by RSH. This does not always imply ACS, even in the presence of organ failure. We suggest using the bladder-to-gastric-pressure difference to differentiate between a localised or systemic ACS. Only the latter should be treated with decompressive surgery.

P302

Prognostic value of abdominal perfusion pressure in mechanically ventilated patients

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Introduction Intra-abdominal hypertension (IAH) is an important outcome-predictor in critically ill patients [1,2]. Abdominal perfusion pressure (APP = MAP – IAP) is suggested as a better resuscitation endpoint [3]. Until now no prospective data have been available looking at the effect of IAP and APP on outcome in patients with acute respiratory failure (ARF) that are mechanically ventilated (MV).

Methods Over a 12-month period patients admitted with ARF were studied prospectively. Patients were screened for IAH (defined as IAP >12 mmHg) with the FoleyManometer method (Holtech, Kopenhagen, Denmark). The IAP was recorded four to six times daily together with the highest and lowest APP, fluid balance, and SOFA score. Until now data have been collected on 142 patients (127 medical and 15 surgical). The major endpoint was ICU mortality. Values are the mean ± SD. The unpaired Student *t* test was used.

Results BMI was 25.1 ± 5.2, male/female ratio 1/1, age 63.9 ± 16.3 years, APACHE II score 23.8 ± 10.2, SAPS-II 52.3 ± 17.3. The SOFA score on day 1 was 9.4 ± 3.6 with 2 ± 1 organ failures. IAP on day 1 was 10.4 ± 3.9 mmHg, while APP was 58.2 ± 15.5. Intra-abdominal hypertension was present in 33.1%. Mortality was 52.9%. The outcome did not differ between patients with or without IAH. Nonsurvivors had a significantly ($P < 0.05$) higher IAP by day 4, but the APP was already significantly lower (<55 mmHg) from day 1 onwards. There was a more positive daily and cumulative net fluid balance in nonsurvivors and the extravascular lung water was also significantly higher on admission in the nonsurvivors.

Conclusion The preliminary results of an ongoing prospective trial, and the first looking at APP in ARF, show that the incidence of IAH is high in ARF. Mortality is also high but in correlation with the severity scores. The persistence of IAH by day 4 was able to discriminate between survivors and nonsurvivors. However, the presence of a low APP (<55 mmHg) was already able to discriminate between survivors and nonsurvivors from day 1 onwards. Close monitoring of IAP and especially APP seems warranted in patients with ARF.

Acknowledgement Grant from the ESICM Chris Stoutenbeek Award 2003.

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P303

Influence of intra-abdominal hypertension on renal artery and vein flow in the porcine kidney

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Background In man, intra-abdominal hypertension (IAH) has been shown to impair renal perfusion due to decreased renal artery flow (RAF). Renal venous hypertension and decreased renal venous flow (RVF) are other potential contributing mechanisms. We used a porcine model of IAH to evaluate the role of RVF and renal venous pressure (RVP) in renal dysfunction due to IAH.

Methods We studied nine anesthetized and ventilated pigs in the prone position (46 ± 3 kg) after insertion of a renal vein catheter and after placement of flow probes around the renal artery and vein. Following baseline measurements, RAF, RVF and RVP were measured during incremental intra-abdominal pressure (IAP) levels (10, 20 and 30 mmHg during 45 min each) by infusing warmed saline into the peritoneal cavity. Standard hemodynamic parameters, obtained from Swan–Ganz monitoring, were also recorded.

Results RAF and RVF decreased in parallel at an IAP of 20 and 30 mmHg (Table 1) without dropping to zero flow. RVP paralleled the increase in IAP, but always exceeded IAP by 3–4 mmHg. Renal perfusion pressure (RPP = MAP – RVP) decreased significantly with increasing IAP, in spite of significantly increased MAPs. RAF/CO decreased from 44% to 34%, indicating a flow redistribution away from the kidney in IAH. In parallel, renal vascular resistance (RVR = RPP / RAF) increased from 0.75 to 1.1 mmHg.min/ml with increasing IAP (Table 1).

Table 1 (abstract P303)

	IAP			
	Baseline (6 mmHg)	10 mmHg	20 mmHg	30 mmHg
RVP (mmHg)	10 ± 2	13 ± 2*	24 ± 2*	33 ± 2*
RPP (mmHg)	92 ± 4	91 ± 5	89 ± 5	82 ± 5*
RVF (ml/min)	144 ± 10	155 ± 10	140 ± 9	112 ± 9*
RAF (ml/min)	182 ± 11	174 ± 11	151 ± 11*	127 ± 10*
RAF/CO (%)	44 ± 6	35 ± 6	38 ± 6	34 ± 6*
RVR (mmHg.min/ml)	0.75 ± 0.5	0.89 ± 0.6	0.99 ± 0.8	1.10 ± 0.8*

*$P < 0.05$ vs baseline.

Conclusion Decreased renal perfusion in IAH is not only due to decreased RAF, but also due to a regional effect of redistribution away from the kidney. Renal venous hypertension can account for this observation.

P304

Aggressive resuscitation prevents gut ischemia due to intra-abdominal hypertension in LPS-induced shock

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Critical Care 2006, **10(Suppl 1):**P304 (doi: 10.1186/cc4651)

Introduction Septic patients may develop intra-abdominal hypertension (IAH) with decreased SMA flow and gut ischemia. The effect of aggressive resuscitation on IAH and gut dysfunction in sepsis has not been well studied.

Hypothesis Aggressive resuscitation in sepsis prevents gut ischemia despite IAH.

Methods Seven pigs were used for intervention and three pigs served as controls. All pigs were sedated and ventilated, and arterial, PA and SMV catheters were inserted. SMA flow was measured with an intra-abdominal transonic flowmeter and IAP was measured directly. Intervention animals received 80 µg *E. coli* 0127:B8 LPS i.v. over 1 hour. Blood samples were taken and hemodynamics measured before and hourly after LPS. Saline and norepinephrine were used for resuscitation (target MAP > 65 mmHg, urine > 0.5 ml/kg/hour, mixed venous SO_2 > 70%). SO_2 was maintained >85%. ANOVA analysis was used for result evaluation.

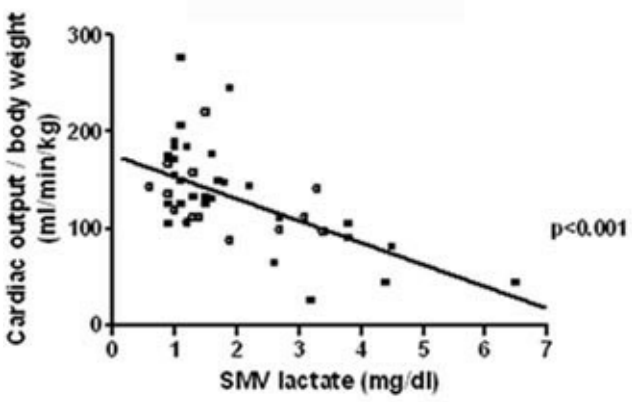
Results After i.v. LPS administration, the animals developed shock and three succumbed after 6 hours. The MAP, CO, DO_2 and VO_2 were stable until animals were moribund. We saw a positive correlation between infused volume and IAP. The IAP exceeded 30 mmHg by 6 hours. However, the abdominal perfusion pressure,

Table 1 (abstract P304)

Time (hours)	CO (ml/min/kg)	MAP (mmHg)	IAP (mmHg)	SMA DO_2 (ml/min)	SMV lactate (mg/dl)
0	121 ± 9	86 ± 7	9 ± 1	492 ± 69	2.2 ± 0.4
2	143 ± 15	73 ± 7	15 ± 2	568 ± 71	1.7 ± 0.3
4	143 ± 11	80 ± 8	22 ± 2*	493 ± 63	1.5 ± 0.3
6	115 ± 23	69 ± 5	34 ± 2*	249 ± 124	2.8 ± 0.7

*$P < 0.001$.

Figure 1 (abstract P304)



Cardiac output versus SMV lactate.

SMA flow and SMV lactate were unchanged as long as CO and CI were stable. CO and CI correlated inversely with SMV lactate. No changes in the IAP were observed in the control animals.
Conclusions Significant IAH develops in a model of LPS sepsis. However, gut ischemia is prevented by adequate CO and intestinal DO_2.

P305

Does intravesical pressure as an estimation of intra-abdominal pressure predict effects on portal circulation?

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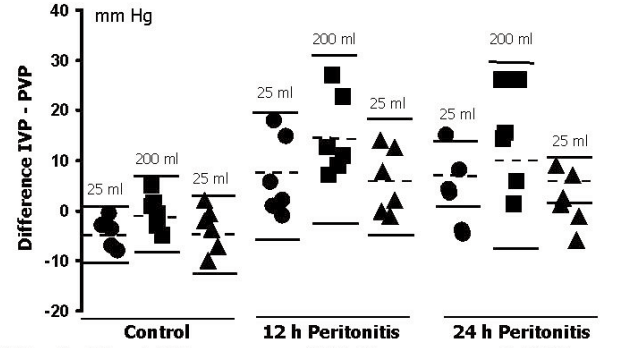
Critical Care 2006, **10(Suppl 1):**P305 (doi: 10.1186/cc4652)

Introduction In the clinical setting, the measurement of intravesical pressure (IVP) has evolved to the gold standard for estimating intra-abdominal pressure (IAP) in critically ill patients. However, in order to study the interplay between flow and pressure in selected regions of the splanchnic circulation (e.g. in the portal vein), direct pressure measurements might be indispensable once IVP proves not accurate enough as an indirect estimate. The intention of our present study was therefore to compare IVP, a surrogate measure of IAP, and portal vein pressure (PVP) simultaneously with portal vein flow (Qpv) measurements in a pig model of fecal peritonitis.
Methods In six anesthetized, mechanically ventilated, and instrumented pigs fecal peritonitis was induced by inoculating autologue feces pellets suspended in saline. The IVP, PVP, and Qpv were measured before as well as 12 and 24 hours after peritonitis induction. The IAP was measured by sequentially filling with 25 and 200 ml urine and subsequently re-empting the bladder to 25 ml. The Qpv was measured by ultrasound Doppler flowmetry. IVP values at each filling step were compared with the simultaneously recorded PVP values using a Bland–Altman plot.
Results During peritonitis, IVP overestimates PVP, especially when the bladder is filled with large fluid volumes (200 ml). Furthermore, under these conditions even the precision of IVP as an estimate of PVP vanishes, as shown in the plots by the larger SD. Regardless of the increases in IVP and PVP, Qpv also increased with peritonitis.
Conclusions We conclude that IVP should be interpreted cautiously as an estimate of IAP in the presence of fecal peritonitis in pigs. Under these experimental conditions, the use of a rather small filling volume is recommended to increase the accuracy of the measurements. IVP (and PVP) alone do not predict effects on portal vein flow, at least up to moderately increased levels.
Acknowledgement MM was supported by a grant from the Alexander von Humboldt Stiftung.

Figure 1 (abstract P305)



	Control	12 h Peritonitis	24 h Peritonitis
$IVP_{25\ ml}$ (mm Hg)	6 [4;7]	21 [18;24]	24 [21;24]
$IVP_{200\ ml}$ (mm Hg)	9 [9;10]	31 [25;34]	33 [30;35]
$IVP_{25\ ml}$ (mm Hg)	6 [4;7]	20 [19;23]	21 [18;26]
PVP (mm Hg)	9.0 [6;12]	16 [12;19]	18 [16;26]
Q_{pv} (ml / min)	935 [907;940]	1175 [1130;1467]	1810 [1285;1960]

P306

Influence of intra-abdominal hypertension on microvascular flow in the porcine renal cortex

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Critical Care 2006, **10(Suppl 1):**P306 (doi: 10.1186/cc4653)

Background In man, intra-abdominal hypertension (IAH) has been shown to impair renal perfusion. Renal microcirculation is difficult to study *in vivo* and little is known about the effect of increased intra-abdominal pressure (IAP) on kidney microcirculation. For the first time, we evaluated renal cortex microcirculation with side-stream dark field (SDF) imaging in a porcine model of IAH.
Methods We studied five anesthetized and ventilated pigs (46 ± 3 kg) during incremental IAP levels (10, 20 and 30 mmHg during 45 min each) by infusing warmed saline into the peritoneal cavity. The renal venous pressure (RVP) was measured with a renal vein catheter. After right mini-lumbotomy and gentle removal of the renal capsule, the SDF device was positioned intermittently on the renal cortex, avoiding pressure artefacts. Subsequently, representative video-clips (10 s) were captured and the microvascular flow index (MFI) was scored blindly by three independent observers, based on the semiquantitative method of Boerma and colleagues [1].
Results The MFI decreased significantly from 2.51 ± 0.30 to 1.76 ± 0.26 ($P < 0.03$) when the IAP increased from 10 to 30 mmHg. The RVP increased significantly from 10 ± 4 to 34 ± 5 mmHg ($P < 0.00003$) with the IAP increasing from 6 to 30 mmHg. There was an inverse correlation ($r = -0.63$, $P < 0.003$) between the MFI and RVP (Fig. 1).
Conclusion Increased IAP impairs renal cortex microcirculation in a porcine model of IAH. Renal venous hypertension may account for this observation.

Reference

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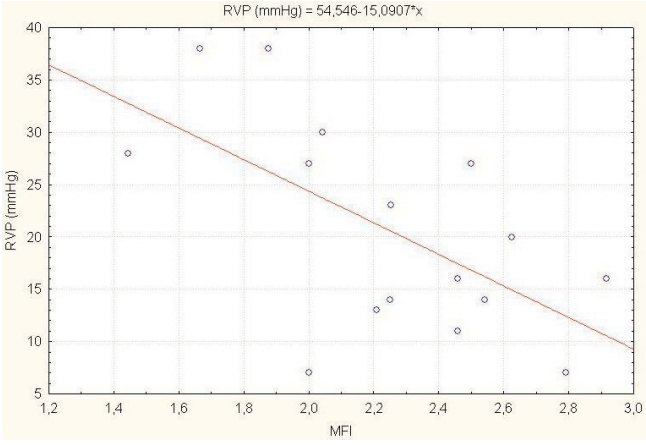
Figure 1 (abstract P306)



P307

Ultralow volumes in transvesical intra-abdominal pressure measurement

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Critical Care 2006, **10(Suppl 1):**P307 (doi: 10.1186/cc4654)

Background Intra-abdominal pressure (IAP) is measured routinely in patients at risk for intra-abdominal hypertension (IAHT) and abdominal compartment syndrome. Transvesical measurement of the IAP has become most widely used technique, but concerns remain about its accuracy. We recently showed that the use of 50 or 100 ml saline for measurement may lead to overestimation of the IAP. The goal of this study was to determine the minimal instillation volume at which an IAP curve can be obtained, and to study bladder compliance at volumes below 20 ml.
Methods Intra-abdominal pressure was measured transvesically using a custom-designed IAP monitoring set (BBraun, Zaventem, Belgium) in 10 critically ill patients at risk for IAHT. Mean age of the patients was 56 years. Four patients were admitted to the ICU after an emergency abdominal surgical procedure or abdominal trauma, the other patients were referred to the ICU because of acute liver failure with ascites ($n = 3$), severe sepsis ($n = 1$), hemorrhagic shock ($n = 1$) or retroperitoneal bleeding and hematoma ($n = 1$). Measurements were performed after a median 1 day of bladder drainage.
After priming the system with normal saline the IAP was measured, starting without any extra instillation of saline, and continued with 1 ml increments up to 10 ml, after a 1-min equilibration period after each instillation. After each instillation, an 'oscillation test' was performed, by gently tapping the abdomen until an oscillating curve could be observed on the monitor. The minimal volume at which the oscillation test was positive was recorded. These values were compared to the IAP obtained using 20 ml saline. Data are presented as the mean (±SD).
Results At 2 ml installed saline volume an oscillation curve could be obtained in all patients. Mean IAP2ml was 9.3 mmHg (±3.9), mean IAP10ml was 9.6 mmHg (±4.2) and mean IAP20ml was 10.1 mmHg (±4.2).
In three patients there was no difference between IAP2ml and IAP20ml, but in six patients the IAP reading at 20 ml was 1 mmHg higher than that at 2 ml (an average increase of 11.4%), and in one patient the difference was 2 mmHg (14.2%).
Conclusion In this sample of ICU patients at risk for IAHT, 2 ml saline was sufficient for IAP signal transduction. Higher volumes for transvesical IAP measurement resulted in higher pressure readings in some ICU patients, even at instillation volumes below 20 ml. Using ultralow volumes for IAP measurement may therefore be preferable.

P308

Evaluation of the Spiegelberg method and the bladder method with different intravesical volumes for measurement of intra-abdominal pressure in a porcine model of intra-abdominal hypertension

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Background Measurement of intravesical pressure (IVP) is generally accepted as the gold standard for indirect, intermittent assessment of intra-abdominal pressure (IAP). However, data about bladder priming volumes are not uniform: 50–100 ml is considered adequate but little is known about smaller volumes (10–15 ml) to prevent falsely high pressures in less compliant bladders. This study compared bladder pressure measurements with different priming volumes for assessment of IAP in a porcine model of intra-abdominal hypertension (IAH). In addition, we compared the Spiegelberg method for direct, continuous intraperitoneal assessment of IAP versus the intermittent IVP method.
Methods We studied five anesthetized and ventilated pigs (46 ± 3 kg) in the prone position after insertion of a suprapubic bladder catheter and an intraperitoneal pressure catheter (Spiegelberg, Hamburg). We measured IVP with increasing priming volumes (10, 20, 30, 40, 50 ml) at four different IAP levels (baseline, 10, 20, 30 mmHg during 45 min each) achieved by infusing warmed saline into the peritoneal cavity. Pressure–volume (PV) bladder curves were constructed for each IAP level. Simultaneously, the Spiegelberg pressure (SP) was recorded. The mean difference (bias) between IVP and SP measurements and the limits of agreement were calculated according to the method of Bland–Altman.
Results Bias for SP as compared with IVP was maximally 0.9 ± 1.9 mmHg (Table 1). Limits of agreement between SP and IVP (over all IAP levels) were better for lower priming volumes. Bladder PV curves showed no significant difference for different priming volumes (at all IAP levels). However, at an IAP of 25 mmHg, as an example of a critical IAP in clinical practice, the range of IVP values was 20.1–29.9 mmHg, even with 10 ml as the preferred distending volume.

Table 1 (abstract P308)

IVP versus SP	Bias ± SEM (mmHg)	Agreement (mmHg)
IVP (10 ml) – SP	0.1 ± 1.6	−4.8 to 4.9
IVP (20 ml) – SP	0.4 ± 1.8	−5.7 to 6.6
IVP (30 ml) – SP	0.9 ± 1.9	−6.5 to 8.2*
IVP (40 ml) – SP	0.5 ± 1.8	−5.7 to 6.8
IVP (50 ml) – SP	0.9 ± 1.9	−6.0 to 7.8

*$P < 0.05$ vs 10 ml priming volume.

Conclusion In this model of porcine IAH, measurement of IAP was not significantly influenced by priming volumes between 10 and 50 ml. The classical IVP measurement demonstrated good agreement with the Spiegelberg method.

P309

Quantitative relationship between increased intra-abdominal pressure and intrathoracic pressures and volumetric filling parameters in the pig

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Background The central venous pressure (CVP) and the pulmonary artery occlusion pressure (PAOP) are dependent on intrathoracic pressure (ITP). A few studies reported 9–73% transmission of intra-abdominal pressure (IAP) to the thoracic compartment. In a porcine model of intra-abdominal hypertension (IAH), we studied this transmission and the impact on pressure and volume parameters of the cardiac preload.
Methods In nine anesthetized pigs (46 ± 3 kg), ventilated with a constant tidal volume and 5 cmH_2O PEEP, the IAP was increased stepwise from baseline to 30 mmHg. The ITP was measured from a balloon catheter (air) in the distal oesophagus and the abdominothoracic pressure transmission (APT = [ITP − PEEP × 0.735] / IAP) was calculated. A pulmonary artery catheter was used to

assess cardiac filling pressures and the transmural CVP (CVPt = CVP – ITP) and PAOPt were calculated. All pressures were measured end-expiratory. The global end diastolic volume index (GEDVI) and extravascular lung water index (EVLWI) were measured by transpulmonary thermodilution (PICCO; Pulsion).

Results With increasing IAP, the ITP increased significantly (Table 1). The APT decreased significantly from 48% to 27% (mean 35%) with unchanged EVLWI. While the CVP and PAOP parallelled changes in IAP, the CVPt, PAOPt and GEDVI remained constant.

Table 1 (abstract P309)

	IAP			
	Baseline (6 mmHg)	10 mmHg	20 mmHg	30 mmHg
ITP (mmHg)	5 ± 1	6 ± 1*	8 ± 1*	9 ± 3*
CVP (mmHg)	7 ± 2	9 ± 2	14 ± 3*	12 ± 4*
PAOP (mmHg)	9 ± 1	11 ± 2	12 ± 2*	13 ± 4*
GEDVI (ml/kg)	14.7 ± 2.4	14.4 ± 2.5	15.5 ± 2.6	19.3 ± 3.7
CVPt (mmHg)	2 ± 2	2 ± 2	2 ± 2	3 ± 2
PAOPt (mmHg)	5 ± 2	5 ± 1	6 ± 2	4 ± 2

*$P < 0.05$ vs baseline.

Conclusion About 35% of the IAP is transmitted to the thoracic compartment, but the APT decreases with increasing IAP, due to decreasing thoracic compliance. In the setting of IAH, the CVPt and PAOPt or volumetric parameters are superior in the assessment of cardiac preload.

P310

Intra-abdominal pressure and Sequential Organ Failure Assessment score: is there a correlation?

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Introduction The aim of this study was evaluating the correlation between intra-abdominal pressure (IAP) and Sequential Organ Failure Assessment (SOFA) [1] in critically ill patients admitted to our ICU.

Methods Reported are the preliminary results of a prospective study. During a 10-month period 18 patients consecutively admitted with secondary or tertiary abdominal sepsis were enrolled in this study and divided into two groups: in the first group five patients underwent abdominal surgery with open laparostomy before ICU admission; in the second group 13 patient were treated without surgical intervention. The SOFA score and IAP were recorded once every 8 hours, for the first 3 days from admission, for a total of 162 records. The IAP was measured with the Kron open system single measurement technique [2]. The Pearson correlation coefficient between the IAP and SOFA score was calculated for all patients and separately for the laparostomy and the nonlaparostomy groups.

Results No evident correlation has been found between IAP and SOFA score in the group of all patients. A Pearson linear correlation of 0.46 occurred in the nonlaparostomized group. A less significant value in the laparostomized group was found but with an inversed correlation.

Conclusion These preliminary results suggest that a correlation between IAP and SOFA could be found in selected critically ill groups.

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P311

Effect of vasopressin and norepinephrine on renal blood flow in a canine model of raised intra-abdominal pressure

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Introduction Increasing intra-abdominal pressure (IAP) is associated with a decrease in renal blood flow [1]. Abdominal perfusion pressure (APP) is calculated as the mean arterial pressure (MAP) – IAP. We investigated whether restoration of APP in dogs with the use of vasopressin (VP) and norepinephrine (NE) could increase renal blood flow under conditions of raised IAP.

Methods Ten mongrel dogs (average weight 20 ± 3 kg) were anaesthetized and mechanically ventilated with 100% oxygen and halothane. The IAP was altered by filling a 3 l intraperitoneal bag with varying volumes of normal saline and the IAP was measured by the urinary catheter technique. Ultrasonic transit-time flow probes were placed around the ascending aorta and left renal artery. After baseline readings, the IAP was increased to 10, 20 and 30 mmHg. Preload was maintained by a continuous infusion of 500 ml/hour normal saline. At each level of IAP, the MAP was restored to achieve the baseline APP with VP and NE infusion, followed by decompression. The MAP, IAP, and renal blood flow (RBF) were measured.

Results The average baseline MAP was 75 ± 10 mmHg. The mean baseline RBF was 180 ± 60 ml/min. Incrementally increasing the IAP from baseline resulted in a progressive decrease in RBF (Table 1). The RBF (ml/min) achieved following the use of NE and VP to return the APP to the baseline APP of 70–75 mmHg is shown (Table 1). RBF after decompression (no vasopressor) is also shown.

Conclusion In dogs an increase in IAP results in an incremental decrease in RBF. Using VP to restore the APP to baseline does not reverse the decrease in RBF. At moderate levels of IAH, using NE improves restoring APP to baseline and improves RBF, but does not return it to baseline values.

Reference

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Table 1 (abstract P311)

	Pre-vasopressor	NA	VP	Decompression	*P* value
IAP 10 mmHg	141.80 ± 51.60	162.00 ± 60.50	141.00 ± 32.30	157.9 ± 45.90	0.58
IAP 20 mmHg	94.70 ± 31.65	111.30 ± 36.60	94.8 ± 35.60	136.04 ± 27.07	0.03
IAP 30 mmHg	61.80 ± 31.70	98.50 ± 22.90	55.20 ± 9.20	134.50 ± 25.80	0.01

P312

Indocyanine green clearance as a predictor of outcome in liver transplant patients

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Introduction Invasive measurement of indocyanine green clearance (ICG) has been shown to predict the outcome after liver transplantation in a small series of patients. A non-invasive technique using ICG plasma disappearance rate (PDR) has recently been shown to correlate well with invasive techniques. We report our experience of ICG PDR in a large cohort of liver transplant patients.
Methods The ICG PDR was measured by the LiMON (PULSION Medical Systems) finger probe after injection of 0.25 mg/kg ICG in 79 patients after orthotopic liver transplantation. Clinical and laboratory markers of overall organ and liver graft function were recorded at the time of ICG measurement. Associations with duration of ICU admission, early graft failure and 3-month survival were also analysed. Values are presented as the median (interquartile range).
Results Twenty-four out of 79(30%) were transplanted for acute liver failure (ALF). Eighty-one grafts were implanted, two patients undergoing retransplantation for primary graft failure. Twenty-one (27%) patients died, five of whom had ALF. Variables for the whole group at the time of ICG clearance were: APACHE II 17 (11.5–22), SAPS 46 (33–63), lactate 2 mmol/l (1.2–3.5), INR 1.4 (1.2–1.7), AST 563 IU/l (158–1268) and bilirubin 75 mmol/l (27–128).
Correlations were observed between the ICG PDR and SAPS ($r = -0.45$, $P < 0.001$), APACHE II ($r = -0.23$, $P = 0.04$), bilirubin ($r = -0.57$, $P = < 0.001$) and length of ICU stay ($r = -0.32$, $P = 0.014$). No relationship was seen with typical markers of graft function (lactate, AST and INR). In grafts implanted into patients with chronic liver disease ($n = 57$), the ICG correlated with SAPS and bilirubin ($r = -0.55$, $P < 0.001$; $r = -0.62$, $P < 0.001$ respectively). However, for those with ALF, only the bilirubin had an association with ICG PDR ($r = -0.44$, $P = 0.029$). The median ICG PDR in survivors was significantly higher than in those who died; 15 (10.2–21)%/min vs 9.8 (5–16.3)%/min ($P = 0.01$). No significant difference was seen between survivors or nonsurvivors in the ALF group, although similar significant differences were observed between survivors and nonsurvivors in the chronic liver disease group. In those whose death was directly attributable to poor graft function, the median ICG PDR was lower; 4.8 vs 10.5%/min (NS).
Using a receiver–operator characteristic curve, a cutoff value for ICG-PDR of 9.5%/min identified graft failure (requiring retransplantation) or patient death with a sensitivity of 78% and specificity 50%.
Conclusion Non-invasive ICG PDR is a useful marker of outcome in patients undergoing orthotopic liver transplantation. The multifactorial nature of ICG clearance is demonstrated by strong correlations with composite measures of organ function.

P313

Value of serial serum lactate evaluation in liver transplant patients at the ICU

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Objective To determine the role of serial serum lactate evaluation in patients submitted to orthotopic liver transplant (OLT) and its correlation with classic hepatic laboratorial parameters.
Design A retrospective case–control study in a 16-bed medical–surgical ICU.
Methods Patients submitted to OLT with an ICU stay >72 hours were retrospectively studied during the immediate postsurgery period at the ICU. For comparative purposes, a control group of OTL patients that were discharged from the ICU uneventfully was studied ($n = 23$, mean age years, mean ICU stay days). Patients with complications were evaluated ($n = 17$, mean age years, mean ICU stay days): nine vascular complications (seven with documented venous thrombosis, two with documented arterial thrombosis), one hepatic aspergillosis, one acute cellular rejection, two graft primary nonfunction, one biliary system stenosis and three intrahepatic colestasis. These patients were further divided based on a biochemical pattern of liver laboratory parameters: hepatocellular (increased ALT and AST) or cholestatic (increased GGT and total bilirubin). Serial serum lactate measurements were evaluated, and compared with the biochemical profile of liver function parameters. Hemodynamic instability during surgery was also considered, as well as APACHE II and SAPS II scores. A statistical analysis was performed. Patients with twofold and 1.5-fold increases in any biochemical parameter were identified and were cross-examined by a chi-squared test, considering $P < 0.05$ significant.
Results In the control group, serum lactate decreased rapidly, along with other biochemical parameters. Patients with complications presented a higher serum lactate at first measurement (9.4 vs 6.7 mmol/l, $P = 0.046$), and a higher SAPS II score (22.3 ± 9.6 vs 40.1 ± 15.5, $P < 0.001$). Female sex and hemodynamic instability also correlated with the presence of complications. All vascular complications were characterized by an increase in serum AST and ALT. A 1.5-fold increase in lactate correlated strongly with a similar increase in ALT and AST ($P < 0.001$) and less with an increase in cholestatic parameters ($P = 0.02$). A twofold increase in serum lactate correlated well with a similar increase in AST and ALT ($P = 0.005$) but not with cholestatic parameters.
Conclusions A 1.5-fold increase in serum lactate after OLT correlated well with all complications observed. A twofold increase correlated only with complications that led to an increase in ALT and AST, particularly vascular.

P314

Monitoring of lactate and base deficit: what is their role in the predictive outcome of severe trauma?

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Background The evaluation of cellular metabolism in the critically ill patient, through measurement of the arterial lactate and arterial base deficit parameters, has proved to be a good means to guide the therapy and provide the outcome. We wanted to verify the prognostic ability of the blood lactate level and of the base deficit in patients with severe trauma surveyed during their recovery.
Methods The values of the blood lactate level and of the base deficit were considered in 33 patients with severe trauma (ISS > 15) and observed from their arrival in the ICU (T0) for 24 hours (T24). The data of dead and live patients were analysed with the Student *t* statistical method.
Results Ten of the 33 recovering (ISS 30) patients died. In the dead patients, medium values of lactate were more elevated than in discharged patients: T0 – dead patients 3.98 ± 4.03 mmol/l (min

0.5, max 11.8) vs live 2.13 ± 1.33 mmol/l (min 0.5, max 6.8); T24 – dead patients 2.57 ± 2.65 mmol/l (min 0.4, max 7.1) vs live 1.22 ± 0.86 mmol/l (min 0.4, max 4) ($P = 0.037$). The analysis of the trend of the base deficit cannot prove a statistically important difference: at T24 dead patients −2.57 ± 3.44 (min −9, max 2.1), and survivors 1.05 ± 7.18 (min −14, max 9.6) ($P = 0.141$).

Conclusions The measurement of lactates seems to be a good index of prognosis. In particular, the values revealed during 24 hours are more predictable, perhaps because they are probable proof of the capacity of recovering the hypoperfusion of tissues and the anaerobic metabolism that is the cause of the development of organ failure and future complications. On the contrary, the analysis of the base deficit has less prognostic capacity because it is conditioned by other factors such as employed solutions, renal compensations, the rate of vascular filling and possible breathing deficit. In conclusion, the monitoring of blood lactate levels can be a good aid in guiding therapy in its initial phases and predicting the outcome of patients.

P315

A novel therapeutic concept for the treatment of acute angioedema attacks in hereditary angioedema patients: multiple successful treatments even in severe swelling attacks with the bradykinin-B2 receptor antagonist Icatibant

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Several forms of angioedema seem to be induced by elevated bradykinin (BK) concentrations. They are either caused by increased BK production, as is the case in hereditary angioedema (HAE) involving the lack of a functional C1-esterase inhibitor, or by reduced BK inactivation (e.g. during ACE-inhibitor treatment). BK-induced angioedema does not respond to the current standard treatment for angioedema caused by increased histamine levels, corticosteroids and antihistamines.

Until now acute attacks of HAE have been treated with intravenously administered C1-esterase inhibitor concentrate derived from human plasma. However, no specific treatment has been approved for ACE-inhibitor-induced angioedema. It would be necessary that such an approach inhibits directly the activation of the bradykinin-B2 receptor by BK.

During the ongoing international phase III HAE study FAST2, we treated several HAE patients subcutaneously with Icatibant, a specific bradykinin-B2 receptor antagonist. In the open-label part of this study we administered Icatibant for the treatment of 21 acute HAE attacks. Eleven attacks were located in the head–neck region, of which three involved the laryngeal area, six the abdominal and four the genital area. Following treatment with Icatibant, patients reported rapid onset of symptom relief and complete remission of symptoms within a few hours. We were especially impressed by the successful treatment of the edema involving the laryngeal area. The study drug was safe and well tolerated. We have noted short-lived local injection site reactions, which resolved spontaneously without intervention.

In our hands Icatibant showed high efficacy for the treatment of acute HAE attacks with a rapid onset of symptom relief. Subcutaneous administration might improve the quality of life for HAE patients. Icatibant could also represent a new therapeutic paradigm for the treatment of ACE-inhibitor-induced angioedema cases but this hypothesis needs to be tested in a clinical study.

P316

Impact of early sepsis on oxygen delivery in the microvasculature

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A defining characteristic of sepsis is progressive blood flow dysfunction in the microvasculature in organs remote to the original site of injury. Previous work has established that microvascular oxygen transport is compromised in sepsis due to a loss of perfused capillaries. In a companion study to this project, which investigated the role of leukocyte traffic in sepsis, it was observed that increased transit times of leukocytes passing through the capillary bed not only resulted in the occlusion of some capillaries but also served to cause some vessels to experience prolonged periods of low flow. The objective of the present study was to examine how the progressive loss of functional capillary density (FCD) impacts oxygen transport and consumption in skeletal muscle during sepsis. Hemodynamic and oxygen saturation data from video recordings are incorporated into an experiment-based mathematical model of oxygen transport in a 3D volume. This modeling helps to further our understanding of the impact capillary loss has on tissue oxygenation and consumption. Sepsis was induced in rats by cecal ligation and perforation (CLP). Rats received crystalloid fluid resuscitation to maintain the blood pressure and hematocrit at baseline levels. Microvascular flow was observed in the extensor digitorum muscle using a dual wavelength intravital video microscopy set-up. The same field of view was recorded at 30-min intervals between 2 and 5 hours post CLP to follow the progression of capillary dysfunction. Individual capillaries were analyzed for oxygen saturations and hemodynamics. As sepsis progressed we observed that the capillaries' hemodynamic profiles transiently change between normal, stopped and fast flow states. Although it has previously been assumed that once a capillary becomes occluded flow is not easily re-established, we observed that capillaries could suddenly become reperfused after being occluded for up to 1 hour or more. The occlusion of capillaries was found to decrease oxygen saturations in nearby vessels by as much as 20%. Subsequent recruitment of previously unperfused capillaries was shown to increase saturations in adjacent vessels by as much as 50%. Changes in perfusion of adjacent vessels had a greater impact on oxygen saturations than changes in hematocrit or velocity in the vessel itself. At 2, 3 and 4 hours post CLP the percentage of stopped flow vessels was 17%, 28% and 48% in CLP compared with 13%, 13% and 20% in sham. The extent of FCD loss is progressive over the course of the injury. However, it is important to note that while the percentage of occluded capillaries increases, the individual vessels constituting this percentage were variable. Our study suggests that in this early stage where the FCD is in transition, affected tissue experiences dynamic changes in tissue oxygenation. This highlights the importance of understanding the mechanisms responsible for this dynamic change in FCD.

P317

A method for improvement of data quality from OPS/SDF devices in visualization of the microcirculation

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Introduction OPS imaging (Cytometrics, Philadelphia, PA, USA) and SDF imaging (MicroVision Medical, Amsterdam, The Netherlands)

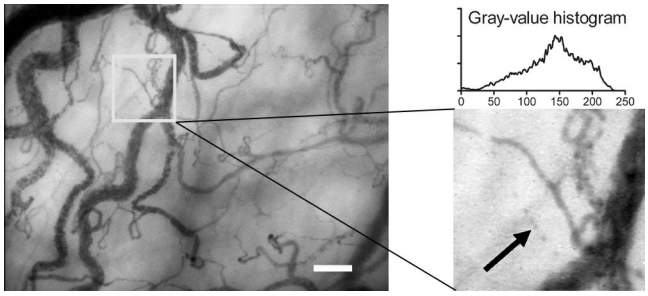
are valuable tools for visualization and study of the microcirculation. Unfortunately, the widespread current practice of using a (digital) video recorder and subsequent transfer to a computer results in data loss. This is due to video compression and nonoptimal use of the available dynamic range. In order to be able to develop and use software for automated data analysis we should strive for the highest possible image quality. Here we describe a simple and cost-effective method for obtaining significant improvement of data quality.

Methods A 10-bit frame-grabber board (NI PCI-1409; National Instruments, Austin, TX, USA) was used for online capture of noncompressed video data from an SDF device. The 10-bit data was real-time converted to optimized 8-bit data by a dynamic scaling algorithm, compressing the excess 1024 gray values into the standard 256 gray values and thereby mathematically correcting for the offset. The converted data were written to hard disk as an uncompressed AVI file. The data stream of 2.5 Gb/min was handled by a 3 MHz Pentium-4 PC with two 250-Gbyte hard disks in the Raid 1 mode. Software was written in LabView (version 7.1; National Instruments).

Results The system routinely delivers excellent dynamic range and resolving power in a clinical setting. Figure 1 is an example from a sublingual measurement in a healthy volunteer. The white bar equals a distance of 100 mm, the right panel is a magnification the marked area and the arrow indicates single erythrocytes within a capillary.

Conclusion A major improvement in the dynamic range (typically a factor 2) can be obtained by 10-bit data acquisition followed by 8-bit conversion by a dynamic scaling algorithm. Furthermore, noncompressed video data offer a better image quality in terms of resolving power of single erythrocytes and extremely small vessels. It is expected that the improved data quality will ease automatic analysis by future software.

Figure 1 (abstract P317)



P318

Non-invasive assessment of the microcirculation in ICU patients

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Introduction Microcirculation is severely affected in sepsis. The non-invasive evaluation of microcirculation and its association with the severity of sepsis has not been sufficiently studied.

Objective To compare microcirculation parameters with sepsis severity.

Methods We studied 23 patients of a general ICU (age 56 ± 21 years) and 11 healthy volunteers (age 28 ± 4 years). Severity of sepsis was assessed with the SOFA score (5 ± 2), APACHE II score (13 ± 5) and sepsis severity category (SIRS $n = 15$, severe sepsis $n = 4$ and septic shock $n = 4$). An InSpectra® near-infrared spectrometer was used to measure the thenar muscle tissue oxygen saturation (StO_2) before, during and after a 3-min occlusion of the brachial artery. For the occlusion we used a brachial cuff and raised the pressure 50 mmHg above the measured systolic blood pressure. For the StO_2 curve analysis we used the InSpectra® Software Analysis program. For the statistical analysis we used SPSS 11.5 for Windows® and applied one-way ANOVA.

Results The StO_2 baseline value was significantly lower in patients with severe sepsis when compared with healthy controls (65 ± 15 [49, 85] vs 83 ± 6 [72, 93], $P = 0.009$). During the 3-min occlusion of the brachial artery the StO_2 decrease rate was significantly lower in the septic shock group compared with healthy controls (15.5 ± 6.3 [6.5–21.4] vs 38.7 ± 10.3 [22.1–52.9], $P < 0.001$) as well as compared with the SIRS group (15.5 ± 6.3 [6.5–21.4] vs 25.4 ± 7.2 [17.8–43.4], $P = 0.036$). The StO_2 decrease rate was also significantly lower in the severe sepsis group when compared with healthy controls (15.0 ± 0.6 [14.4–16.0] vs 38.7 ± 10.3 [22.1–52.9], $P < 0.001$) as well as compared with the SIRS group (15.0 ± 0.6 [14.4–16.0] vs 25.4 ± 7.2 [17.8–43.4], $P = 0.028$). After the release of the occlusion, the StO_2 increase rate was significantly lower in the SIRS, severe sepsis and septic shock groups when compared with healthy controls (402.1 ± 140.1 [206.2–653.5] vs 643.8 ± 241.4 [389.0–1275.0], $P = 0.002$; 322.4 ± 162.6 [185.5–520.5] vs 643.8 ± 241.4 [389.0–1275.0], $P = 0.005$; and 219.3 ± 136.3 [82.4–404.5] vs 643.8 ± 241.4 [389.0–1275.0], $P < 0.001$, respectively).

Conclusions Tissue oxygen saturation is related to the severity of sepsis. Additionally, tissue oxygen consumption is significantly lower in patients with septic shock or severe sepsis compared with healthy subjects or patients with SIRS. The lower StO_2 increase rate in ICU patients may indicate affected endothelium reactivity.

P319

Changes in microcirculation during weaning trials from mechanical ventilation

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Objective We hypothesized that a decrease in tissue oxygen saturation (StO_2) could be detected in patients during weaning failure. To this end, we determined the changes in StO_2 during weaning trials from mechanical ventilation using near-infrared spectroscopy (NIRS).

Patients and methods We studied 16 consecutive, mechanically ventilated patients (age 61 ± 15 years, SOFA score 4.5 ± 1.4), whose physician had judged them ready to wean, during a 2-hour T-piece weaning trial. The weaning trial was defined as successful when the patient was able to sustain spontaneous breathing without distress. Oxygenation, respiratory rate (RR), and minute ventilation (VE) were measured before and either at 2 hours after disconnection from the ventilator in patients with successful weaning trial, or at the time of reconnection to the ventilator in those with a failed one. The thenar muscle StO_2 was measured non-invasively by NIRS (InSpectra; Hutchinson Technology, USA), at the same time points, by the arterial occlusion method.

Results Eleven patients had successful and five had failed weaning trials. The SaO_2, respiratory rate, and VE on mechanical ventilation were not different between the two groups. During the weaning trial, the SaO_2 was decreased in the failure group (from 99% to 92%, $P = 0.027$), the RR was increased (from 20 to 43

breaths/min, $P < 0.05$) while the VE did not change significantly (from 11 to 12.8 l/min, $P = 0.55$). These variables did not change significantly in the success group. The StO_2 baseline on mechanical ventilation was not different between failure and success group patients (72.8% and 78.2%, respectively). At the end of the weaning trial the StO_2 baseline was decreased to 65% in failure group patients ($P = 0.05$), while it did not change in the success group. The StO_2 decrease rate on mechanical ventilation was not different between the two groups. At the end of the weaning trial, the StO_2 decrease rate was significantly lower in failure group patients compared with that of the success group (13.3 ± 2.6 vs 22.5 ± 10.9, $P = 0.026$).

Conclusion These results indicate that microcirculation, as it is monitored by the NIRS technique, might be impaired in patients who fail to wean from mechanical ventilation. Further study is needed to define the role of this method during weaning from mechanical ventilation.

P320

Changes in the microcirculation during human endotoxemia measured with near-infrared spectroscopy

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Objective Aiming at a better understanding of the microcirculatory deficits that characterize the septic condition, we measured local hemoglobin oxygen saturation (= tissue oxygen saturation [StO_2]) using near-infrared spectroscopy (NIRS) (Hutchinson Technology, USA) before and during experimental human endotoxemia. The baseline StO_2 may represent the vasodilatory state, the decline in StO_2 during ischemia the tissue oxygen consumption, the slope of increase in StO_2 after the ischemic period vascular reactivity, and the area under the curve after reperfusion the flow debt repayment.

Methods Five healthy subjects received an i.v. dose of 2 ng/kg *E. coli* O:113 lipopolysaccharide (LPS) and five subjects served as controls. Before, 2 and 4 hours after the administration of LPS/placebo the StO_2 was measured in the thenar skeletal muscle before, during and after a 1.5-min period of arterial occlusion (inflating an upper-arm cuff 50 mmHg above the systolic blood pressure). Data are expressed as the mean ± SEM. Differences were tested by paired Student *t* tests. $P < 0.05$ was considered to indicate significance.

Results The control subjects showed that time itself did not change the response to ischaemia as measurements at $t = 0$, 2 and 4 hours demonstrated similar changes in StO_2. LPS administration induced the expected flu-like symptoms, fever, and the decrease in mean arterial pressure and the increase in heart rate. Experimental endotoxemia resulted in an increase in the baseline StO_2 from 79 ± 4% at $t = 0$ to 87 ± 4% at $t = 2$ hours ($P = 0.07$) and 94 ± 1% at $t = 4$ hours ($P = 0.049$) after LPS administration. The decline in StO_2 during ischemia and the slope of increase during reperfusion was not influenced by endotoxemia. However, the area under the curve after reperfusion decreased from 18 ± 4 AU at $t = 0$, to 10 ± 4 at $t = 2$ hours ($P = 0.04$) and 6 ± 1 AU at $t = 4$ hours ($P = 0.03$) after the administration of LPS.

Conclusions During human endotoxemia the vasodilatory state is represented by an increase in baseline StO_2. Oxygen consumption during ischemia and vascular reactivity after reperfusion is not influenced by endotoxemia. After the ischemic period, during reperfusion, flow debt repayment significantly decreases during endotoxemia. NIRS is a valuable tool that will facilitate future experiments that study inflammatory-associated changes in the microcirculation.

P321

Microcirculation parameters are related to hemodynamic indices in postoperative cardiac patients

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Introduction Peripheral microcirculation is affected by extracorporeal circulation, hypothermia and anesthesia in patients undergoing cardiac surgery. The alterations of peripheral microcirculation and their relation to the hemodynamic status in these patients have not yet been studied.

Objective To compare microcirculation parameters with the postoperative hemodynamic status of these patients.

Methods We studied seven postoperative cardiac patients (five males/two females, 69 ± 6 years) during the immediate postoperative period. All were receiving inotropic agents (11 norepinephrine, 15 dobutamine, three adrenaline, four levosimendan). We used Swan–Ganz catheterization to assess the cardiac index and mixed venous blood oxygen saturation (SvO_2) values. We used the InSpectra near-infrared spectrometer (NIRS) to monitor the thenar muscle tissue oxygen saturation (StO_2) and the total hemoglobin index (THI) (which reflects the sum of oxyhemoglobin and deoxyhemoglobin) at baseline.

Results The hemodynamic parameters of our patients were: MAP 79 ± 10 mmHg, CVP 8 ± 4 cmH_2O, PCWP 11 ± 2 mmHg, MPAP 27 ± 7 mmHg, CI 2.6 ± 0.7 l/min/m^2, SVR 1243 ± 318 dyne × s/cm^5, PVR 309 ± 139 dyne × s/cm^5, HR 93 ± 7 bpm, DO_2 706 ± 209 l/min. Laboratory values were: Hb 10.4 ± 1.5 g/dl, lactate 2.4 ± 1.2 mg/dl. We found a significant correlation between StO_2 at baseline and the cardiac index ($r = 0.85$, $P < 0.001$) and between the THI at baseline and the cardiac index ($r = 0.88$, $P < 0.001$). The StO_2 at baseline also significantly correlated with SvO_2 ($r = 0.94$, $P < 0.001$).

Conclusions Non-invasively acquired tissue oxygen saturation values correlate with hemodynamic indices. This suggests that non-invasive monitoring of the microcirculation might be used for the management of postoperative cardiac patients. Further studies are needed to confirm these findings.

P322

Covert oxygen supply failure measured using the LiDCO plus monitor

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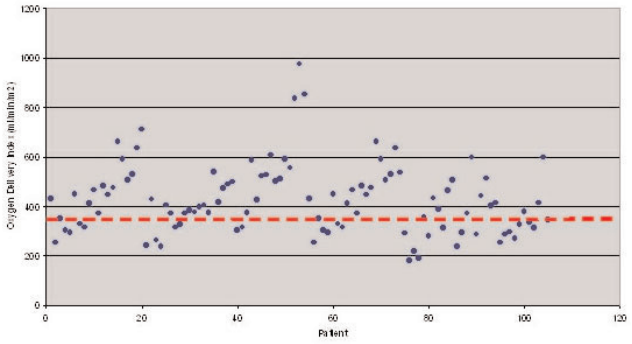
Introduction Oxygen delivery represents one side of the global oxygen flux equation. Normal physiology suggests that cardiac output is linked to tissue metabolic requirement. In sick patients this linkage is frequently abnormal and the ability to maintain tissue oxygen delivery is a prognostic variable. An increasing number of randomised controlled clinical trials and meta-analyses have shown that early manipulation oxygen delivery in certain groups of critically ill patients can reduce morbidity and mortality [1]. Despite a growing bibliography supporting targeting and maintaining oxygen delivery, it is rarely calculated or its level appreciated, despite the fact that the cardiac output has been measured. We have formed a Haemodynamic Nursing/Technical team who institute calibrated

Figure 1 (abstract P322)



Scatter plot: oxygen delivery index.

CO monitoring and protocolised resuscitation of haemodynamically unstable patients using fluid challenges.

Hypothesis This study was designed to assess the range and clinical appreciation oxygen delivery in patients admitted to the ICU.

Methods The cardiac index and oxygen delivery index were measured using the LiDCO plus monitor in 106 critically ill adult patients admitted with a variety of diagnoses, to General Intensive Care at Southampton Hospital.

Results For the purposes of this study the normal range was taken as being the normal value ± 30%. Values below the range would be considered as being low. Indexed results were used to compensate for patient size.

Conclusion Two patients in the study group had a cardiac index below the calculated normal range; however, the DO_2I (Fig. 1) showed a fivefold variation across the group, with 31/106 (30%) patients having a DO_2I considered low. These findings were covert, coincident with anaemia and/or poor respiratory gas exchange. In the majority of these patients there had been a failure to appreciate the low DO_2I and clinical management changes were subsequently considered. The continuous measurement of the cardiac index and DO_2I enabled early identification and enhanced standard of care for patients with low DO_2I. These patients may represent the subgroup of critical care patients, cited by RCT evidence, whose survival may be enhanced by CO augmentation and optimisation of oxygen delivery. Because these patients were high risk with potentially serious management implications from DO_2 measurement errors, clinical confidence in the data was provided by calibration with lithium dilution.

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P323

Pulse contour analysis for cardiac output measurement in patients after off-pump coronary artery bypass grafting: a comparison of FloTrac and $PiCCO_{plus}$ with intermittent thermodilution

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Introduction Pulse contour analysis calibrated by transpulmonary thermodilution ($PiCCO_{plus;}$ Pulsion Medical Systems, Munich, Germany) has shown in the past years to be a reliable alternative to the pulmonary artery catheter for cardiac output (CO) assessment in different clinical settings [1,2]. A new pulse contour analysis device, which does not need an external calibration (FloTrac/Vigileo; Edwards Lifesciences, Irvine CA, USA), recently became available. The aim of this study was to compare the CO determined by the FloTrac sensor (FCO) and by the $PiCCO_{plus}$ system (PCO) with the CO assessed by intermittent thermodilution (ICO).

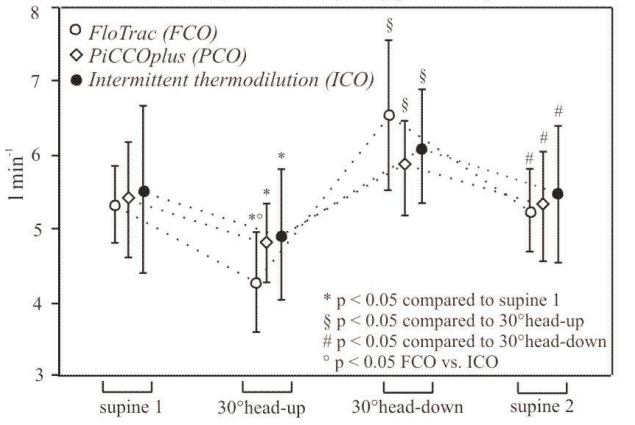
Methods With local ethic committee approval, patients after elective off-pump coronary artery bypass grafting were studied under different conditions in the ICU. For one set of data (A = 'haemodynamic stable') the CO was assessed following haemodynamic stabilization and calibration of the $PiCCO_{plus}$. Triplicate FCO and PCO values were recorded within 3 min before the ICO was determined by three repeated injections at four time points with intervals of 15 min. For the second set of data (B = 'haemodynamic changes') triplicate FCO, PCO and ICO measurements were recorded 15 min after inducing CO changes by different body positions (supine 1, 30° head-up, 30° head-down, supine 2). Mean arterial pressure was maintained ≥70 mmHg by adjustment of norepinephrine infusion. Statistical analysis was performed using ANOVA with post-hoc Bonferroni/Dunn correction, *t* test and Bland–Altman analysis for absolute CO values and percentage changes (Δ = trend analysis) of CO during A and B. $P < 0.05$ was considered statistically significant.

Results Seventy-two matched sets of data were obtained from nine patients (ASA III, female/male ratio = 2/7, age = 63.0 ± 9.5 years, BMI = 24.8 ± 2.2 kg/m^2). CO values recorded during A ranged from 3.30 to 6.56 l/min, no significant CO changes between measurement points were recorded (ΔFCO = −0.8 ± 14.8%, ΔPCO = −0.9 ± 15.3%, ΔICO = −1.9 ± 12.8%). Bland–Altman analysis revealed a mean bias ± 2SD (limits of agreement) of −0.13 ± 1.08 l/min for FCO-ICO and of 0.08 ± 0.91 l/min for PCO-ICO. Differences of ΔCO were comparable (mean bias ± 2SD = 1.1 ± 24.8% for ΔFCO − ΔICO and 1.0 ± 24.8% for

Table 1 (abstract P323)

	→30° head-up	→30° head-down	→supine 2
ΔFCO	−24.1 ± 22.7%	+29.4 ± 17.4%	−20.8 ± 18.0%
ΔPCO	−12.0 ± 7.3%	+17.5 ± 4.4%	−10.8 ± 2.3%
ΔICO	−12.6 ± 8.0%	+20.3 ± 6.7%	−13.9 ± 4.8%

Figure 1 (abstract P323)



CO changes induced by body positioning.

ΔPCO – ΔICO). A range of CO values from 2.85 to 8.60 l/min were obtained during B with significant changes of FCO, PCO and ICO between the measurement points (Table 1 and Fig. 1). The mean bias ± 2SD was −0.14 ± 1.82 l/min for FCO-ICO and −0.17 ± 1.13 l/min for PCO-ICO. For ΔFCO – ΔICO a mean bias ± 2SD of −2.8 ± 36.4% was observed, whereas for ΔPCO – ΔICO the mean bias ± 2SD was 0.9 ± 13.2%.

Conclusions These preliminary results indicate that cardiac output in patients after off-pump coronary artery bypass grafting can be reliably monitored by both tested pulse contour analysis devices (FloTrac and $PiCCO_{plus}$ system) during stable haemodynamic conditions. However, the FloTrac system showed a tendency to overestimate rapid decreases and increases of cardiac output when compared with the $PiCCO_{plus}$ system.

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P324

Continuous arterial pulse cardiac output validation in hyperdynamic conditions

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Introduction Assessment of continuous cardiac output using the arterial pulse cardiac index (APCI) is nowadays available also with only standard radial artery catheterization with a transducer (Vigileo System, FloTrac™; Edwards Lifesciences, Irvine, CA, USA) [1,2]. It does not require calibration (thermodilution or any) but rather bases its calculations on arterial waveform characteristics in conjunction with patient demographic data. The aim of the study was to assess the level of agreement between a continuous APCI and continuous cardiac index (CCI) and intermittent cardiac index (ICI) obtained with a pulmonary artery catheter (Intellicath) in cirrhotic patients with hyperdynamic conditions.

Methods Hemodynamic measurements were obtained in 14 liver-transplanted patients. ICI measurements were collected after ICU admission and every 8 hours until the 48th postoperative hour. Continuous data were collected every hour after ICU admission to the 48th postoperative hour. Statistical analysis was performed using the method described by Bland and Altman. Statistical significance was considered $P < 0.05$.

Figure 1 (abstract P324)

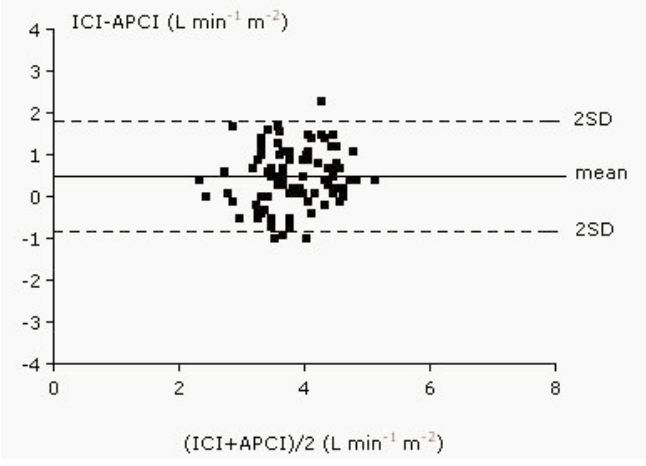
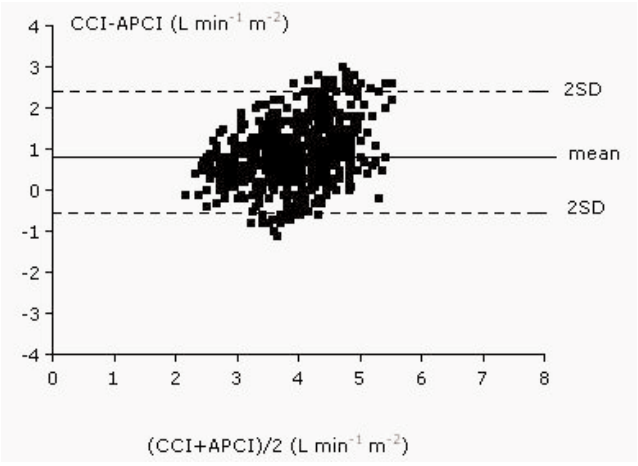


Figure 2 (abstract P324)



Results Data are presented standardized by body surface area. The mean difference between APCI–ICI (bias ± 2SD) was 0.48 ± 1.40 l/min/m² together with 95% confidence intervals of −0.92 to 1.88 l/min/m². The mean difference between APCI–CCI (bias ± 2SD) was 0.90 ± 1.49 l/min/m² together with 95% confidence intervals of −0.59 to 2.39 l/min/m².

Conclusions APCI obtained with the Vigileo System provided comparable measurements of cardiac output in hyperdynamic conditions. Larger population studies are needed to confirm these preliminary data.

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P325

A calibrated pulse waveform analysis algorithm, which determines continuous cardiac output, compared with a noncalibrated algorithm

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Introduction We compared two pulse waveform analysis algorithms for measuring continuous cardiac output; PulseCO (LiDCO UK Ltd), which requires a transpulmonary indicator dilution (TPID) calibration; and the Pressure Recording Analytical Method (PRAM) (most~care, FIAB, Italy), which does not require calibration but requires the user to define whether the patient is septic or nonseptic. No study has compared these two methods simultaneously in adults.

Methods Arterial pulse waveforms were collected prospectively from 11 patients (seven male, age 36–75 years) requiring haemodynamic monitoring, and were stored electronically and then replayed through each device. Nine patients were deemed 'septic' on the study day by standard clinical criteria. Each patient had a (TPID) cardiac output (CO) measurement prior to pulse wave collection (lithium dilution or thermodilution) to allow prospective calibration of the PulseCO software. The duration of continuous waveform collection was between 55 and 145 min, and these were replayed through the septic and nonseptic settings of the PRAM. Thirty second CO measurements were collected with the

proprietary data acquisition software. Comparisons were made between: PulseCO(c) (TPID calibrated) to PRAM(cp) (set to clinical picture, i.e. septic or nonseptic); PulseCO(c) to PRAM(bf) (set to 'retrospective best fit'); and PulseCO(c) to PRAM(c) (in line with the clinical picture and mathematically calibrated to the TPID). It was only possible to include seven patients in the PRAM(bf) analysis.

Results One patient was in extremis at the time of data collection, requiring epinephrine boluses, and was excluded, leaving 10 patients in the analysis group. The mean flow, bias and precision (±2SD) of PulseCO(c) to PRAM(cp), of PulseCO(c) to PRAM (bf), and of PulseCO(c) to PRAM(c) were: 6.86, −0.58 and ±6.03 l/min; 6.24, 0.88 and ±1.55 l/min; and 6.67, −0.21 and ±2.23 l/min, respectively. The 95% limits of agreement for PulseCO(c) to PRAM(cp), for PulseCO(c) to PRAM (bf), and for PulseCO(c) to PRAM(c) were 88%, 24.9% and 34%.

Conclusions The CCO algorithm in the PRAM does not trend acceptably with PulseCO. Even though the precision of PRAM(bf) was acceptable (in seven patients) the settings were inconsistent with the clinical presentation. The noncalibrated PRAM is currently not suitable for continuous cardiac output monitoring in the ICU.

P326

Do the data obtained by the PiCCO system enable one to differentiate between direct ALI/ARDS and indirect ALI/ARDS?

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Critical Care 2006, **10(Suppl 1):**P326 (doi: 10.1186/cc4673)

Introduction It is known that measurement of the intrathoracic blood volume (ITBV) is a more accurate estimate of cardiac preload than pressure measurements using central venous or pulmonary artery occlusion pressures. Extravascular lung water (EVLW) is defined as the value of the intrathoracic thermal volume minus the ITBV. An increase in EVLW is the pathophysiological basis for the development of pulmonary edema (PE). There is evidence to suggest that therapy to reduce EVLW may improve outcome in the critically ill patient. The bedside assessment of EVLW may be very useful in identifying and quantifying PE, and hence in selecting patients who might benefit from a fluid restriction/depletion therapeutic strategy based on EVLW monitoring. The PiCCO (Pulsion, Munich, Germany) provides an estimate of the ITBV, EVLW, and permeability index (PI) via a single transpulmonary thermodilution technique. PE is defined as the abnormal accumulation of fluid in the extravascular space of the lung. ALI/ARDS is characterized by pulmonary edema. PE consists of increased hydrostatic PE (cardiogenic PE) and increased permeability PE (ALI/ARDS). Increased permeability PE (ALI/ARDS) is further classified into direct lung injury type and indirect lung injury type. PI was calculated as the ratio of EVLW to ITBV, which was previously shown to reflect permeability of the alveolar–capillary barrier. The early recognition and differential diagnosis of direct lung injury and indirect lung injury may be challenging.

Objective To clarify whether differentiation with direct injury ALI/ARDS and indirect injury ALI/ARDS is possible by parameters obtained from PiCCO systems.

Materials and methods We studied 10 patients, four with direct ALI/ARDS and six with indirect ALI/ARDS (sepsis induced). Direct ALI/ARDS consisted of two aspiration and two pneumonia. All patients in indirect ALI/ARDS were sepsis. Nine of the patients were male, one was female; aged 27–85 years. All patients were mechanically ventilated in the pressure mode. GEDV, ITBV and EVLW were measured by the PiCCO and the PI was calculated. Data are presented as the mean ± SD. For statistical analysis a paired *t* test was performed.

Results One hundred and twenty measurements were available for analysis. ITBVI and EVLWI were significantly higher in indirect ALI/ARDS than in direct ALI/ARDS. PI (PVPI = EVLW/ITBV) was significantly higher in direct ALI/ARDS than in indirect ALI/ARDS. See Table 1.

Table 1 (abstract P326)

	Direct	Indirect	*P* value
ITBVI	984 ± 331.7	1279 ± 312.1	0.0001
EVLWI	13.2 ± 4.7	16.8 ± 6.5	0.014
PI	0.59 ± 0.27	0.44 ± 0.22	0.006

Conclusions Measurement of the ITBV, EVLW and PI using the PiCCO system contributes to differentiating between direct and indirect ALI/ARDS and to determining the therapeutic strategy for critically ill patients. These data are an important variable for increased permeability PE, direct injury and indirect injury ALI/ARDS, and may be very helpful for guiding fluid therapy in critically ill patients. There is a possibility that data such as the ITBI, EVLWI and PI obtained from the PiCCO system might be included in the diagnostic criteria ARDS in the future.

P327

Combined gas exchange and pulse wave monitoring for detecting anaerobic metabolism in critically ill patients

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Introduction The anaerobic metabolism causes lactate to increase. This is accompanied by a reduction in bicarbonate concentration in the blood, causing CO_2 production (VCO_2) to accelerate, evidenced as an increased respiratory CO_2 output. Over the physiological range of CO_2 content the CO_2 tension is linearly related to CO_2 content, and the venoarterial CO_2 tension difference ($DPCO_2$) could be used as a surrogate for the difference between mixed venous and arterial CO_2 contents. Under anaerobic metabolism the respiratory quotient increases. The venoarterial CO_2 tension difference/arteriovenous O_2 content difference ratio [$DPCO_2/C(a\text{-}v)O_2$] therefore increases. We tested the $DPCO_2/C(a\text{-}v)O_2$ ratio and mixed venous oxygen saturation (SvO_2) values as potential predictors of anaerobic metabolism.

Methods Fifty-one consecutive adult patients (head injury, subarachnoid haemorrhage, sepsis) admitted to our ICU were prospectively studied. The $DPCO_2/C(a\text{-}v)O_2$ ratio, SvO_2, oxygen delivery index (DO_2I), and arterial lactate (Lac) values were collected at T1 (ICU admission) and at T2 (after 24 hours). The DO_2I was calculated using the cardiac index (CI) measured by the Pressure Recording Analytical Method (PRAM). PRAM is a pulse contour system for beat-to-beat quantification of the CI. It does not need calibrating factors, and allows the stroke volume (SV) to be calculated avoiding the inaccuracies derived from instant variations of arterial impedance. Radial (80%) or femoral (20%) arteries were used for the blood pressure analysis. The presence of anaerobic metabolism (e.g. hyperlactatemia, Lac+) was defined by an increase in Lac >2 mmol/l. Linear correlations and the ROC test were applied.

Results For a threshold value of $DO_2I > 330$ ml/min/m^2, an inverse relationship ($R^2 = 0.69$; $P < 0.05$) between Lac and SvO_2 at T1 was found. For a $DO_2I < 330$ ml/min/m^2, good direct correlations

between Lac and the $DPCO_2$/Da-vO_2 ratio calculated at T1 (R^2 = 0.89; $P < 0.05$), and at T2 (R^2 = 0.88; $P < 0.05$) were found. The SvO_2 did not show any significant relationship with Lac for a DO_2I < 330 ml/min/m^2. ROC curves to predict Lac+ were constructed. The areas under the ROC curves (AUC) were 0.78 and 0.47 for the $DPCO_2$/Da-vO_2 ratio and SvO_2, respectively. The AUC for the $DPCO_2$/Da-vO_2 ratio was significantly greater that that for SvO_2 ($P < 0.05$). From the ROC curve an optimal cutoff value of 1.5 (sensitivity = 0.78, specificity = 0.75) was determined for the $DPCO_2$/Da-vO_2 ratio predicting the presence of Lac+.

Conclusions Pulse wave analysis plays a key role in the continuous monitoring of critically ill patients. It provides beat-to-beat values of the SV, and consequently allows the DO_2I to be frequently calculated. The $DPCO_2$/Da-vO_2 ratio is simple and quick to calculate and would be a valuable approach in clinical practice. Our findings showed that $DPCO_2$/Da-vO_2 ratio values are directly related to Lac. For DO_2I < 330 ml/min/m^2 the $DPCO_2$/Da-vO_2 ratio seems a more reliable predictor of anaerobic metabolism than SvO_2. Combined gas exchange and pulse wave monitoring might be a very useful approach to detect anaerobic metabolism in ICU patients.

P328

Feasibility study of continuous non-invasive blood pressure measurement in critically ill children

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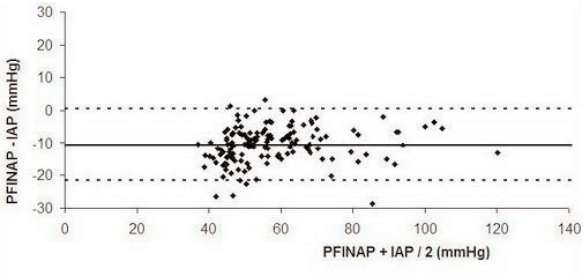
Critical Care 2006, **10(Suppl 1):**P328 (doi: 10.1186/cc4675)

Introduction Arterial finger blood pressure can be measured continuously and non-invasively using the Finapres method. There are numerous studies on the absolute blood pressure levels and tracking of blood pressure changes in adults [1]. The accuracy and precision of Finapres are according to the standards of the Association for the Advancement of Medical Instrumentation. Recently BMEYE developed finger cuffs specifically designed for the pediatric population. We present the first feasibility study comparing the blood pressure measurements of a pediatric prototype device (PFINAP) with intra-arterial blood pressure (IAP) in critically ill children.

Methods Thirty-six mechanically ventilated and sedated children, with a median age of 4 months (4 days–10 years) and a median body weight of 5 kg (2–22 kg) were included. The IAP and PFINAP were recorded simultaneously for a period of 10 min. Both signals were stored with a 200 Hz sample rate. Standardized intervals of 30 s were used for further analysis. The two methods were compared using the Bland–Altman method.

Figure 1 (abstract P328)



Results One hundred and thirty-seven out of 144 non-invasive blood pressure measurement (95%) signals were obtainable. The bias for systolic, diastolic and mean arterial pressures was −15.9 mmHg (SD 9.8), −8.0 mmHg (SD 5.9) and −10.5 mmHg (SD 5.6), respectively (Fig. 1). Repeatability for the bias of MAP (1.96 × SD of the difference between repeated measurements) was 6.9 mmHg. The use of vasoactive drugs or a low temperature of the hand did not influence the bias.

Conclusion The bias and precision found in this study are comparable with the results of previous studies in adults. In adults, accuracy and precision strongly improves after reconstruction of finger blood pressure [2]. A similar software adjustment for the pediatric population is under construction.

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P329

Arterial pressure based cardiac output in the septic patient

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Introduction In the treatment of severe sepsis and septic shock inotropes, vasopressors and vasodilatation drugs are needed to improve cardiac performance and microcirculation. The cardiac output is used to measure the cardiac performance. Pulmonary artery catheter (PAC)-based cardiac output measuring is often used but major complications can occur. A cornerstone and also a quality indicator of intensive care medicine is the prevention of complications within the intensive care. Alternative methods to measure cardiac output are developed to minimize complications. Until now, every new introduced method has been shown to have limitations. One of the latest alternatives is arterial pressure-based cardiac output (APCO) measuring.

Objective To assess the usefulness of APCO in critically ill patients with severe sepsis and septic shock.

Methods Patients with severe sepsis or septic shock who needed a PAC to guide therapy were connected to the APCO FlowTrac™ (Edwards Lifesciences, Irvine, CA, USA). Data collected from the APCO were evaluated and compared with the intermitted cardiac output measurement using the PAC. Results of both observational methods are compared using the Blend–Altman method.

Patients In this study the results of the first 10 patients are analysed. The mean age is 72 years (36–86 years).

The mean APACHE II score is 23 (18–31). The severe sepsis originated from the abdomen in five patients. The other five cases originated from the lungs.

Results A total of 208 cardiac output measurements have been obtained in critically ill patients of different origin. Comparing the different cardiac output measurements in the individual patient, we found a comparable trend in both methods. The presence of a tricuspid and or mitral valve regurgitation should be known when using the PAC-based cardiac output, especially when comparisons are made. There is an interesting difference in subgroup analysis when valvular abnormalities are considered. Significant differences were found between patients with and without valvular abnormalities (Mann–Whitney U test; $P < 0.001$). A moderate

correlation was seen for the group of patients with valvular abnormalities between the magnitude of the cardiac output and the size of the difference between monitoring methods (Pearson's $r = 0.53$; $P < 0.001$), whereby bigger differences were found for higher cardiac output volumes. Correcting for this output-size effect, the difference between monitoring methods remained significantly higher (mean diff.: 1.53; 95% limits of agreement: −1.57 to 4.63) for patients with valvular abnormalities (Mann–Whitney U test; $P < 0.001$).

Conclusion To us, the exact algorithm used by the APCO to calculate the cardiac output is unknown. Nevertheless we find comparable cardiac output measurements in patients with severe sepsis and septic shock. Because of this we think there is a place in clinical use of the APCO in the treatment of critically ill patients with severe sepsis and septic shock. More research is needed to fully understand the APCO and its implications.

P330

Measurement of CO by flow probe, USCOM and PAC in conscious sheep at rest and after dobutamine

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The PAC remains in clinical use as a measure of CO and haemodynamic trends, despite reports of inefficacy and patient risk. The flow probe (FP) accurately measures flow but is restricted to animal use by the necessity for surgical implantation. USCOM is a novel non-invasive 2D independent CW Doppler device for measurement of CO and haemodynamic change. We compared the USCOM and PAC Baxter intermittent thermodilution (PAC) with FP measurement of baseline CO and dobutamine-induced changes in conscious sheep. FPs were implanted on the ascending thoracic aorta of five sheep, and after 2 weeks recovery a PAC was inserted. In conscious sheep, transcutaneous transpulmonary USCOM signals were acquired and calibrated at baseline to the FP as USCOM calculates flow volumes from a human anthropometric algorithm. Simultaneous FP, USCOM and PAC signals were acquired at baseline and after dobutamine (5, 10, 20 mg/hour), and stored to Spike 2 software while the Doppler data were recorded on the USCOM device. Mean values for baseline measures by FP ($n = 862$), by USCOM ($n = 829$) and by PAC ($n = 741$) were 4.26 ± 0.67 l/min, 4.51 ± 0.90 l/min and 5.34 ± 1.26 l/min, respectively, increasing to 5.33 ± 1.55 l/min, 5.25 ± 1.45 l/min and 6.09 ± 1.61 l/min after dobutamine infusion.

Table 1 (abstract P330)

	Sheep 1	Sheep 2	Sheep 3	Sheep 4	Sheep 5	Total
USCOM	0.925	0.764	0.850	0.528	0.659	0.745
PAC	0.114	0.722	0.818	0.517	0.207	0.323

Table 2 (abstract P330)

	CO diff – total (%)	CO diff – base (%)	CO diff – dobutamine (%)
FP vs USCOM	−2	−5.5	1
USCOM vs PAC	−19	−15	−19
FP vs PAC	−19	−20	−18

The mean error between paired FP and USCOM measures at baseline was 5.5%, and between FP and PAC was 20.4%, and after dobutamine was 0.6% and 17.9%. For all measures FP and USCOM showed good correlation ($r = 0.745$), while FP and PAC were poorly correlated ($r = 0.323$).

USCOM may be a non-invasive alternative to PAC for measurement and monitoring of haemodynamics in animals and humans.

P331

Pneumoperitoneum influence on the cardiovascular system evaluated by the PiCCO system

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Introduction In laparoscopy the pneumoperitoneum, increasing intra-abdominal pressure, could impair cardiac performance and determine adverse cardiopulmonary effects. We have assessed the influence of laparoscopic surgery on selected hemodynamic–volumetric parameters by the PiCCO device (pulse contour analysis and transpulmonary technique).

Methods Under general anaesthesia 16 patients, age 62 ± 13 years, ASA II–III (exclusion criteria: cardiovascular disease, neurological disease, pulmonary disease), nine male/seven female, were enrolled in two groups: Group A eight patients submitted to laparoscopic surgery; Group B, eight patients submitted to open surgery. In this randomised, controlled study the cardiac index (CI), global ejection fraction (GEF), mean arterial pressure (MAP), systemic vascular resistance index (SVRI), intrathoracic blood volume (ITBVI), index of ventricular contractility (Dp/Dtmax) and stroke volume index (SVI) were recorded. The hemodynamic and volumetric data are studied at T0 (after induction of anaesthesia), T1 (during pneumoperitoneum pressure at 12 ± 3 mmHg) and T2 (after deflation of the gas). Statistical analysis: ANOVA and Bonferroni multiple comparisons post-test to compare changes in the groups. All data are given as means ± SD and $P < 0.05$ is considered statistically significant.

Results The hemodynamic parameters are not changed significantly between groups and in each group except for SVRI during pneumoperitoneum ($P = 0.0077$) (Table 1).

Table 1 (abstract P331)

	Mean hemodynamic values					
	Group A			Group B		
	T0	T1	T2	T0	T1	T2
MAP (mmHg)	83.8 ± 11	83.8 ± 12	76.8 ± 11	80 ± 3	78.4 ± 4	79 ± 7
CI (l/min/m^2)	3.38 ± 1	2.3 ± 0.8	2.4 ± 0.6	3.0 ± 0.3	2.5 ± 0.4	3.0 ± 0.1
GEF (%)	24.8 ± 5.5	21.8 ± 7.3	23 ± 5.6	30 ± 4	27 ± 5	28 ± 0.8
SVRI (dyn × s/cm^5 × m)	1866 ± 623	3200 ± 1051*	1462 ± 397	1900 ± 143	1980 ± 220	2000 ± 160
ITBVI (ml/m^2)	1011 ± 180	965 ± 272	965 ± 135	856 ± 64	870 ± 120	970 ± 69
Dp/Dtmax (mmHg/s)	889 ± 275	766 ± 248	875 ± 94.7	889 ± 220	1000 ± 113	1100 ± 228
SVI (ml/m^2)	45.9 ± 14.5	38.8 ± 14	41.9 ± 10	48 ± 4	43 ± 8	48 ± 7

* $P < 0.05$.

Acknowledgement Grant from Dr A Annunziata.

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P332

Non-invasive assessment of cardiac index: comparison between PiCCO and LiDCO

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Introduction The aim of the study was to compare measurements of cardiac index (CI) obtained with PiCCO (P) and LiDCO (L) before and after fluid challenge (FC) in eight critically ill patients.
Methods We studied eight patients (seven males), aged 20–82 (49 ± 23) years, admitted to our ICU for head injury (four patients), septic shock (one patient), ARDS (one patient), SAH (one patient), PO NCH (one patient). The APACHE II score was 22–32 (27.75 ± 5.2), SAPS II was 44–77 (59.12 ± 11.4). They were all monitored with P and L systems, to evaluate the CI, and received FC to optimize fluid loading. Haemodynamic measurements were made before and after FC with colloids (5 ml/kg in 30 min). Only data of calibration provided from PiCCO and LiDCO measurements were considered. Statistical analysis was performed with correlation and the Bland and Altman test.
Results Twenty-two samples of data were collected. The CI P range was 3.75–7.1 (4.4 ± 1.29) l/min/m^2 before FC and 2.75–7.41 (4.94 ± 1.42) l/min/m^2. The CI L before FC was 2.05–7.3 (4.4 ± 1.75) l/min/m^2 and was 2.7–6.84 (4.56 ± 1.37) l/min/m^2 after FC. The correlation coefficient found is 0.823 ($P < 0.001$). The 95% CI was 0.6156–0.942. The overall mean CO P – CO L difference was 0.19 l, with ±1.96 SD of –1.53 and 1.91 l, respectively. One measurement (4.5%) extended beyond the lower SD limit.
Conclusion CI measurements obtained with the L system provided acceptably comparable measurement with those of the P even if a larger population study is needed to confirm these preliminary data.

P333

Effects of midline thoracotomy on pulse pressure variations during pressure-control ventilation

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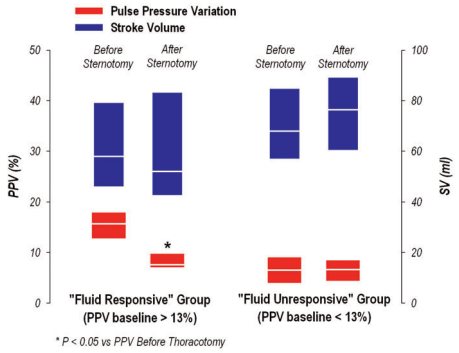
Objective During mechanical ventilation, the heart–lung interaction induces a cyclic oscillation of the arterial pulse pressure. The measure of this respiratory changes, called pulse pressure variation (PPV), is one of the most reliable index of fluid responsiveness. It is used as a functional hemodynamic monitoring in several conditions (general anesthesia, sepsis, ALI/ARDS). During cardiac surgery, midline thoracotomy significantly alters heart–lung interaction and, consequently, PPV. The aim of the study was the evaluation of the effects of sternotomy on PPV during pressure-control ventilation (PCV).

Figure 1 (abstract P333)



Methods Nineteen patients (age 62 ± 10 years) undergoing elective CABG in a tertiary university hospital were enrolled. A Swan–Ganz catheter, an arterial catheter and a central venous catheter was inserted in order to collect pressure waveforms. After the induction of general anesthesia all the patients were mechanically ventilated (PCV), setting pressure values in order to obtain a tidal volume of 8 ml/kg. Hemodynamic data were collected 5 min before and after sternotomy. PPV was calculated offline from the collected waveforms, according to the formula reported by Michard and colleagues [1].
Results The PPV, cardiac index, stroke volume, mean arterial pressure, airway pressure and tidal volume did not change after sternotomy. We subsequently differentiated patients according to PPV values (Fig. 1). In the subgroup of patients with PPV > 13% (7/19 patients), we found a good correlation between PPV and Paw (Pearson correlation 0.861 $P = 0.03$; $R^2 = 0.74$ $P = 0.049$); after sternotomy, PPV was significantly reduced (15.4 ± 2.8% vs 8.2 ± 1.6%, $P = 0.043$) and it was no more correlated with Paw. In the subgroup of patients with PPV < 13% (12/19 patients), we did not find any correlation between PPV and Paw, and sternotomy had no effects on hemodynamic data.
Conclusions During PCV, airway pressure affects PPV only when patients are in a 'fluid responsive' status (PPV > 13%); similarly, sternotomy reduces PPV only when baseline is above the threshold value of 13%. It may thus be possible that midline thoracotomy makes a 'fluid responsive' patient unresponsive to a fluid challenge by leading his heart to work on the plateau portion of the Frank–Starling curve. This hypothesis would be confirmed by the lack of correlation between airway pressure and PPV after opening the thorax.

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P334

Influence of ventilatory settings on the value of static hemodynamic variables and pulse pressure variation

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Background Volume expansion is the first-line therapy proposed to improve hemodynamics. However, volemic evaluation remains a clinical problem mainly in mechanically ventilated patients. The cyclic change in the arterial pressure waveform during positive pressure mechanical ventilation as pulse pressure variation (dPP)

has been proposed to identify responders to fluid administration. Despite this, there are no data about the performance of dynamic parameters during the use of different ventilatory settings in normovolemia and hypovolemia.

Objectives To evaluate the influence of positive end expiratory pressure (PEEP), tidal volume (VT) and inspiratory to expiratory ratio (I:E) on the value of hemodynamic variables, including dPP, during normovolemia and hypovolemia in pigs. To compare the ability of hemodynamic variables (right atrial pressure [RAP], pulmonary artery occluded pressure [PAOP], right ventricular end diastolic volume [RVEDV], mixed venous oxygen saturation [SVO_2] and dPP) to identify hypovolemia during different ventilatory settings.

Methods Ten anaesthetized pigs (67 ± 3.5 kg) were mechanically ventilated with VT 8 ml/kg, PEEP 5 cmH_2O, I:E ratio 1:2 and monitored with a pulmonary artery catheter for continuous cardiac output, RVEDV and SVO_2 measurement and a femoral artery catheter for systemic blood pressure and dPP recording. Animals were also ventilated in random order with VT 16 ml/kg, PEEP 15 cmH_2O or I:E = 2:1 in normovolemia (PAOP 12–15 cmH_2O), after withdraw of 20% of animal estimated volemia (hypovolemia) and after infusion of withdrawn blood (transfusion).

Results During normovolemia, use of PEEP 15 cmH_2O decreased the systolic volume (SV) (77.6 ± 23.5 vs 64.5 ± 16.4 ml, $P < 0.05$) and SVO_2 (78.8 ± 7.7 vs 67.4 ± 12.9%, $P < 0.01$), and increased the RAP (10.5 ± 2.1 vs 13.4 ± 2.1 mmHg), PAOP (14.6 ± 1.6 vs 17.4 ± 1.7 mmHg, $P < 0.001$) and dPP (15.8 ± 8.5 vs 25.3 ± 9.5%, $P < 0.001$). VT 16 ml/kg caused an increase in dPP (15.8 ± 8.5 vs 31.6 ± 10.4%, $P < 0.001$) and I:E = 2:1 did not affect hemodynamics. During hypovolemia, the high PEEP level affected significantly all studied variables except RVEDV but dPP was strongly influenced by high VT (40.5 ± 12.4% vs 84.2 ± 19.1%, $P < 0.001$). During the transfusion phase, SV and SVO_2 ($P < 0.001$) decreased with PEEP 15 cmH_2O while RAP ($P < 0,001$), PAOP ($P < 0.05$) and dPP ($P < 0.001$) increased their values; VT 16 ml/kg caused further increase of dPP from 10.6 ± 5.6 to 32.4 ± 8.6% ($P < 0.001$). ROC curves analysis showed that dPP, SVO_2 and RVEDV were better indicators of hypovolemia in all ventilatory settings with areas under the curve of 0.93, 0.91 and 0.87, respectively.

Conclusions For the same volemic state, the results lead us to conclude that: use of a high PEEP level causes increase of filling pressures (RAP and PAOP), reduction of SVO_2 and increase of dPP; VT causes a great influence on the dPP value; and RVEDV is the hemodynamic variable that is less influenced by ventilatory settings. The dPP, SVO_2 and RVEDV are better indicators of hypovolemia than RAP and PAOP independently of the ventilatory settings.

P335

Comparative evaluation of pulse contour analysis, thermodilution and partial CO_2 rebreathing techniques for cardiac output assessment in critically ill patients during different levels of positive end expiratory pressure

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Objective To investigate the precision and accuracy of continuous pulse contour cardiac output (PCCO) and the partial carbon dioxide rebreathing technique (NICO) under different levels of positive end expiratory pressure (PEEP).

Design A prospective, interventional study in the ICU of a university hospital.

Participants Ten patients undergoing elective CABG surgery.

Methods After admission to the ICU each patient was ventilated using one of three steps of PEEP for a time period of 30 min, followed by a 15-min equilibration period. All three PEEP settings were applied in randomly assigned order in every patient. A: PEEP 5 cmH_2O; B: PEEP 10 cmH_2O; C: PEEP 15 cmH_2O. The ventilatory settings were adjusted to achieve a tidal volume of 6–8 ml/kg/BW. Hemodynamic measurements were performed in sequence every 3 min during the subsequent 30-min period. The cardiac output (CO) was simultaneously measured using PCCO and NICO. At the end of each 30-min period a bolus thermodilution-derived CO was obtained from thermodilution curves detected in the femoral artery (TPTDCO). Three intermittent consecutive boli consisting of 10 ml ice-cold saline were randomly injected over the ventilatory cycle.

Results The comparison between the continuous cardiac output measurement methods NICO vs PCCO showed a bias of 0.4 ± 1.02 l/min (bias ± SD), $r = 0.58$; between NICO vs TPTDCO 0.0 ± 1.22 l/min; $r = 0.47$; and between TPTDCO vs PCCO 0.24 ± 0.45 l/min; $r = 0.93$ at a PEEP level of 5 cmH_2O. Mean bias at a PEEP level of 10 cmH_2O was 0.30 ± 1.17 l/min; $r = 0.58$; 0.1 ± 1.12 l/min; $r = 0.59$; 0.22 ± 0.61 l/min; $r = 0.89$, respectively. With increasing PEEP to a level of 15 cmH_2O the mean bias was NICO vs PCCO 0.5 ± 1.37 l/min; $r = 0.45$; NICO vs TPTDCO 0.7 ± 1.37 l/min; $r = 0.4$; and TPTDCO vs PCCO −0.29 ± 0.99 l/min; $r = 0.92$.

Conclusions The results of this clinical investigation show agreement between TPTDCO and PCCO to satisfy clinical requirements in a setting of postoperative patients after cardiac surgery independent of the level of applied PEEP. In contrast, the NICO monitor show agreement in clinical range until a PEEP level of 10 cmH_2O. With further increasing levels of PEEP the NICO monitor is of limited use in these patients.

P336

Stroke volume variation for assessment of the responsiveness to volume loading in canines with hemorrhagic shock: study on the comparison with hemodynamic parameters

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Objective To assess the significance of stroke volume variation and intrathoracic blood volume index on the responsiveness to volume loading in canines with hemorrhagic shock.

Methods Healthy mongrel canines were studied first to standardize the modified Wiggers' blood loss shock method. The MAP reached 50 mmHg and was maintained for 60 min. Graded volume loading was performed with each volume loading step (VLS) consisting of 7 ml/kg Ringer's given for 2 min. The same VLSs were preformed after a period of 15 min of stability. Successive responsive VLSs were performed (increase in SV >5% after VLS) until a continuous change in SV <5% (nonresponsives) was reached. The values of HR, MAP, CVP, PAWP, ITBI, and SVV were determined immediately before and 5 min after volume loading. The responsives and nonresponsives were identified as two groups.

Results (1) Responsive of VLS: 14 canines were studied and a total of 134 VLSs were performed. In 94 VLSs, an increase in SV of more than 5% was reached. In 40 VLSs, an increase in SV of less than 5% was reached (nonresponsives). (2) Comparison between the pre-VLS values of hemodynamic variables: the pre-VLS values of MAP, ITBI (79.6 ± 27.6 mmHg, 569.9 ± 341.4 ml/m^2) in responsives were less than nonresponsives (98.8 ± 15.2 mmHg, 784.2 ± 407.1 ml/m^2). The pre-VLS values of SVV (14.5 ±

4.0%) in responsives were more than nonresponsives (9.0 ± 2.7%), ($P < 0.05$), but no difference occurred in the values of HR, CVP, and PAWP. (3) Comparison between the change in the values of hemodynamic variables after VLS: the values of HR, CVP, PAWP, ITBI, and SVV in responsives differed from those of nonresponsives ($P < 0.05$). (4) Correlation between the pre-VLS values of hemodynamic variables and the change in SV after VLS (delta SV): statistically significant correlations were found between delta SV after VLS and the values of ITBI and SVV before fluid loading ($r = 0.356$ and 0.531, respectively) ($P < 0.05$). No correlation was found between delta SV and the value of HR, MAP, CVP, and PAWP before fluid loading ($P > 0.05$). (5) Correlation between the pre-VLS values of hemodynamic variables and delta SV: statistically significant correlations were also found between delta SV and delta CVP, delta PAWP, delta ITBI, and delta SVV after fluid loading ($r = -0.371$, −0.448, 0.438 and −0.376, respectively) ($P < 0.05$). (6) Assessment of the volume: using ROC analysis, the area under the curve for SVV was 0.872, and ITBI was 0.689, statistically more than those of HR, MAP, CVP, and PAWP. A SVV value of 9.5% or more will predict an increase in the SV of at least 5% in response to a VLS with a sensitivity of 92.6% and a specificity of 62.5%.

Conclusion Assessment of SVV and ITBI on the responsiveness to volume loading were more useful indicators than HR, MAP, CVP, and PAWP. It as a functional preload parameter and, for online monitoring, may help to improve the hemodynamic management.

P337

Monitoring of cardiac output in cardiogenic shock and low-output heart failure: LiDCO vs pulmonary artery catheter thermodilution

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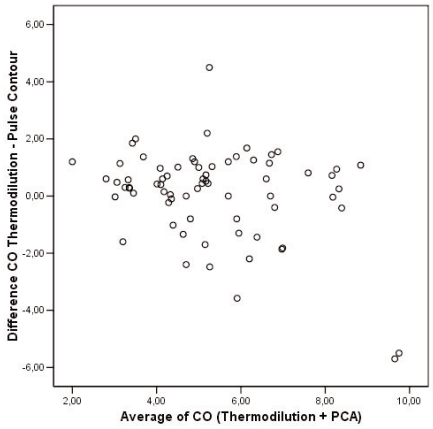
Introduction Determination and possibly monitoring of cardiac output (CO) is essential in cardiogenic shock (CS) and low-output heart failure (HF). The value of pulse contour analysis in these patients is unknown.

Hypothesis The aim of the present study was to assess the feasibility of LiDCO-pulse contour analysis in patients with CS and HF and to compare LiDCO with the standard pulmonary artery catheter (PAC).

Methods A total of 27 patients (17 male, age 62 ± 13 years, SAPS II 52 ± 19; mechanical ventilation $n = 24$; CS and HF, group 1, $n = 14$; control, group 2, $n = 13$) and a total of 72 measurements were included (a mean of 2.17 consecutive measurements/patient). The CO was measured using PAC and LiDCO simultaneously in all patients. The LiDCO was calibrated according to the manufacturer.

Results CO-PAC and CO-LiDCO showed a significant correlation ($r = 0.66$, $P = 0.001$) for the group as a whole. The correlation was lower in group 1 ($r = 0.45$, $P = 0.004$) vs group 2 ($r = 0.58$, $P = 0.001$). There was good agreement between the two methods for the entire group (mean difference 0.086, 95% CI −0.29 to 0.47). Respective values were 0.08 (95% CI −0.37 to 0.54) for group 1 and 0.09 (95% CI −0.58 to 0.7) for group 2.

Figure 1 (abstract P337)



Conclusion There was a somewhat lower correlation between CO-PAC and CO-LiDCO in patients with CS and HF when compared with controls. From a clinical standpoint, agreement between the two methods was fairly good.

P338

Passive leg rising and pulse contour monitoring

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Introduction Passive leg rising is proved to be a predictive tool of fluid challenge in the ventilated patient. Pulse contour analysis remains an innovative technique, so there are many dark sides to explore in usual clinical practice.

Objective To evaluate the PiCCO parameter responses to the passive leg rising position in ICU patients.

Patients and methods All patients with PICCO monitoring under mechanical ventilation and deeply sedated were enrolled. When physicians needed fluid challenge, we noted parameters delivered beat to beat (Philipps Monitor), heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), continuous cardiac index (CCI) and stroke volume variation (SVV), in the supine position (SP), then at 1 and 5 min in the Tredelembourg position (TP) (bed at 45°, patient position unchanged on bed), then in the supine position and after 200 ml gelatine fluid challenge.

Results We analysed nine measures in three ICU patients with septic shock: two received norepinephrine and one epinephrine as amine support. All patients were mechanically ventilated and deeply sedated. The TP leads to a decrease in HR, an increase in

Table 1 (abstract P338)

	HR	SAP (mmHg)	DAP (mmHg)	MAP (mmHg)	CCI (l/min.m^2)	SVV%
SP	120 ± 21	110 ± 25	65 ± 20	80 ± 22	4.2 ± 0.76	16 ± 7
TP (1 min)	115 ± 20	114 ± 24	66 ± 17	82 ± 20	4.2 ± 0.8	10.8 ± 6.6
TP (5 min)	113 ± 20	118 ± 24	68 ± 17	84 ± 20	4.18 ± 0.77	11.6 ± 7
SP	119 ± 27	108 ± 26	64 ± 19	79 ± 22	4.1 ± 0.7	17.4 ± 10
Fluid challenge	109 ± 27	124 ± 24	73 ± 17	90 ± 20	4.27 ± 0.9	9 ± 4.3

arterial pressure, a decrease in SVV, without any effect on the pulse contour cardiac index. Fluid loading increases arterial pressure but decreases the HR and SVV (Table 1).

Conclusion The TP mimics the effect of fluid loading. PiCCO parameters, especially SVV, can detect changes induced by the TP.

P339

Assessment of stroke volume variation

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Critical Care 2006, **10(Suppl 1):**P339 (doi: 10.1186/cc4686)

Introduction The specific interactions of the lungs and the cardiovascular system under mechanical ventilation cause cyclic variations of left ventricular stroke volume (SVV). Real-time measurement of SVV using arterial pulse contour analysis is useful to predict volume responsiveness and to monitor volume therapy in mechanically ventilated patients. In this study, SVV was evaluated using simultaneous recordings with the LiDCO plus system (LiDCO Ltd. Cambridge, UK) and the Vigileo (Edwards Lifesciences, Irvine, CA, USA) cardiac output monitor.

Methods At baseline the LiDCO pulse contour cardiac output was calibrated using the bolus thermodilution technique. The setup and zeroing procedure of the Vigileo cardiac output monitor was carried out in compliance with product specifications. Nine postoperative cardiac surgical patients were included. All measurements were carried out during standard clinical care. In stable clinical conditions, changes in SVV were forced by changes in tidal volume (Vt), the level of PEEP and leg-raising procedures. In all patients a total of 134 data pairs were evaluated using linear regression and Bland–Altman statistics.

Results The mean SVV measured with LiDCO was 10.1 ± 5.3% (SD), and that measured with the Vigileo was 11.7 ± 5.9%. The correlation coefficient regarding SVV measured with the two different devices was $R^2 = 0.678$ (slope 0.944, SE 0.057) (Fig. 1). The computed bias was significantly different from 0 (−1.70 ± 3.3%, $P < 0.001$) (95% CI −2.28 to −1.13). The upper and lower limits of agreement were 5.01 and −8.42% (Fig. 2). The calculated agreement between negative and positive changes in SVV using the LiDCO plus system and the Vigileo cardiac output monitor was correct in 80.6%.

Conclusions The agreement in SVV measured with the LiDCO and Vigileo cardiac output computer is acceptable. We found a slight, but significant, difference in SVV between the LiDCO and Vigileo cardiac output monitoring systems. For adequate interpretation of differences of SVV, more disclosure of the used mathematical models is essential.

Figure 1 (abstract P339)

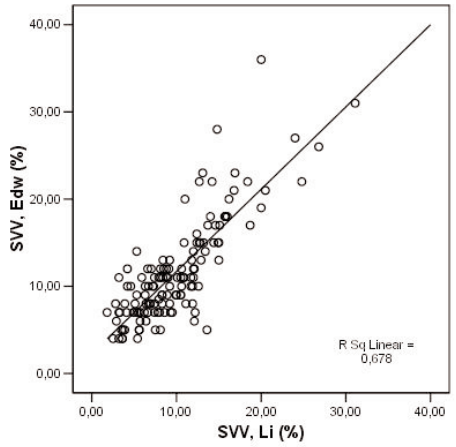
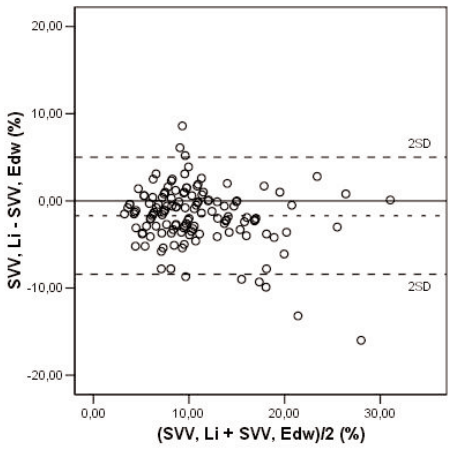


Figure 2 (abstract P339)



P340

Continuous central venous oxygenation measurement by CeVOX in patients undergoing off-pump coronary artery bypass grafting

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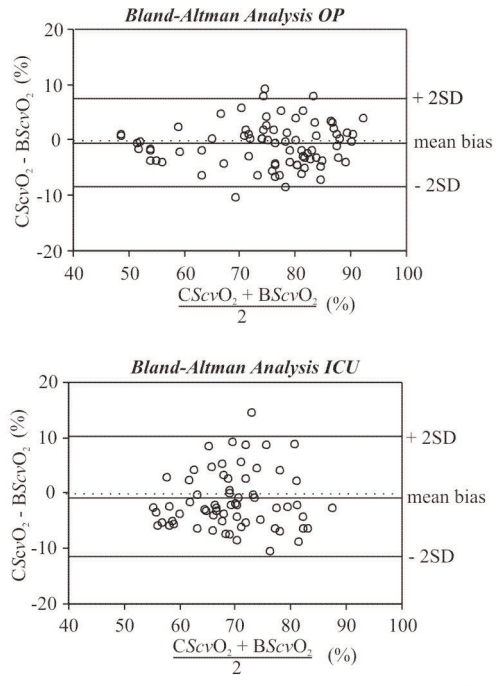
Introduction Less invasive measurement of central venous O_2 saturation ($ScvO_2$) has shown to be a valuable alternative to the determination of mixed venous O_2 saturation for monitoring of O_2 supply/demand [1,2]. The aim of this study was to compare $ScvO_2$ measured continuously by the new CeVOX (Pulsion Medical System, Munich, Germany) device ($CScvO_2$) with $ScvO_2$ determined by blood gas co-oximetry ($BScvO_2$).

Methods Ten ASA III patients undergoing elective off-pump coronary artery bypass grafting were studied during the operation (OP) and during their ICU stay. In addition to the standard hemodynamic monitoring according to institutional policy, a CeVOX fiber-optic probe was introduced into a standard central venous catheter placed via internal jugular vein access. OP and ICU measurement started after *in-vivo* calibration of CeVOX. $BScvO_2$ and $CScvO_2$ readings were recorded at intervals of 30 min during OP and of 120 min during ICU. Data were statistically analyzed using Bland–Altman analysis, Pearson correlation and *t* test for the periods during OP, ICU, a set of three consecutive measurements during OP immediately after calibration (OP_{cal}) and 4 hours later ($OP_{4\ h}$) as well as immediately after calibration on the ICU (ICU_{cal}) and 14 hours later ($ICU_{14\ h}$). Trend analysis was performed, calculating differences (Δ) between consecutive measurements. $P < 0.05$ was considered significant.

Results One hundred and twenty-nine matched sets of data were obtained (OP: $n = 78$, ICU: $n = 51$) with a wide range of $ScvO_2$ values ($BScvO_2 = 48.0–91.0\%$, $CScvO_2 = 49.0–94.0\%$). The OP observation time was 4.0–6.5 hours and the ICU measurement sequence was 14.0–20.0 hours. Bland–Altman analysis revealed an overall mean bias ± 2SD (limits of agreement) of −0.7 ± 7.8%

Figure 1 (abstract P340)



$CScvO_2$: Continuous central venous oxigenation measured by CeVOX
$BScvO_2$: Central venous oxigenation measured by blood gas co-oximetry

Table 1 (abstract P340)

	OP_{cal}	$OP_{4\,h}$	ICU_{cal}	$ICU_{14\,h}$
Mean bias ± 2SD (%)	−0.3 ± 7.2	−0.1 ± 8.4	−0.7 ± 8.6	−1.9 ± 14.0
r^2	0.849	0.853	0.832	0.358

for $CScvO_2$ – $BScvO_2$ during OP and −1.1 ± 11.6% during ICU (Fig. 1). There was no significant difference between $CScvO_2$ and $BScvO_2$ (OP: $P = 0.120$, ICU: $P = 0.167$). The correlation coefficient (r^2) for $CScvO_2$ vs $BScvO_2$ was 0.885 (OP) and 0.592 (ICU). Statistics for OP_{cal}, $OP_{4\,h}$ and ICU_{cal} were comparable, whereas for $ICU_{14\,h}$ the bias ± 2SD increased and r^2 decreased (Table 1). Trend analysis showed no significant difference (OP: $\Delta BScvO_2 = -1.3 \pm 9.0\%$, $\Delta CScvO_2 = -1.1 \pm 8.6\%$, $P = 0.663$; ICU: $\Delta BScvO_2 = -0.4 \pm 6.8\%$, $\Delta BScvO_2 = -0.4 \pm 5.8\%$, $P = 0.828$).

Conclusions These preliminary results indicate that $ScvO_2$ can be reliably assessed by CeVOX. Scheduled recalibration at intervals <14 hours may be mandatory.

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P341

Noninvasive approach to follow-up hemodynamics in patients with intra-aortic balloon counterpulsation: expediency and value

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Introduction Evaluation of hemodynamics in patients with complicated acute myocardial infarction (AMI) is crucial. Intra-aortic balloon counterpulsation (IABC) in patients with AMI complicated by cardiogenic shock (CS) is supposed to be monitored exclusively by invasive methods for assessment of hemodynamics. However, noninvasive methods might have a place in monitoring these patients.

Objective To evaluate hemodynamic indices (HI) by intermittent thermodilution (ITD) in patients with AMI, complicated by CS managed with IABC, and to compare with HI evaluated by continuous impedance cardiography (ICG).

Methods Cardiac output (CO) and stroke volume (SV) were measured by both ITD and ICG methods for patients with AMI complicated by CS, admitted within 12 hours from the onset of pain and managed by IABC. The standard eight-electrode ICG registration was used. The average values of COICG and SVICG derived from the last 10 min of the ICG record (60 SV instantaneous readings) were used to compare the results of ITD.

Fourteen patients were investigated according to the study protocol, eight (57.1%) men and six (42.9%) women. The average age was 72.8 ± 6.9 years. Anterior AMI was diagnosed for nine (64.3%) patients, inferior for four (28.6%), circular for one (7.1%) patient. Primary PTCA was successfully performed for seven (50%) patients, six (42.9%) underwent cardiac surgery within the first 2 weeks, and primary PTCA was unsuccessful for one (7.1%) patient, who died within the first 18 hours. The mortality rate was 78.6% (11 patients).

Results The measured COITD ranged from 2.8 ± 1.3 to 3.9 ± 1.1 l/min, SVITD from 26.8 ± 8.2 to 34.4 ± 10.8 ml. While the COICG ranged from 4.2 ± 1.4 to 4.9 ± 2.2 l/min, the SVICG ranged from 40.4 ± 14.2 to 51.4 ± 12.1 ml. The correlation coefficient (CF) was calculated comparing CO values derived from ICG and ITD; it ranged from 0.24 to 0.98 in separate patients. A weak correlation of ICG and ITD measurements was observed before initiation of IABC – 0.24–0.27 in separate cases. CF improved during IABC (0.58–0.98) and at the termination of IABC (0.67–0.97). The observed correlation was more pronounced in patients without a high dose of inotropes and ranged 0.58–0.98 while for patients with a high dose of inotropes it was less pronounced (0.29–0.5).

Conclusion Significant correlation of SV was observed between the ICG and ITD methods during IABC. However, higher values of CO and SV were measured by ICG. Non-invasive evaluation of hemodynamic indices by continuous monitoring of ICG during AMI, complicated by CS and managed by IABC, is a reliable method for further application. The correlation of hemodynamic parameters measured by two methods was more pronounced in patients without a high dose of inotropes.

P342

Increasing cardiac output by epinephrine after cardiac surgery: effects on indocyanine green plasma disappearance rate and splanchnic microcirculation

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Introduction Most clinical studies have so far focused on the regional effects of epinephrine (i.e. hepato-splanchnic blood flow) in septic patients. In cardiac surgical patients, however, inotropic (i.e. epinephrine) support is often necessary for optimizing cardiac output postoperatively. We tested whether increasing cardiac output by epinephrine leads to an improved regional (i.e. hepato-splanchnic) blood flow and function.

Methods After approval by our ethics committee and written consent, we postoperatively studied 12 patients (mean age 71 ± 8 years) with elective coronary artery bypass grafting ($n = 2$) or aortic

valve replacement ($n = 10$). All patients had a reduced left ventricular function and underwent extended hemodynamic monitoring by a pulmonary artery (CCO-PAC) for clinical indication. Microcirculation within the splanchnic area was assessed by gastric tonometry, liver blood flow and function non-invasively by transcutaneous measurement of the ICG-PDR. Since fluid loading led to no increase in cardiac output, patients were considered nonfluid responsive. Measurements were made on ICU admission and after 1 hour of epinephrine treatment. The mean epinephrine dosage was changed from 0.02 to 0.08 µg/kg/min. All patients were on pressure-controlled mechanical ventilation and respirator settings remained unchanged throughout the study period. Data are the mean ± SD. $P < 0.05$ was considered statistically significant.

Results The heart rate significantly increased from 97 ± 11 to 106 ± 12/min. Central venous (10 ± 3 vs 10 ± 4 mmHg) and left atrial (10 ± 5 vs 11 ± 5 mmHg) pressures were unchanged. The cardiac index and stroke volume index significantly increased from 2.7 ± 0.5 to 3.2 ± 0.5 l/min/m^2 and from 28 ± 6 to 31 ± 5 ml/m^2. Although systemic O_2 delivery and O_2 consumption significantly increased, the ICG-PDR did not change significantly (i.e. from 18.0 ± 5.6 to 19.5 ± 6.4%/min). The gastric mucosal PCO_2 and the PCO_2 gap (difference between regional and end-tidal PCO_2) significantly increased from 5.4 ± 1.0 to 5.9 ± 1.1 kPa and from 1.2 ± 0.8 to 1.5 ± 0.7 kPa, respectively.

Conclusion Increasing cardiac output by epinephrine was associated with no change in the ICG-PDR but with a significant deterioration in gastric mucosal blood flow in patients after cardiac surgery.

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P343

Cardiac output measurement in preterm neonates: validation of USCOM against echocardiography

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Objective measurement of cardiac output (CO) in preterm neonates is important for optimisation of haemodynamic management, and may have outcome benefits. Doppler ultrasound is the preferred method for measurement of CO; however, the pulmonary and aortic diameters for calculating flow volumes are small, and measurement using 2D ultrasound requires expertise and experience, particularly for analysis of transpulmonary flow. The USCOM (USCOM Ltd, Sydney, Australia) is a novel 2D independent device using CW Doppler and anthropometrics to determine both right and left flow volumes. The device is simpler to operate and less expensive than the conventional echocardiography.

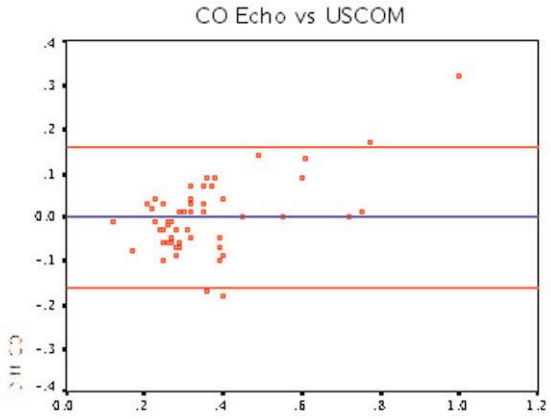
This study was to compare 2D echo and USCOM CO measurements in preterm neonates.

After IRB approval 66 paired measures of transpulmonary CO were acquired in 37 preterm neonates (mean weight 1.13 ± 0.47 kg) using conventional echocardiography, combining 2D and CW Doppler, and the USCOM device. Signals were acquired and analysed independently and in a blinded fashion, and values compared by two-tailed *t* tests and Bland–Altman bias analysis.

Mean values of transpulmonary CO were 0.36 ± 0.19 l/min by echocardiography and 0.37 ± 0.14 l/min by USCOM and were not significantly different ($r = 0.9134$, $P < 0.005$). The mean difference between measures was 0.00 ± 0.08 l/min, with a mean of the means of 0.36 ± 0.16 l/min and a mean percentage error of –3.7%. The smaller SDs associated with USCOM convert to smaller 95% CIs and a possible increased sensitivity for detection of haemodynamic change.

These results suggest that the USCOM is as accurate for measurement of neonatal CO as conventional echocardiography, and may be a simple cost-effective alternative for neonatal haemodynamic management.

Figure 1 (abstract P343)



P344

Transthoracic contrast echocardiography in the detection of patent foramen ovale

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A patent foramen ovale (PFO) is a common clinical finding and is becoming increasingly implicated in several important pathophysiological conditions, including cryptogenic embolic stroke, migraine with aura, decompression sickness and, more rarely, acute myocardial infarction [1]. Echocardiographic techniques are the principal means for diagnosis and assessment of a PFO [2]. The development of transthoracic echocardiography (TTE) with harmonic imaging coupled with the use of contrast and provocation testing has potentially enhanced our ability to detect a PFO transthoracically.

Methods A total of 20 patients with an unexplained embolic event were recruited. We compared four routes of contrast delivery (upper extremity vein in a dependent position, upper extremity vein in an elevated position, right femoral vein and lower extremity vein) with provocation manoeuvres on the detection of PFO using both TTE and transoesophageal echocardiography (TOE). The route of contrast delivery was performed in a random fashion. Studies were interpreted in real time by an echocardiographer in an unblinded manner as in real-life clinical practice. All studies were digitally recorded and later reviewed independently by a second BSE-accredited echocardiographer blinded to the sequence and site of contrast injections.

Results The mean age of the 20 patients was 24 ± 10.7 years and 12 (60%) were male. All patients were in sinus rhythm. Six patients

(30%) were exsmokers and four (20%) current smokers. Two patients were on treatment for hypertension and five (25%) patients had hyperlipidaemia (total cholesterol >5 mmol/l). One patient suffered with type 1 diabetes mellitus. The prevalence of PFO detected by the TTE approach combined with a provocation manoeuvre was 50% (10/20). The prevalence in divers was 100% (5/5) and 38% (5/13) in patients with a cryptogenic stroke/TIA. TOE only detected 5/20 (25%) PFOs. All PFOs detected by TOE were detected by TTE. Valsalva improved the detection rate for all routes of contrast delivery except i.v. access at the ankle. The highest detection rates were seen with contrast injection in the elevated arm or via the right femoral venous route (10/20). Agreement between reviewers was excellent ($P < 0.01$). All non-agreement observed between TTE and TOE occurred when TTE reported a positive result and TOE a negative result. In 9/10 (90%) cases the clearest image was using TTE, with 7/9 (78%) following a provocation manoeuvre. Left ventricular opacification was most marked during femoral vein delivery of the contrast agent coupled with the valsalva manoeuvre and TTE.

Conclusion TTE with harmonic imaging and femoral vein delivery of contrast should be regarded as the gold standard for the echocardiographic detection of PFO. Maximising the contrast load by use of the large antecubital vein and arm elevation improves detection if arm injection is used.

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P345

Simplified parameter to attest systolic right ventricular function obtained by tissue Doppler imaging of the tricuspid annulus

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Introduction The assessment of right ventricular (RV) function is difficult because of its complex geometry, its dependence on the load conditions and the absence of normal physiological values. Longitudinal shortening, the main component of its 'systolic function', can be studied by Doppler tissue imaging (DTI) of the tricuspid valve annular at the RV free wall, which analyses the longitudinal component of the RV 'function'.

Objective To estimate the ability of the tricuspid valve annular DTI to diagnose a RV dysfunction.

Patients and methods Forty intensive care patients without any cardiopulmonary pathology underwent an echographic exploration with DTI and form the reference group. This group allows one to test the feasibility of the technique and to confirm the normal values suggested by the literature. Forty-five other patients with a RV dysfunction attested by a dilation of the right ventricle, a RV/LV ratio >0.6, a dilation of the VCI without respiratory variation and the presence of pulmonary hypertension more than 45 mmHg underwent the same echo-Doppler study. Parameters obtained from DTI are: the systolic peak velocity (Stric) and the velocity time integral (VTITric) of the annular tricuspid free wall side.

Results The feasibility of the method is excellent, since all the patients could be analyzed. The reference group presents values that are in conformity with the data of the literature: Stric = 15.8 ± 5.45 cm/s and VTItric = 2.76 ± 0.48 cm, which correlated well together ($r = 0.81$, $P < 0.001$). The values of the RV dysfunction group are different: Stric = 8.87 ± 2.22 cm/s and VTItric = 1.33 ± 0.39 cm but correlated well together ($r = 0.82$, $P < 0.001$). Threshold values of Stric < 12 cm/s and VTIStric < 2 cm diagnose a RV dysfunction with, respectively, a sensitivity of 92% and 97% and a specificity of 95% and 96%.

On the other hand there is no correlation between these two parameters and the RV shortening fraction measured by echography or the pulmonary artery pressure attested by conventional Doppler. This underlines the difficulties to analyse the RV function with the conventional tools.

Conclusion Recording the tricuspid annular velocity by pulsed-wave DTI at the free wall is easy and very simple. These parameters would allow one to diagnose early systolic RV dysfunction, a frequently underestimated pathology among patients with aggressive ventilation.

P346

Noninvasive monitoring of cardiac output in critically ill patients: transesophageal Doppler vs transesophageal echocardiography

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Introduction Transesophageal Doppler (TED) increases prognosis in perioperative time [1] by detecting cardiac output (CO) variations [2]. Transesophageal echocardiography (TEE) is progressively considered as an alternative to the pulmonary artery catheter in the ICU. The purpose of this study is to compare cardiac output measurement using two ultrasound-based technologies: TED vs TEE.

Methods Twenty-one ventilated patients in septic shock were enrolled in two ICU units. The CO was recorded successively with TEE (COTEE) (Toshiba) and with TED (COTED) (Hemosonic 100 Arrow® and DOPTEK-ODM®) at the initial phase of septic shock. COTEE was obtained by measurement of the aortic velocity (ITVAo) in the transgastric view and by measurement of the aortic area in the transesophageal view (CSA): CSA × ITVAo × HR. An average of three measurements was recorded for each technique. A Bland–Altman study was used to compare the two techniques.

Results Bad correlation was found between the two ultrasound-based technologies (correlation coefficient = 0.09; P = NS) with an overestimation of COTED on COTEE of 1.4 ± 5.4 l/min. These differences were found with the two Doppler types used.

Conclusion Comparison of two non-invasive techniques to obtain CO output proves a low correlation between absolute value measurements of CO. Even though prolonged use is possible with TED, the absolute values obtained with TED have to be carefully interpreted.

Figure 1 (abstract P346)

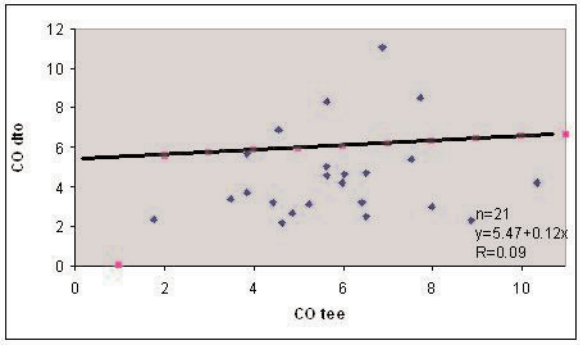
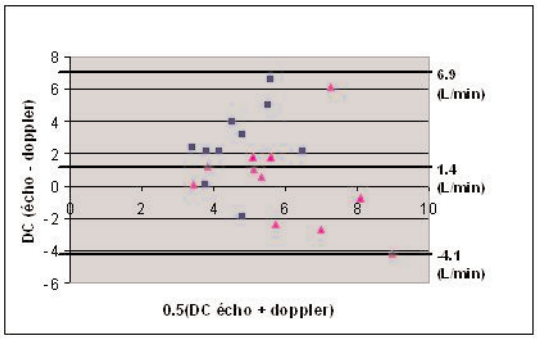


Figure 2 (abstract P346)



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P347

Cardiac pump performance in patients who underwent coronary artery bypass grafting

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Introduction The measure of ventricular performance, as an independent parameter of cardiovascular function, must be performed by a beat-to beat assessment of systolic function independent of load conditions, and is useful both as an index of contractility and as an index of ventricular functional reserve. We analyzed three different parameters of ventricular performance: the preload adjusted peak power (PAPP) [1], as an index of contractility; the cardiac cycle efficiency (CCE) [2], as a measure of ventricular arterial coupling; and the ejection fraction (EF), as an index of global ventricular function.
Materials and methods Fourteen patients who had undergone elective coronary artery bypass grafting were studied during the operation. All patients had preoperative EF >35%, good function of the cardiac valve and no contraindication to transoesophageal echocardiography (TEE). The arterial pressure was connected to a Pressure Record Analytical Method (PRAM) monitor to continuous measure the stroke volume index (SVI), cardiac cycle efficiency (CCE), and stroke volume variation (SVV) by pressure wave analysis. All the TEE examinations were obtained with a multiplane transesophageal probe (5-MHz probe). PAPP was obtained by the product of the peak systolic aortic pressure and the peak velocity of the aortic blood flow. EF was estimated from the end-diastolic and end-systolic area in the mid-papillary transgastric view. The parameters from PRAM and TEE were recorded simultaneously, and were performed during apnoea, after induction of anaesthesia, and after cardiopulmonary bypass (CPB). In eight patients dobutamine 2.5 μg/kg/min was infused before CPB to assess ventricular reserve.
Results No significant difference was found between preoperative and postoperative hemodynamic data. There was a good correlation found between PAPPpre vs CCEpre (R 20.80; $P <$ 0.001), PAPPpre vs SVIpre (R 20.95; $P < 0.001$) and PAPPpre vs EFpre (R 20.92; $P < 0.001$). The same good correlation was found for postoperative data between PAPPpost vs CCEpost (R^2 0.94; $P < 0.001$), PAPPpost vs SVIpost (R^2 0.95; $P < 0.01$) and PAPPpost vs EFpost (R^2 0.90; $P < 0.001$). There was an improvement of the PAPP value after infusion of dobutamine (2.4 ± 0.9 vs 3.2 ± 0.8) in all eight patients where it was made, but the small samples did not allow statistical analysis in this preliminary study.
Conclusion The PAPP, CCE and the EF could be used to assess ventricular and ventricular–arterial performance in clinical practice by the new low-invasive monitoring systems.

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P348

Incidence and efficacy of pulmonary artery catheters in the ICU of a developing country: a prospective, controlled study

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Background Existing randomized controlled trials on pulmonary artery catheter (PAC)-guided strategies reveal a modest risk reduction that does reach statistical significance. Risk reduction appears to be greatest in surgical series. This is primarily inserted for patients with systemic shock requiring haemodynamic support. However the efficacy of data collected from its use and the cost–benefit ratio are debatable. We would like to propose a study to look at the following objectives in the setting of a Third-World country ICU.
Objectives The incidence, indications, complication rate and outcome of PAC use in our ICU over a period of 3 months, comparing cases with matched controls.
Design An observational, prospective, controlled study in the ICU of a tertiary care university hospital serving an urban population of a Third-World country with limited resources.
Methods Over a period of 3 months every patient admitted to the ICU who had a PAC inserted for any indication was included. An equal number of patients matched for age and diagnosis but without a PAC were used as controls. Sample size calculation: as we do not have an incidence of PAC use available for our ICU as yet, a sample size calculation was not possible; however, we propose to study the incidence as well as indications and outcome by carrying out this study over 3 months. Data collection was carried out by the first author and an ICU resident. The data were collected by means of a data collection form.
Results and conclusion Fourteen patients and controls were enrolled in the study. The incidence of PAC use was 19% of all ICU admissions. Statistical analysis using Fisher's exact test and Student's t test revealed a P value of 0.677 for outcome with a nonsignificant difference between the two groups; a P value of 0.003 for length of stay, proving a significant difference between the two groups; and a P value of 0.455 (nonsignificant) for the mean age of patients with PACs. Pneumonia and sepsis were two of the leading causes for ICU admission; while 'fluid management' and 'haemodynamic monitoring' were two leading indications for PAC insertion. There were complications present in 30% of the

patients, including line sepsis, balloon rupture and coiling. Cost analysis showed a total cost of Rs.16,532/per patient for PAC insertion and monitoring. Despite being a limited study, we can clearly see that the cost effectiveness and outcome of patients with the PAC seems ambiguous. In a developing country where resources are limited, thought must be given to the risk and benefit ratio of placing this invasive monitor and the use of the information provided properly justified.

P349

Hemodynamic monitoring in severe sepsis and septic shock in German ICUs

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The first-line therapy in severe sepsis and septic shock is volume resuscitation, since relative and absolute hypovolemia are key symptoms of this illness. In addition a small subset of patients present with a septic cardiomyopathy (10–15%), a type of heart failure that barely responds to inotropes. Rapid restoration of blood flow and of tissue oxygenation respectively is of utmost importance in order to prevent organ dysfunction. So it is reasonable to postulate hemodynamic monitoring to diagnose pathophysiologic features and to guide therapy in these severely ill patients; more so since it has been shown recently that a substantial reduction in mortality could be achieved following therapeutic goals [1].
The objective of the study was to evaluate monitoring habits in German ICUs in patients with severe sepsis and septic shock.
A prospective observational cross-sectional study was performed in the ICUs of a representative hospital sample randomly selected from a complete registry of German hospitals stratified by size (≤200; 201–400; 401–600; >600 beds; university hospitals). From a total of 3877 patients screened, 415 patients (11%) fulfilled the ACCP/SCCM criteria for severe sepsis or septic shock. In these patients, monitoring routines – arterial blood pressure (ABP), central venous pressure (CVP), pulmonary artery catheter (PAC) and pulse contour analysis (PCA) – were ascertained by physicians trained in critical care medicine and compared with the data of a questionnaire that had been answered by the director of the ICU.
In general there was a pronounced difference between the statements of the ICU directors answering the questionnaire and the monitoring devices actually used. Only CVP measurement had been performed in all ICU patients in all hospital strata, and there was no gap between the questionnaire and instituted device. Patients in hospitals >400 beds were monitored with invasive ABP measurement in the majority of all cases, while middle-sized hospitals did this less frequently (60–75%). The PAC had been used in only a small subset of patients (<12%), although especially in larger hospitals the ICU director stated to use it more frequently (university: 40.4%). PCA, an excellent device to guide volume resuscitation [2], had seldom been in use as well. Even in major hospitals less than 15% of all patients monitored their patients in this way.
Acknowledgements Competence Network Sepsis is funded by the BMBF Grant No: 01KI0106. Sponsored by Lilly Germany.
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P350

Arterial to end-tidal carbon dioxide pressure difference and correlation of the difference with end-expiratory pressure in critically ill patients with severe lung injury

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Setting The general ICU of Hyllel Yaffe Medical Center, Israel.
Objective End tidal carbon dioxide ($ETCO_2$) monitoring is a non-invasive way to estimate blood carbon dioxide (PCO_2). The purpose of this study was to determine whether $ETCO_2$ measurement reliably indicates PCO_2 in mechanically ventilated patients and analyses the effects of positive end-expiratory pressure (PEEP) on volumetric capnography and respiratory system mechanics in mechanically ventilated patients.
Methods Twenty normal subjects (control group) and 20 patients with acute respiratory distress syndrome (ARDS group) were studied. Respiratory system mechanics – compliance and Bohr's dead space (physiologic dead space to tidal volume ratio [VD/VT(Bohr)]) – at different levels of PEEP were measured. $ETCO_2$ and carbon dioxide in arterial blood ($PaCO_2$) measurements were recorded. $ETCO_2$ was measured using a mainstream $ETCO_2$ monitor by Mannen Medical. All patients were ventilated with a Dreger Evita2 ventilator. Demographic data and primary diagnosis were recorded. Linear regression was used to analyze $ETCO_2/PCO_2$ pairs. Statistical significance was considered $P < 0.05$.
Results See Table 1. The mean dead-space fraction was markedly elevated (0.58 ± 0.01) at PEEP 11 cmH_2O and 0.66 ± 0.02 at PEEP 15 cmH_2O early in the course of ARDS. Large differences were found between $PaCO_2$ and mixed expired carbon dioxide ($PETCO_2$) in ARDS patients. The difference between arterial and end-tidal PCO_2 correlated closely with VD/VT.
Conclusions Our studies confirm that $PETCO_2$ is a poor estimate of $PaCO_2$ in patients with respiratory failure in PEEP values greater than 11 cmH_2O. Furthermore, the $PaCO_2$–$PETCO_2$ gradient is not stable over time and cannot predict variations of $PaCO_2$. The use of $PETCO_2$ instead of $PaCO_2$ could be deleterious in patients in whom strict control of $PaCO_2$ values is required.

Table 1 (abstract P350)

Volumetric capnographic indices at different PEEP levels in control and ARDS patients

	PEEP 5 cmH_2O	PEEP 7 cmH_2O	PEEP 9 cmH_2O	PEEP 11 cmH_2O	PEEP 13 cmH_2O	PEEP 15 cmH_2O
Et PCO_2 control	36 ± 7	38 ± 4	40 ± 5	40 ± 8	42 ± 7	43 ± 8
Et PCO_2 ARDS	42 ± 4	43 ± 4	42 ± 2	42 ± 3*	41 ± 8*	44 ± 5*
VD/VT control	0.41 ± 0.01	0.41 ± 0.01	0.42 ± 0.01	0.44 ± 0.02	0.45 ± 0.01	0.47 ± 0.02
VD/VT ARDS	0.52 ± 0.01	0.53 ± 0.01	0.55 ± 0.02*	0.58 ± 0.01*	0.61 ± 0.01*	0.66 ± 0.02*

*Statistically significant.

P351

Tissue perfusion may be assessed at the bedside with $ETCO_2$-derived dead-space estimation

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Introduction Alveolar dead space is determined by the degree of ventilation/perfusion mismatch in the lung. Since the entire cardiac output must pass through the lungs, we hypothesized that global changes in perfusion would correlate with changes in alveolar dead space. Dead space (VD/VT) can be estimated from the modified Bohr equation, which is further modified by substituting end-tidal CO_2 for $PECO_2$ – hence the VDVTest (estimated dead space). We used blood lactate as the endpoint of resuscitation.
Methods Five mechanically ventilated patients with lactic acidosis (lactate >30 mg/dl) were included. Four patients were postlaparotomy, one had multiple trauma. Ages were 36–87 years, APACHE II scores 18–37, and P:F ratio 203–470. We recorded the HR, MAP, CVP and $ETCO_2$ from the ICU monitor. We took simultaneous arterial and central venous blood samples at 30-min intervals for the first 4 hours of the study, then every 1 hour for a total of 12 hours.
Results There was a strongly positive linear trend correlating the VDVTest with lactate levels [$r(76) = 0.800$; $P < 0.001$] (Fig. 1). Furthermore, when plotted against time, the trends in VDVTest and lactate are parallel (example data from study patient 1 are shown; Fig. 2). There was also a significant correlation between the arterial to end-tidal CO_2 gradient ($PaCO_2$–$PETCO_2$) and lactate levels [$r(76) = 0.730$, $P < 0.001$]. There was no meaningful correlation between blood lactate and MAP, CVP, $ScvO_2$ and O_2ER.
Conclusion In this pilot study we demonstrated linear correlation between estimated dead-space and lactic acid levels. We propose that this technique may be a useful end-point of resuscitation during shock. It is convenient to measure, requires no special equipment and is non-invasive. Further study is required to assess the technique's reliability across different patient populations.

Figure 1 (abstract P351)

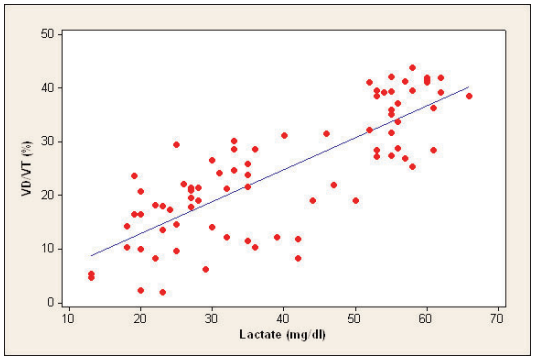
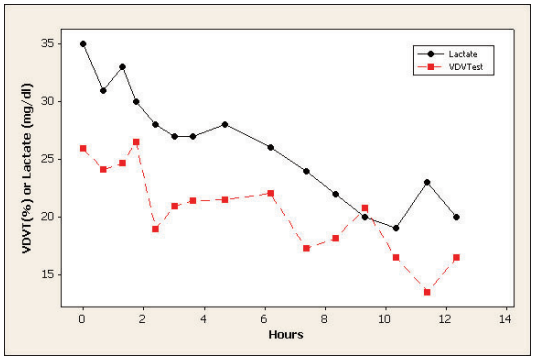


Figure 2 (abstract P351)



P352

Investigation of the pulmonary vascular permeability index and extravascular lung water in patients with SIRS and ARDS under the PiCCO system

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Background and objectives The hallmark of both systemic inflammation response syndrome (SIRS) and acute respiratory distress syndrome (ARDS) is increased capillary permeability, which manifests itself in the lungs as altered alveolar–capillary barrier function and is characterised by accumulation of extravascular lung water (EVLW). It is known that EVLW estimated by transpulmonary single thermodilution correlates closely with gravimetric measurements in experiments on animal studies. The correlation in human beings, however, is uncertain. Furthermore, the pulmonary vascular permeability index (PVPI) in patients with SIRS and ARDS has never been investigated in the literature. The aims of our study were: to evaluate whether PVPI may be an indicator of systemic inflammation disease and the severity of lung injury; and to compare the postmortem lung weight and EVLW measured by transpulmonary single thermodilution.
Materials and methods The PiCCO system (PULSION, Munich, Germany) data from 41 patients (APACHE II score 25 ± 7.5) treated in three hospitals between July 2004 and September 2005 was analysed retrospectively. The patients were divided into two groups. The first included patients who met the criteria of SIRS and the latter did not (SIRS vs non-SIRS). The SIRS groups was further subdivided into two; SIRS with ARDS, and SIRS without ARDS. We also considered four patients upon whom autopsies were carried out within 15 hours after the thermodilution EVLW measurement was performed.
Results The PVPI was significantly higher in the SIRS group ($n = 31$) than the non-SIRS group ($n = 10$) (SIRS vs non-SIRS: 2.37 ± 1.0 vs 1.2 ± 0.21; $P = 0.0013$). The PVPI was highest in the SIRS with ARDS group ($n = 13$) and lowest in the non-SIRS group ($P < 0.001$). Moreover, the PVPI was higher in the SIRS with ARDS group than the SIRS without ARDS group ($n = 18$) (non-SIRS vs SIRS with ARDS vs SIRS without ARDS: 1.2 ± 0.21 vs 1.7 ± 0.44 vs 3.2 ± 1.10). There was a very close relationship between transpulmonary thermodilution and postmortem lung weight ($n = 4$, $R = 0.985$; $P = 0.0015$)
Conclusion Measurement of extravascular lung water using the PiCCO system is very closely correlated with the gravimetric measurement of lung weight. The PVPI may increase due to systemic inflammation. This increase of PVPI may represent subclinical lung injury, which is undetectable by other bedside monitors or clinical examination.

P353

Comparative study on central venous pressure evaluation in jugular or subclavian and femoral accesses

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Objective To compare central venous pressure (CVP) measurements obtained in two different locations (jugular or subclavian veins and femoral veins).
Setting A 16-bed medical–surgical ICU.
Materials and methods The patients enrolled had central venous catheters (CVC) in two different locations, one placed in the internal jugular or subclavian veins and a second in a femoral vein. Simultaneous measurements of CVP were undertaken by two different operators, with a pressure transducer zero-referenced at the mid-chest. Standard CVC with similar features (20 cm length) were used. Patients with intra-abdominal pressure (IAP) >15 mmHg were excluded. The IAP was previously evaluated in all patients using the method described by Sugrue and Hillman. A linear correlation analysis was performed, considering significant $P > 0.05$ and a correlation coefficient >0.85.
Results Twenty four patients were studied and three patients were excluded. The mean age was 61.2 ± 9.3 years, the ICU stay was 9.8 ± 4.1 days, the APACHE II score was 24.8 ± 5.7, and SAPS II was 52.7 ± 10.4. The mean CVP measured with jugular or subclavian access was 12.1 ± 4.1 mmHg and 12.9 ± 4.2 mmHg at the femoral access. A good correlation between measurements was found with a correlation coefficient and $P > 0.001$.
Conclusions CVP can be accurately measured in femoral accesses, using standard CVC in patients with normal intra-abdominal pressure.

P354

Anterior approach internal jugular vein catheterization

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Critical Care 2006, **10(Suppl 1):**P354 (doi: 10.1186/cc4701)

Background Internal jugular vein cannulation has become one of the most commonly attempted central lines used in the operation rooms as well as in critically ill patients. There are three approaches to the internal jugular vein (posterior, conventional, and anterior)
Methods We randomly studied 60 patients who underwent percutaneous internal jugular vein cannulation with the supra-clavicular (anterior) approach (30 patients) or the conventional internal jugular approach (30 patients). The parameters observed included success rates, complications, flow and waveform characteristics and the acceptability of the technique both to the operator and the patient.
Results There were no significant differences between the two groups. First-attempt success and failure was the same in the two groups. Easiness for the operator was higher in the supraclavicular approach ($P = 0.02$). The number of complications (arterial puncture [3–2], pneumothorax [0–0], hemothorax [0–0]) were not different in the two groups. There were two significant differences in flow and waveform characteristics between the two groups. However, the supraclavicular approach was associated with greater patient comfort ($P < 0.00001$) but difficult fixation. Kinking in CXR in the ICU was higher in the supraclavicular group ($P < 0.0001$).
Conclusions We recommend the supraclavicular approach for CVP line placement in the internal jugular vein in cardiac surgery for experienced cardiac anesthesiologists.

P355

Influence of veno-venous renal replacement therapy on transpulmonary thermodilution measurements

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Introduction In principle, various factors may influence the accuracy of transpulmonary thermodilution. We analyzed whether veno-venous renal replacement therapy (RRT) has impact on the measurement of cardiac index (CI), intrathoracic blood volume index (ITBVI) and extravascular lung water index (EVLWI).
Methods With ethics approval, we studied 24 critically ill patients (nine female, 15 male) undergoing monitoring by the trans-pulmonary thermodilution technique for clinical indication and veno-venous RRT. All patients had a 5-F femoral arterial catheter and monitoring system (PV2015L20; Pulsion Medical Systems). Twelve patients had a femoral venous 12-F dialysis catheter *in situ* (Trilyse Expert; Vygon) and 12 patients had one placed in the v. cava superior. All patients received heparin for anticoagulation of the extracorporeal circuit. Measurements of CI, ITBVI and EVLWI were performed in triplicate by injecting 15 ml saline (4-6°C) through the distal port of a triple lumen central venous catheter (Certofix Trio; Braun, Melsungen) into the v. cava superior during RRT, during shortly interrupted therapy (disconnection) and immediately after reconnection.
Results Global hemodynamics were comparable at the three time points (mean ± SD). During RRT, the CI (mean change −0.1 l/min/m^2, $P < 0.01$) and ITBVI (mean change −18 ml/m^2, $P = 0.02$) were significantly lower. However, EVLWI was not influenced by RRT (mean change +0.1 ml/kg, $P = 0.42$).

Table 1 (abstract P355)

Parameter	RRT	No RRT	RRT
HR (1/min)	99 ± 27	100 ± 27	99 ± 27
MAP (mmHg)	74 ± 14	76 ± 12	74 ±13
CVP (mmHg)	14 ± 4	14 ± 4	14 ± 4
CI (l/min/m^2)	3.8 ± 1.4	3.9 ± 1.3	3.8 ± 1.3
ITBVI (ml/m^2)	934 ± 254	945 ± 255	920 ± 247
EVLWI (ml/kg)	8.3 ± 3.7	8.3 ± 3.6	8.4 ± 3.6

Conclusion Running RRT had no clinically relevant impact on the accuracy of the measurement of CI, ITBVI and EVLWI by transpulmonary thermodilution.

P356

Heart dysfunction evaluated by troponin, stroke work analysis and QT dispersion can predict outcome in patients with septic shock

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Critical Care 2006, **10(Suppl 1):**P356 (doi: 10.1186/cc4703)

Introduction Sepsis is the leading cause of mortality in ICUs. The mortality rate approaches 29%. As far as the heart is concerned,

adequately volume-resuscitated patients in septic shock present a hyperdynamic circulatory state with high cardiac output and reduced systemic vascular resistance, and this profile seems to persist throughout the septic event regardless of the outcome. Myocardial depression in patients with septic shock is characterized by biventricular dilatation and decreased systolic contractile function, all in the presence of an overall hyperdynamic circulation. In addition, sepsis and septic shock is characterized by an impaired sympathetic modulation of the heart, suggesting that a central autonomic regulatory impairment contributes to the circulatory failure that is seen. The purpose of this study was to analyze echocardiographic, ultrasonographic, hemodynamic and serum cardiac markers in patients with septic shock and to evaluate their relationship to the outcome.

Methods Prospective study on a six-bed ICU of a university hospital and a five-bed medical ICU of a tertiary care hospital. Data were collected over a period of 2 years. We studied 68 septic patients that met the ACCP/SCCM consensus criteria for sepsis and septic shock. All patients had continuous monitoring of blood pressure (BP) and heart rate (HR). Blood samples were collected on the first day of the septic shock and on days 3, 5, 7, and 10, and were analyzed for troponin, CPK, CK-MB, SGOT, SGPT, and LDH. Pulmonary artery catheterization was performed in all patients and the results were recorded for the days in question. Cardiac ultrasonography and echocardiography was also performed on the aforementioned days. Measurements of the patients' QT intervals on a 12-lead electrocardiogram (ECG) were also made. The QT interval was corrected (QTc) using the heart rate according to the Bazett's formula. The QT dispersion (QT-d) was defined as the difference between the maximum and the minimum value of the QTc in different leads. QT-d was measured and recorded for all the aforementioned days`

Results The patients were divided into survivors and nonsurvivors. We had 28 patients in the nonsurvivor group and 40 patients that recovered from their septic shock. The mortality rate was approximately 41%. The APACHE II scores for both groups were similar with no significant difference during the study. A hyperdynamic circulatory state with high cardiac output and low vascular resistance was observed throughout the study, and no significant difference was shown in any of the patients in either group. All the serum cardiac markers except troponin showed no significant difference. Troponin and stroke work analysis, however, showed a significant difference between the two groups. Troponin levels showed a significant difference from day 1 of the study and continued to the end, whereas the stroke work analysis difference became evident from day 5 and onwards. The QT-d measured from the ECG on days 1 and 3 were significantly increased especially in the nonsurvivor group (49 ± 20 ms vs 34 ± 11 ms). QT-d measurements of the following days had similar patterns to day 3 in either group.

Conclusion Heart dysfunction was evident by the troponin serum values, by the QT-d and by the hemodynamic stroke work analysis. All these variables presented a significant difference between survivors and nonsurvivors during the study. The establishment of heart dysfunction seems to correlate to patient outcome.

P357

Levosimendan: experience of an adult ICU

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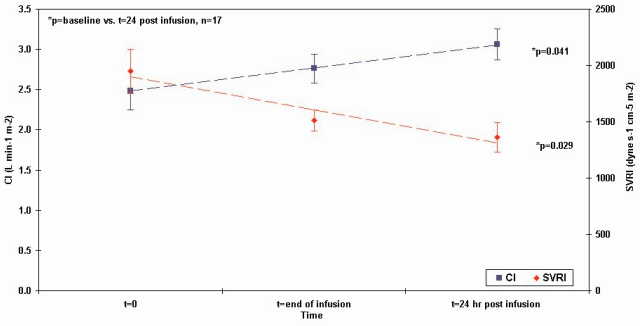
Critical Care 2006, **10(Suppl 1):**P357 (doi: 10.1186/cc4704)

Introduction The prognosis of patients admitted to the ICU with cardiogenic shock is poor.

Table 1 (abstract P357)

Key outcome measures
Reason for admission to the ICU
APACHE II score at initiation of levosimendan
Levosimendan dose and duration
Concurrent inotrope use
Cardiac studies
Adverse effects
Mortality

Figure 1 (abstract P357)



Levosimendan increases the cardiac index (CI) while lowering the systemic vascular resistance index (SVRI).

Method Data were collected retrospectively between January 2004 and June 2005. Cardiac studies and inotrope use were evaluated using Wilcoxon matched-pairs testing.

Results Twenty-eight patients received levosimendan. Ten (34%) patients were admitted following cardiac surgery and nine (31%) post acute myocardial infarction. The mean APACHE II score at time of levosimendan was 19 (SE = 0.96). No patients received a loading dose. The median maintenance dose was 0.1 µg/kg/min for a median of 24 hours (range = 3–58). A reduction in the mean dose of dobutamine (8.26 vs 3.77 µg/kg/min, $n = 7$, $P = 0.031$) and milrinone (0.22 vs 0.12 µg/kg/min, $n = 8$, $P = 0.031$) was seen 24 hours post levosimendan. A single patient developed atrial fibrillation and there were no new reports of ischaemia. ICU mortality was 62%.

Discussion Levosimendan had a favourable impact on the cardiac index, systemic vascular resistance index and inotrope use in our critically ill ICU patients at high risk of death. It was well tolerated in terms of arrhythmias and cardiac ischaemia.

P358

Hemodynamic and echographic effects of levosimendan in patients with cardiogenic shock refractory to catecholamines

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Critical Care 2006, **10(Suppl 1):**P358 (doi: 10.1186/cc4705)

Background Levosimendan is a novel inodilator that has proved effective in treating advanced congestive heart failure but has been poorly evaluated in cardiogenic shock.

Figure 1 (abstract 358)

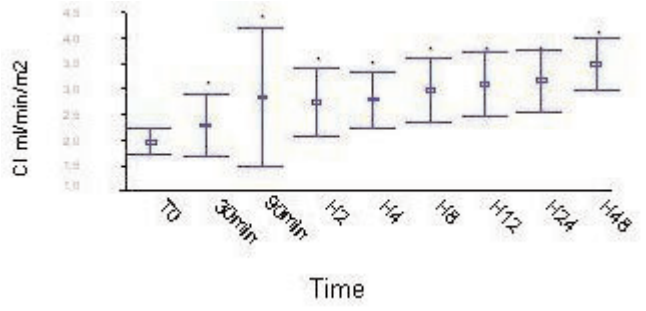
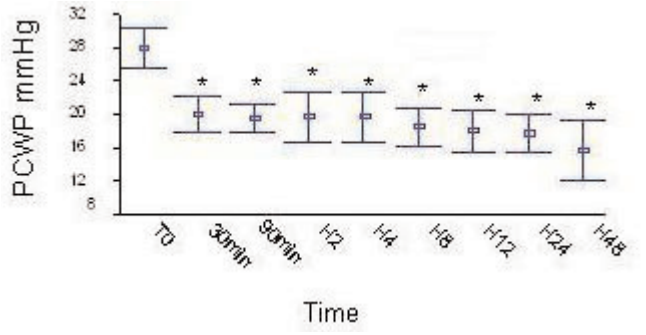


Figure 2 (abstract 358)



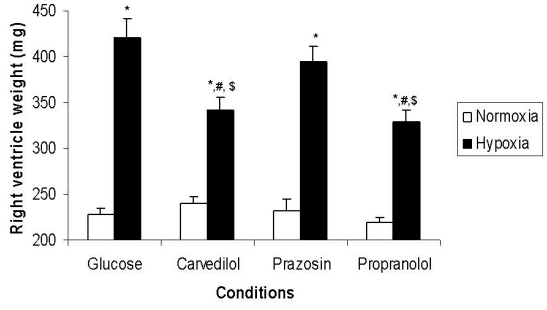
Objective To characterize the hemodynamic and echographic effects of levosimendan in patients with cardiogenic shock refractory to catecholamines.

Methods Nine patients (53.3 ± 19 years, five male/four female) with persisting cardiogenic shock following acute myocardial infarction (five cases), peripartum cardiomyopathy (two cases) or dilated cardiomyopathy (two cases) were candidates for levosimendan infusion. In all patients, a high dose of inotropic treatment failed to improve hemodynamic parameters. Levosimendan was introduced at a loading dose of 12 μg/kg followed by a continuous infusion of 0.1 μg/kg/min for 24 hours. Hemodynamic measurements were performed using a Swan–Ganz thermodilution catheter (744HF75; Edwards Life Sciences, Carolina, USA) at baseline and at 30 and 90 min, 6, 12, 24 and 48 hours after the start of levosimendan. Transoesophageal echocardiography was performed at baseline, 12 and 24 hours and then after 7 and 15 days in survivors.

Results Levosimendan induced a significant decline of pulmonary capillary wedge pressure and systemic vascular resistances, followed by a significant increase in the cardiac index and mixed venous oxygen saturation. Changes in the heart rate and mean arterial blood pressure were not significant. The left ventricular ejection fraction was improved from 24% to 40% within 48 hours.

Conclusion This study showed that the use of levosimendan in cardiogenic shock improved hemodynamics and left ventricular performance. Additional clinical trials on hemodynamics and mortality are needed to safely broaden its indications in cardiogenic shock.

Figure 1 (abstract P359)



Right ventricle weight according to altitude and treatment. *Hypoxia (acclimatized rats) vs normoxia; #treatment vs glucose; §carvedilol or propanolol vs prazosin. Mean ± SE, $P < 0.05$.

P359

Carvedilol inhibits right ventricular hypertrophy induced by chronic hypobaric hypoxia

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Right ventricular hypertrophy induced by chronic hypoxia is mainly due to a mechanical stress upon the ventricular wall secondary to pulmonary arterial hypertension. However, the hypoxic chronic activation of the sympathetic nervous system can contribute to the development of right ventricular hypertrophy either via myocardial adrenergic receptors and/or a vasoconstriction and remodeling of pulmonary arteries. To highlight the specific role of the sympathetic nervous system on hypoxia-induced right ventricular hypertrophy, and particularly the efficiency of carvedilol, our study compared physiological, myocardial and pulmonary arterial morphometric data in rats treated by α-prazosin, or β-propranolol or αβ-carvedilol antagonist and exposed to chronic hypobaric hypoxia (2 weeks at 380 mmHg barometric pressure). In chronic hypoxia, both the systolic right ventricular pressure and Fulton's ratio (right / [left + septum] ventricular weight) were lower in rats treated by prazosin (−16.7% and −13.6%), propranolol (−28.6% and −12.7%) and carvedilol (−15.9% and 14.3%), respectively, when compared with glucose ($P < 0.05$). Surprisingly, prazosin was unable to reduce right ventricle hypertrophy induced by chronic hypoxia, whereas the left ventricular weight increased. The wall thickness index of pulmonary arteries increased in chronic hypoxia and was reduced by carvedilol. In conclusion, the hypoxia-induced activation of the adrenergic system participates in the development of right ventricular hypertrophy. Carvedilol is effective in reducing hypoxia-induced right ventricular hypertrophy, pulmonary arterial hypertension and muscularisation of pulmonary arteries.

P360

Low-dose vasopressin improves cardiopulmonary functions in sheep with combined burn and smoke inhalation injury

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Background Arginine vasopressin (AVP) is increasingly used for hemodynamic support in critically ill patients. However, the effects

on reactive nitrogen species and pulmonary function are still not fully understood. We hypothesized that infusion of low-dose AVP improves cardiopulmonary performance by limiting nitrate/nitrite (NOx) and peroxynitrite ($ONOO^-$) formation.

Methods Chronically instrumented sheep were randomly allocated to: healthy controls (sham), injured controls (40%, third-degree burn; 4 × 12 breaths of cotton smoke, <40°C), or an injured intervention group treated with a continuous AVP infusion (0.02 U/min) from 1 hour post injury to the remainder of the 24-hour period of study ($n = 6$ each/group). Physiologic variables and NOx plasma levels (chemiluminescence) were analyzed intermittently. Post mortem, lung tissue was harvested for the determination of the wet/dry weight ratio and airway obstruction. In addition, 3-nitrotyrosine concentrations (stable biomarker of $ONOO^-$) in lung and heart tissues were measured using immunohistochemistry and ELISAs. Data are expressed as the mean ± SEM. For statistical analysis a two-way ANOVA for repeated measurements with appropriate post-hoc comparisons (Student–Newman–Keuls) was performed.

Results There were no differences between groups at baseline. All variables remained stable in sham animals throughout the entire experiment. Compared with injured controls, AVP reduced NOx plasma levels (24 hours: 9.5 ± 1.2 vs 4.5 ± 0.9 µmol/l), improved PaO_2/FiO_2 ratio (24 hours: 214 ± 20 vs 431 ± 38, each $P < 0.001$) and decreased the degree of pulmonary edema and airway obstruction. In addition, AVP improved myocardial contractility, as indexed by increased left ventricular stroke work index (24 hours: 52 ± 7 vs 87 ± 10 g/m/m^2). Compared with injured controls, AVP prevented the increase in 3-nitrotyrosine concentrations (lung: 43 ± 4 vs 32 ± 3 nM; heart: 37 ± 5 vs 22 ± 3 nM; $P < 0.01$ each).

Conclusion This study suggests that low-dose AVP infusion may be a rational approach to attenuate cardiopulmonary dysfunctions resulting from combined burn and smoke inhalation injury. The effects of AVP in this model may be related to inhibition of the cytotoxic $ONOO^-$.

P361

Effects of enalaprilat sodium on plasma NTproANP and NTproBNP levels in healthy volunteers

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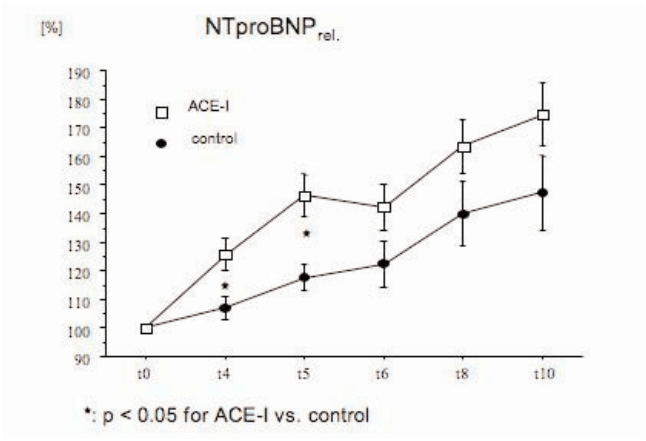
Background The N-terminal prohormones of the A-type and B-type natriuretic peptides (NTproANP and NTproBNP) are increasingly used as humoral markers for myocardial dysfunction in various clinical settings [1]. No data are available on the effects of angiotensin-converting-enzyme inhibition (ACE-I) on the plasma levels of these hormones.

Materials and methods Ten healthy males were cross-over and double-blind treated with 20 mg enalaprilat sodium or placebo (t0) following 7 days on a sodium enriched-diet and an induction period of 4 days with increasing doses of enalapril. After 4 hours (t4) 15 ml/kg NaCl 0.9% was infused over 60 min. Hemodynamics were determined and blood was sampled at t0, t4, t5, t6, t8, and t10 hours. NTproANP and NTproBNP were determined by radioluminescence and electrochemoluminescence immunoassays, respectively. Data were analyzed as raw data and as relative changes in comparison with baseline levels.

Results Arterial blood pressure was significantly lower after enalapril treatment during the fourth day of induction and during t0–t8 in comparison with control. Raw NT-proANP levels did not change throughout the observation period; relative NTproANP levels showed a short-lasting increase from t4 to t6 during control and ACE-I (after sodium loading). Raw and relative plasma NTproBNP levels increased from t0 to t10 during placebo and enalapril ($P < 0.001$). No between-group differences were observed in raw NTproBNP levels, while relative NTproBNP levels were significantly higher after ACE-I in comparison with control at t4 and t5 (Fig. 1).

Figure 1 (abstract P361)



Conclusions This suggests that ACE-I does not affect baseline and stimulated plasma NTproANP levels but augments the reactivity of the BNP system in sodium-loaded healthy individuals. ACE-I may thus interfere with NTproBNP determinations in sodium-retaining states.

Reference

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P362

Early administration of β-blockade in high-risk, acute coronary syndrome patients

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Critical Care 2006, **10(Suppl 1):**P362 (doi: 10.1186/cc4709)

Introduction Acute coronary syndromes represent the life-threatening phase of coronary artery disease. Over two decades ago, two large randomised controlled trials showed a reduction in early mortality when intravenous (i.v.) β-blockade was given acutely to patients presenting with ST elevation myocardial infarction [1,2]. β-Blockers also limit infarct size, reduce life-threatening arrhythmias, relieve pain, prevent myocardial rupture and reduce reinfarction rates. More recent data suggest that the early administration of β-blockade with thrombolytic therapy or prior to primary percutaneous coronary intervention also has significant benefits. Despite evidence, the use of β-blockade in patients presenting with acute myocardial infarction remains poor and i.v. β-blockade is rarely used.

Objectives and methods To assess the use of early (within 24 hours) β-blockade in patients presenting with acute ST elevation myocardial infarction (MI). A prospective audit was carried out on consecutive patients admitted to our coronary care unit over a 6-month period.

Results In 6 months 87 patients were admitted (males 60, female 27). The average age was 65.5 years. Sixteen per cent of patients (14/87) had had a previous MI and 41% (36/87) had three or more risk factors for coronary artery disease. Presenting ECG, 54% (47/87) of patients had either an anterior (median TnT 7.3 ng/ml) or lateral (TnT 2.43 ng/ml) MI and 46% (40/87) a posterior (TnT 6.11 ng/ml) or inferior MI (TnT 4.24 ng/ml). The majority of patients received reperfusion therapy, 47% (41/87) thrombolysis and 44% (38/87) were treated with primary percutaneous intervention. Nine out of 87 did not receive reperfusion therapy due to late presentation. The mean pulse on admission 75 (±23) bpm and systolic BP 135 (±39) mmHg. Only seven patients received intravenous β-blockade within the first 24 hours, with no adverse reactions reported. Twenty-one out of 87 patients were already taking a β-blocker at the time of admission. Fifty-three out of 87 received oral β-blockade within the first 24 hours and 67/87 patients were discharged on β-blockade. The average delay in initiating β-blockade, 8.4 hours from admission. Contraindications to β-blockade existed in 14% (12/87) of patients (5/87 second/third-degree heart block, 5/87 severe heart failure and 2/87 asthma).
Conclusion During the acute phase of acute MI, β-blockade is indicated in all patients without an absolute contraindication, and a large evidence base supports their use. Our results have shown that the early (<24 hours) use of β-blockade, and in particular i.v. β-blockade, is low. This may in part be due to clinicians' lack of awareness of the benefits of early i.v. β-blockade, and ongoing education is required.

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P363

Evaluating the values of blood troponin T in relation to the values of cardiac ejection fraction in patients suffering subarachnoid hemorrhage due to ruptured cerebral aneurysms

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Objective To evaluate the values of blood troponin T (T-T) in relation to the values of cardiac ejection fraction (EF) in patients suffering subarachnoid hemorrhage (SAH) due to ruptured cerebral aneurysms (RCA).
Patients and methods The present study was approved by the local ethical committee and informed consent was obtained from all patients and/or their relatives. During 1 April to 30 November, 10 patients were transferred to Kanemaru Hospital under suspicion of SAH: they complained of sudden headache and/or showed disturbed consciousness. The diagnosis for RCA with SAH was obtained by checking the views from cranial computed tomography (CT) and cerebral angiography. We also examined blood samples to evaluate the blood T-T and also their cardiac function using an echocardiogram machine (Sonos 4500; Philips). To compare, we divided the patients into the two groups in relation to the results of blood T-T: patients who showed negative results (N-G) and patients who showed positive results (P-G), respectively. Cardiac functions were evaluated using the values of cardiac EF. T-T was measured using the kit Trop-T sensitive (Roche). These values were obtained from blood samples drawn from patients after more than 4 hours since the onset of the SAH attack. Data were expressed as means (±SD). Statistical analysis was performed using Statview software and $P < 0.05$ was thought statistically significant.
Results In two patients, paired values could not be obtained and we removed them from the study. Eventually, eight patients were enrolled. Two female patients of all the eight patients showed positive results in T-T and the other six patients (two male and four female) showed negative results. The age was 70 (12.6) years with the range of 43–80 in N-G and was 80.5 (0.7) years with the range 80–81 in P-G, respectively. In N-G, the EF value was 73.1% (6.2) with the range of 64–81, and in P-G was 39.5% (7.8) with the range of 34–46, respectively. There was a significant difference in the cardiac EF values between the two groups ($P = 0.0003$). However, no patient with normal cardiac function showed a positive value of T-T. In addition, patients with disturbed cardiac EF values less than 55% showed positive results in the T-T test. The patients in P-G also showed giant negative T waves in their electrical cardiogram.
Discussion Catecholamine-induced cardiomyopathy can occur in several kinds of diseases, one of which is SAH. It can induce disturbed cardiac function. Many patients with SAH due to RCA need surgical procedures, such as neck clipping. However, we also need to obtain correct information about their general conditions including the state of cardiac functions. Evaluations with measuring cardiac EF and blood T-T could give us good information to understand cardiac conditions. The information might also help surgeons and anesthesiologists to decide when the surgical procedures should be done or not. We can obtain the values of blood T-T easily without special equipment and a talented technique.
Conclusion Some patients who suffered SAH due to RCA showed disturbed cardiac dysfunctions. In assessing them, we recommend measuring blood troponin T as an adjunctive method.

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Cardiac troponin in the general adult critical care unit: solution or problem

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Cardiac troponin T (cTnT) and troponin I (cTnI) are the most sensitive and specific biochemical markers of myocardial injury available, but do not indicate the mechanism of such injury [1]. There are many problems with their interpretation in the critical care setting.
A recent editorial has highlighted that frequent determination of troponin in the ICU patient can lead to 'troponinitis'! [2]. The editorial quotes various studies, including those showing association between elevated cTnI levels and mortality. After analysis of 346 samples measured over 22 months from our general adult ICU (annual admissions 850), we also found a statistical relationship between levels of elevated cTnI and both ICU and hospital mortality (Table 1) using chi-square testing. However, we have not found this to be clinically significant. A hospital mortality of 51.2% may be high, but not so high as to precipitate the withdrawal of intensive care treatment.
Due to the low specificity and positive predictive value of cTnI in mixed adult general critical care patients, it is difficult for us as intensivists to place elevated troponin levels in their clinical context. We also have difficulty in using elevated troponin levels to influence patient management in the absence of a classical history and ECG changes. Thrombolysis, ACE-inhibitors and β-blockers can be doubled-edged swords in the critically ill; echocardiography in the resting patient provides scant meaningful information; a pulmonary artery catheter is invasive – and all this before we consider the risks associated with coronary angiography. We therefore believe that cardiac troponins in a mixed adult ICU should only be requested when it could confirm an acute coronary

Table 1 (abstract P364)

Plasma cTnI	<0.199 µg/l	0.2–0.99 µg/l	>1.0 µg/l	*P* value
n	67	149	125	
Median APACHE II score	14	17	20	NS
Median ICU LOS	6	5	4	NS
ICU mortality	13 (19.4%)	39 (26.1%)	51 (40.8%)	<0.01
Hospital mortality	19 (28.3%)	61 (40.9%)	64 (51.2%)	<0.01
Post-ICU mortality	6 (11.1%)	22 (20%)	13 (17%)	NS

syndrome. In the ICU setting, this would almost always entail obtaining new ECG changes before requesting a cTnI level.

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High incidence of elevated serum creatine kinase in the ICU: an underestimated problem

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Introduction An elevation in the serum creatine kinase (CPK) level (without a simultaneous rise in the MB fraction or massive ischaemic cerebral infarction) correlates with the extent of muscular damage. Although usually asymptomatic, it could evolve into a life-threatening condition of rhabdomyolysis complicated by acute renal failure and/or disseminated intravascular coagulation. Critically ill patients may present with an elevated CPK for a number of different reasons. We performed an observational prospective pilot study during 31 days in a mixed ICU in a tertiary referral teaching hospital in order to study the incidence of elevated CPK levels and its possible influence on outcome.

Subjects and methods With the exception of cardiac surgery patients and children below the age of 16, all patients admitted to the ICU were included. Patients were excluded when either an elevated troponin I >0.50 ng/ml, an elevated CPK–MB fraction (>6% of total CPK) or a cerebral infarction was present. A CPK level >170 IU/l was arbitrarily defined as elevated. The number of patients with CPK levels >2000 IU/l were also identified. We sought to compare differences in 28-day mortality and length of stay (LOS) in the ICU (max 28 days) and LOS in the hospital (max 28 days).

Results See Table 1. Most patients with an elevated CPK level were surgical patients (including trauma). A cause could be identified in 86% of all cases. Of the unidentified causes, 80% were in medical patients. No statistical significance was observed for mortality or LOS.

Conclusions Elevated CPK is frequently observed in a mixed ICU population. Surgical patients are more prone to elevated CPK levels than medical patients. Unexplained CPK elevation is more observed in medical patients. LOS, mortality and the number of patients with a LOS >28 days rise in parallel with the level of elevation of CPK independent of the APACHE II score, although no statistical significance could be observed. Further investigation of the true incidence, complication rate and independent risk factors for elevated CPK seems to be indicated.

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Role of homocysteine in the development of the cerebral and cardiovascular pathology in young persons

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Cerebral and cardiovascular pathology is the leading cause of the death and invalidity in industrially developed countries. During recent years new data allowed to increase significantly the presentations of the pathogenesis of these diseases. They revealed that hyperhomocysteinemia increases the risk of early development of atherosclerosis and thrombosis of the coronary, cerebral and peripheral arteries independently of the traditional risk factors and it is the prognostic marker of the lethal outcome.

The objective of this study was to appreciate the role of homocysteine in the development of the cerebral and cardiovascular pathology (ischemic stroke, myocardial infarction) in young persons. We examined 28 patients during an acute period of the ischemic stroke (IS) and 10 patients with acute myocardial infarction (AMI) (mean age 45.1 ± 1.15 and 40.9 ± 2.34 years). Clinical evaluation of the neurological status of the patients with IS was conducted traditionally and according to the international clinical scales determining neurological deficiency (Bartela, NIH-NINDS, Orgogoso, Scandinavian, Index of the Disorders of Adoptive Activity) at patient's admission. The control group consisted of 15 healthy subjects (mean age 44.7 ± 1.02 years). The homocysteine concentration in the blood was analyzed in all fasting patients on the immunochemoluminescent analyzer 'IMMULITE One' (USA) using the assay kit of 'DPC' production (USA).

We revealed the presence of the moderate hyperhomocysteinemia in the patients with IS and AMI. The mean concentration of the serum homocysteine exceeded the mean concentration of this metabolite in healthy subjects by 57% and 48%, respectively.

The patients with IS had dependence of the clinical course of the disease on the homocysteinemia level. In mild (n = 7) and moderate (n = 9) neurological deficiency, the mean concentration of homocysteine was 8.1 ± 0.65 and 10.8 ± 1.44 µmol/l respectively. In expressed and gross (n = 11) neurological deficiency, the mean concentration of homocysteine was 16.0 ± 2.44 µmol/l, which exceeded the control value by 85%. In two patients with gross neurological deficiency and the highest values of homocysteine, the disease finished by fatal outcome. All patients with increased homocysteine concentration had atherosclerotic

Table 1 (abstract P365)

CPK (U/l)	*n* (%)	Age (years)	APACHE II score	LOS ICU	LOS hospital	Mortality (%)	LOS > 28 days [*n* (%)]
<170	35 (50)	64.2 ± 13.7	18.8 ± 7.3	4.9 ± 5.7	15.9 ± 9.4	2 (5.7)	6 (17.1)
>170	35 (50)	55.1 ± 17.4	16.0 ± 8.4	6.1 ± 6.7	16.2 ± 9.5	4 (11.4)	9 (25.7)
>2000	10 (14.3)	51.2 ± 16.5	13.5 ± 6.2	9.1 ± 7.6	19.7 ± 10.8	2 (20)	6 (60)

Data presented as *n* (% of total) or mean ± SD.

changes of the vessels that were uncharacteristic for their age. All patients had the atherothrombotic subtype of IS.
The development of AMI and the severe degree of the atherothrombotic subtype of IS in young persons may thus be conditioned by increased homocysteine concentration provoking early formation of the atherosclerotic changes of the vessels and thrombosis. The obtained data may be useful in the composition of programs of the prophylactic measures.

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The use of medical early warning scores in high-risk acute coronary syndrome patients in a district hospital setting

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Introduction Clinical deterioration is often preceded by a change in physiological parameters. Inappropriate action to these changes can lead to increased mortality. One way to identify the critically ill patient is through physiologically based early warning scores (EWS) [1,2]. Use of EWS scores is advocated by the Royal College of Physicians, the Intensive Care Society and the Department of Health. Several generic scoring systems are available, although specific cardiac scoring systems also exist. The TIMI risk score for patients with unstable angina and non-ST elevation myocardial infarction (UA/NSTEMI), validated in several large patient cohorts, is broadly applicable, easily calculated and stratifies a patient's risk of future events [3].
Aims and methods To assess the incidence of SIRS at the time of presentation in acute coronary syndrome (ACS) patients, and to assess the use of medical EWS (modified EWS [MEWS] [1], patient at-risk score [PARS] [2]) in high-risk ACS patients in a district hospital setting to determine whether they correlate with the validated TIMI UA/NSTEMI score. Over a 6-month period all patients diagnosed with NSTEMI, identified via the hospital coding system, were identified and a retrospective review was performed.
Results Seventy-four patients were identified (age 70.4 ± 10.8 years), of which 46/74 (62%) were male. Male patients were younger 67.3 ± 10.6 vs 75.3 ± 9.4 years ($P < 0.01$) with a mean TIMI score 5 vs 5.3 (P = NS). The admission route was split 49%/51% between A&E and primary care. Patients were managed by cardiologists in 40% of cases. Most patients were managed on CCU, 53/74 (71%), median age 69.3 ± 10.7 vs 73.1 ± 11 years (P = NS). Over 60% of patients had a positive smoking history and 7/74 (8%) had undergone previous revascularisation.
In 22 (30%) patients a SIRS response was noted. Patients with a SIRS response tended to have a slightly higher 12-hour troponin T measurement (1.2 vs 0.7 ng/ml, $P = 0.2$), TIMI score (5.32 vs 5, $P = 0.15$) and were older (74 vs 68.8 years, $P = 0.06$).
The median (range) MEWS and PARS scores were 1 (0–5) and 1 (0–8), respectively. There was no association between MEWS and TIMI scores ($r = -0.1$, $P = 0.5$), or PARS and TIMI scores ($r = 0.2$, $P = 0.1$). There was a positive association between MEWS and PARS scores ($r = 0.5$, $P < 0.001$).
Conclusion EWS are used to identify patients at risk and to highlight the fact that a patient is critically ill. Recording a patient's physiological variables should be part of the daily ward routine. The TIMI risk score for patients with UA/NSTEMI should be used in patients with symptoms and signs suggestive of an ACS and not medical EWS.
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Inpatient management of high-risk acute coronary syndrome patients in a district hospital setting

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Introduction European guidelines recommend that 'high-risk' acute coronary syndrome patients presenting to non-interventional centres should be transferred to a tertiary care centre for diagnostic coronary angiography ± coronary revascularisation within 72 hours of admission [1].
Aims and methods To assess the contemporary management of non-ST elevation myocardial infarction (NSTEMI) patients in a district hospital setting. Over a 6-month period patients diagnosed with NSTEMI, identified via the hospital coding system, were identified and a retrospective review was performed.
Results Seventy-four patients were identified (age 70.4 ± 10.8 years), of which 46/74 (62%) were male. Male patients were younger 67.3 ± 10.6 vs 75.3 ± 9.4 years ($P < 0.01$) with a mean TIMI score 5.2 vs 5.4 ($P = 0.3$). The admission route was split 49%/51% between A&E and primary care. Patients were managed by cardiologists in 40% of cases; 53/74 (71%) were managed on CCU, median age 69.3 ± 10.7 vs 73.1 ± 11 years ($P = 0.17$) for patients not on CCU. Over 60% of patients had a positive smoking history and 7/74 (8%) had undergone previous revascularisation. At the time of admission 61/74 (82%) patients received aspirin, 41/74 (55%) received LMWH and only 51/74 (69%) received clopidogrel. Once the 12-hour troponin T result was available, LMWH and clopidogrel use increased to 45/74 (61%) and 54/74 (73%), respectively. Only 33/74 (45%) patients were transferred for further inpatient investigation, 11 from cardiologists and 22 from noncardiologists. Four patients underwent outpatient diagnostic angiography. Patients who were transferred were younger, 64.3 vs 75.2 years ($P < 0.001$), although had similar TIMI risk scores to those not transferred, 5.2 vs 5.3 ($P = 0.56$), and had 12-hour troponin T values, 0.7 vs 1 ng/ml ($P = 0.29$). Other than age there were no other significant differences in the specific TIMI risk score features. In the cohort, 15/23 (65%) <65 years, 16/23 (70%) 65–75 years and only 2/28 (7%) >75 years were transferred. Prior to transfer no patients received a GPIIb/IIIa receptor antagonist. In the 41/74 patients who were not transferred, four (10%) died during their inpatient stay (TIMI score 5.5 vs 5.3 for survivors, $P = 0.5$). Patients who died were older 76.5 vs 70 years ($P = 0.25$). Only 23/41 (56%) of patients not transferred were discharged on Clopidogrel with no significant difference in age.
Conclusion The use of antiplatelet and anticoagulant therapies in the treatment of high-risk ACS patients is suboptimal. It might be more appropriate to start these therapies on admission and not once troponin results become available, with a view to discontinuing treatment subsequently in those deemed unlikely to benefit. The low rate of compliance with the guidelines might be partly explained by uncertainties about the management of the elderly.
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P369

Clinical factors of extension and severity of the coronary disease in patients with acute coronary syndrome

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Introduction The presence of multicoronary artery disease is a predictor of a worse prognosis in patients who suffer from an acute coronary syndrome (ACS). The objective of this study is to identify all clinical factors that are indicative of multicoronary artery disease in those patients who are suffering from an ACS.
Materials and methods One hundred patients with an ACS, admitted to our CCU, were studied prospectively. Sixty-nine percent presented a non-ST segment elevation myocardial infarction (NSTEMI) and 13% a ST segment elevation myocardial infarction (STEMI). During their hospitalization we registered cardiovascular risk factors; we determined the presence of microalbuminuria (MA) (>3 mg/dl) in a 24-hour urine sample. We also took blood samples in the first 24 hours of their admittance to the CCU for a complete hemogram, levels of total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, glucose, HbAc1, high-sensibility C-reactive protein (HS-CRP) and a follow-up of levels of troponin, CK and CK-MB. All patients were submitted to a coronary angiography in the first 72 hours to give a clinical score to their coronary artery disease (disease of one, two or three arteries).
Results We observed that the antecedents of diabetes mellitus ($P = 0.000$), hyperlipemia ($P = 0.000$), arterial hypertension, ischemic heart disease ($P = 0.000$), ictus ($P = 0.000$), periphery artery disease ($P = 0.000$), chronic renal insufficiency ($P = 0.000$), type of ACS (NSTEMI, $P = 0.000$), development of cardiac failure during hospitalization ($P = 0.000$), and lowering of ST segment on EKG ($P = 0.025$) present a greater extent of coronary artery disease. In the biochemical parameters we found that levels of tropinin, CK and CK-MB were significantly inferior in patients with a more extended coronary artery disease ($P = 0.05$), and high levels of fibrinogen corresponded to a more severe coronary artery disease ($P = 0.03$). The levels of HS-CRP and MA did not evidence differences in the severity of coronary artery disease.
Conclusions By means of numerous clinical factors and biochemical parameters it is possible to determine easily the severity and extension of coronary artery disease of each patient during his/her stay in the CCU.

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Coronary occlusions in first non-ST segment elevation myocardial infarction

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Background Patients with ST segment elevation myocardial infarction usually have a total coronary thrombotic occlusion, and acute reperfusion reduces mortality in this setting. In contrast, patients with non-ST segment elevation myocardial infarction (NSTEMI) represent a more heterogeneous group in which a non-occlusive thrombus has been suggested as a main pathophysiologic mechanism. However, some of these patients may also present a total coronary occlusion but they are not identified as an early reperfusion target.
Methods Our objective was to analyze the TIMI flow status in 120 consecutive patients with their first NSTEMI. The admission 12-lead ECG and coronary angiographies were reviewed and coronary occlusion was defined as TIMI flow <3. Patients with Q waves or ST segment elevation with reperfusion criteria were excluded.
Results Mean age was 64 ± 15 years, 78 males (65%). In 77 (64%) patients the culprit lesion was identified, in 33 (27%) there were >1 possible culprit lesions, and no significant stenosis were found in 10 patients. Fifty-one patients (42%) presented TIMI <3 (30 TIMI 0, eight TIMI 1, 13 TIMI 2) in at least one major coronary artery. Collateral flow was found in 20 (17%). Thirty-two percent of patients presented one-vessel, 35% two-vessel and 22% three-vessel disease. Seventy-four patients were treated with GP IIb/IIIa antagonist and in 74 a PTCA was performed (93%). Two patients died during admission.
Among 77 patients, in which the culprit lesion was identified (44% circumflex [CX], 36% left anterior descending coronary artery [LAD] and 19% right coronary artery [RC]), coronary occlusion was present in 38 (50%) (60% CX, 29% LAD and 10% RC, $P < 0.012$). Patients with culprit coronary occlusions were younger (59.5 ± 13 vs 65 ± 12 years, $P = 0.03$), tended to have a higher incidence of smoking and had a larger myocardial necrosis (CK MB mass 108 ± 99 vs 64 ± 60, $P = 0.02$) than those with nonoccluded culprits.
Conclusion The presence of a culprit coronary occlusion, in nearly one-half of the patients with a first NSTEMI, emphasizes the need to better identify, clinically and electrocardiographically, those that could benefit from early thrombolysis or primary angioplasty.

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Temporal trends in the type of recurrent acute coronary syndrome

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Introduction Different pathogenic mechanisms have been suggested for acute coronary syndrome (ACS) with ST segment elevation (STEMI) or without ST segment elevation (NSTEMI) and for unstable angina (UA). Our objective was to analyze the incidence of different types of ACS in relation to the temporal occurrence, as first or recurrent ACS.
Methods Six hundred and twenty consecutive patients admitted to a cardiology ward due to ACS during 12 months were studied. The ACS were divided into UA, STEMI and NSTEMI. Previous ACS episodes, the clinical profile and angiographic information were recorded.
Results The mean age was 67.4 ± 14 years, 447 (72%) males. The ACS type was 251 (40%) UA, 168 (27%) STEMI and 201 (32%) NSTEMI. In 408 (66%) patients it was the first admission due to ACS, 120 (29%) UA, 146 (36%) STEMI and 142 (35%) NSTEMI. The incidence of STEMI was higher in the first episode than among 213 second episodes (169 [27%] UA, 244 [39%] STEMI and 181 [29%] NSTEMI vs 140 [66%] UA, 20 [9%] STEMI and 53 [25%] NSTEMI, $P < 0.001$). The average time between first and second ACS was 51.9 ± 60 months. Patients with recurrent ACS presented more incidence of male sex (174 [82%] vs 273 [67%], $P < 0.001$), diabetes mellitus (69 [33%] vs 102 [25%], $P =$

0.045), hypercholesterolemia (123 [58%] vs 153 [37%], $P < 0.001$), hypertension (124 [58%] vs 202 [49%], $P = 0.034$) and peripheral arterial disease (40 [20%] vs 31 [8%], $P < 0.001$) than patients without recurrent ACS. Patients with recurrent ACS also presented less ejection fraction (52.8 ± 14 vs 56 ± 13, $P = 0.007$) and less incidence of one-vessel disease (46 [22%] vs 140 [34%], $P = 0.001$).

Conclusion STEMI appears more frequently in a first ACS rather than in a recurrent ACS. Patients who suffer from recurrent ACS demonstrated a worst cardiovascular profile

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L-carnitine deficiency in acute myocardium infarction: prevalence and therapeutic effects of repletion

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Anoxia or ischemia causes an accumulation of long-chain fatty acid esters mainly because of the inhibition of B oxidation. These compounds have deleterious effects on cellular and intracellular membranes. They also inhibit mitochondrial adenine nucleotide translocase inducing inhibition of ATP within the mitochondrial matrix, thus rendering it unavailable for myocardial cell contractility. L-carnitine (L-C) protects against these negative effects by decreasing the acylcoenzyme A (acyl CoA) through formation of the corresponding acyl carnitine that is less harmful and diffuses freely across the cell membrane.

To assess the effects of L-C in preserving the ischemic myocardium following acute myocardium infarction (MI) and in limiting the extent of ischemic damage, we studied 14 patients with acute MI (13 male, one female, mean age 55 years, range 38–72 years). Acute MI was anterior in nine patients, inferior in three patients and combined in two patients. Twelve patients admitted concurrently with acute MI (10 male, one female, mean age 56.5 years) served as the control group. Following admission all patients and controls were subjected to reperfusion therapy in the form of primary PCI (12 patients) and thrombolytic treatment (four patients), while only 12 patients were out of the reperfusion window and were started on conservative medical treatment. Twenty-four hours following therapeutic intervention, the study group received oral L-C in a dose of 1.8 g daily, following a baseline study by M-mode and 2D echocardiography together with rest myocardial perfusion imaging using Tc99 sesta MIBI scintigraphy before and after 1 month of L-C administration. Both imaging techniques were repeated and the serum L-C level was measured in our laboratory and maintained at 20 ± 5 mg/l. Echocardiographic parameters assessed included left ventricular end diastolic diameter, left ventricular end systolic diameter and ejection fraction (EF). Scintigraphically the myocardium was divided into 20 segments to assess RWMA with application of a 0–4 scoring system to obtain the initial ischemic segment (summed score) and the difference between the two summed scores in both studies with an estimated LVEF from gated SPECT techniques. Compared with the control group on conventional therapy, the L-C group exhibited a significantly greater EF from a baseline reading of 57% and 49%, respectively, to 53% and 56.7% after L-C treatment, respectively (i.e. 12% improvement in EF in the L-C group vs 7% decline in the control group). Assessed by scintigraphy the summed score for the L-C group declined from 34.8% to 20.5% following treatment vs 17.5% and 21% for the control group (i.e. 41% improvement in the study group vs 16% worsening in the control group), with a significantly lower myocardium salvage (44.3% in the study group vs –20% in control group).

In conclusion, as a metabolic supplement the early administration of L-C to patients with acute MI provides a significant metabolic support to the ischemic myocardium, helping to limit consequence sequences of ischemic damage and to improve viability.

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Acute pulmonary edema with preserved ejection fraction: clinical and prognostic profile in patients with coronary heart disease

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Objective To investigate the differences in the substrates, triggers and prognosis between patients who suffer an acute pulmonary edema (APE) with preserved ejection fractions and those with depressed ejection fractions.

Methods Prospectively, during a period of 22 months all patients admitted to an emergency unit due to APE were studied. We selected for this analysis patients with documented coronary heart disease. Clinical, echocardiographic, and angiographic characteristics of patients with preserved ejection fractions (EF ≥ 50%, $n = 49$ [27%]) were compared with those of patients with depressed ejection fractions (EF < 50%, $n = 130$ [73%]). A follow-up, after a minimum of 1 year, was conducted in 96% of the cases.

Results Patients with EF ≥ 50% were predominantly female (30 [61%] vs 48 [37%], $P < 0.001$), hypertensive (41 [84%] vs 86 [66%], $P = 0.02$), and had an increased history of atrial fibrillation paroxysms (13 [26%] vs 15 [11%], $P = 0.01$). In the acute phase of pulmonary edema those patients with EF > 50% had more rapid atrial fibrillation (12 [25%] vs 8 [6%], $P < 0.001$) and higher systolic blood pressure levels (171 ± 50 vs 152 ± 39, $P = 0.01$). Between both groups, there were no differences in the extension of coronary disease, the incidence and severity of mitral regurgitation, and the presence of restrictive mitral patterns. Patients with EF ≥ 50% presented a lower 1-year global mortality rate (7 [16%] vs 46 [37%], $P = 0.008$) and a similar incidence of recidivism of APE episodes after discharge (14 [31%] vs 34 [33%], $P = 0.85$).

Conclusions Patients with coronary heart disease who suffer an APE with EF > 50% present different clinical profiles than those with EF < 50% and a lower mortality rate in the follow-up. Surprisingly, however, both groups have the same probability of recurrence of APE.

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Is faster always better?

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Background In the past few years it has been found that primary restoration of the IRA following recent myocardial infarction is the best solution for preserving the left ventricular function.

Objective To assess the importance and benefit of early primary PCI.

Methods Our study included 40 patients (35 males, five females, mean age 50.9 years) with first anterior MI. They were divided into two groups. Group A (20 patients) who had the chance of undergoing primary PCI within a mean 5.4 hours of the start of

chest pain and a door to balloon time of 1.6 hours, and group B (20 patients) with delayed hospitalization (i.e. >12 hours) and neither received thrombolytic nor primary PCI, but were scheduled as routine PCI with mean 20.7 days. The LV function and dimensions were assessed by serial echocardiographic readings measuring left ventricle end diastolic volume (LVEDV), left ventricle end systolic volume (LVESV), ejection fraction (EF), regional wall motion scoring index (RWMI) at 24 hours of admission and after 3 and 6 months. Results are expressed as the mean ± SD, with $P <$ 0.05 considered significant.

Results At 3 months, group A showed significant improvement in RWMI (from 1.9 ± 0.3 to 1.27 ± 0.13) with $P = 0.032$ and there was a nonsignificant increase in the LVEDV value (from 101 ±17.6 to 109 ± 20.1), and it was found that there was a minimal change in the EF value in group A (59.6 ± 3.9% at baseline to 58.5 ± 0.5%). At 6 months, there was no more improvement in the RWMI in both groups but the delayed group showed a marked increase in LVEDV (from 98.3 ± 22.3 at baseline to 138 ± 32.96 after 6 months; i.e. 38.9% increase in volume versus <20% changes in the primary group [from 101 ± 17.6 at baseline to 115 ± 32.14 at 6 months], and $P \leq 0.05$). Whereas the EF% value was nearly preserved in group A (59.6 ± 3.9% at baseline to 59.9 ± 6.81%) there was remarkable deterioration in the EF% value in the delayed group (from 57.1 ± 9.3% at baseline to 51.8 ± 10.8% after 6 months). In spite of early restoration of blood flow in the IRA in group A, and the marked improvement in the RWMI, there were only two patients (10%) who had an increase in the LVEDV >20% of the baseline echo (from 87.5 to 116), with a deterioration in the EF%; they were both diabetic and both hypertensive, with an arrival time to hospital of 7.5 hours and a door to balloon time of 2 hours (i.e. > mean time of group A by 30%).

Conclusion Our data showed that early and immediate revascularization (primary PCI) is superior to delayed, but a few minutes of microcirculation obstructions can still affect left ventricular function in spite of prompt revascularization.

P375

PRONECT: a multiprofessional training course in the care of the acute myocardial infarction

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The Acute Myocardial Infarction (AMI) Recognition and Treatment (PRONECT™) course is a 1-day (3-hour) course originally designed to give doctors greater confidence and ability in the recognition and management of adult patients who have AMI. It may also be suitable for many other groups of health professionals. PRONECT™ was developed using principles common to many advanced life support courses and incorporates aspects of clinical governance, multidisciplinary education and interprofessional working. It incorporates precourse reading, informal and interactive seminars, and role-play during three clinically based scenarios. A novel aspect of PRONECT™ is that participants undertake role interchange during scenarios, thereby facilitating mutual understanding. At all times during the course, participants are encouraged to reflect on their actions and to pay particular attention to detail.

Using initial and final theoretical written tests, after the 3-month courses (36 courses), we assessed the knowledge of aspects of AMI among 900 doctors. The average (±SD) knowledge score was higher for those who had completed a PRONECT™ course, pre-test (545 students) = 23.8 (8.44 ± 1.30) points and post-test (834 students) = 25.3 (9.85 ± 2.12) points ($P < 0.05$). In addition, those in the post-PRONECT™ group also showed significantly better knowledge about AMI (85.6% [714 doctors]) and acquired skills in treatment an AMI. We have demonstrated evidence that doctors' knowledge of AMI can be improved by attending courses such as PRONECT™.

P376

Advanced cardiac life support: comparative analysis between the results of theoretical valuation in two teaching modalities

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The advanced cardiac life support (ACLS) course is a continued medical educational proposal in cardiopulmonary resuscitation and cardiovascular emergencies. The course is part of program of Emergency Cardiovascular Care by the American Heart Association (AHA), which in the United States is one the most successful initiatives of public health of the past decades. The manager of the course and training of this program in Brazil is the National Council of Resuscitation (CNR), which has several regional training centers that develop these activities.

In Minas Gerais the training center was created in 1998, it belongs to the local society of critical care (SOMITI) and administers the courses of ACLS and basic life support. The courses follow the AHA protocol. Every 4 years, the protocol is revised, and the training topics are replaced to become more updated in techniques and didatics as well. In September 2000 at the World Council on Science in Resuscitation, in California, the last review happened, when the guidelines were standardized all over the world and the course of ACLS was remodeled. The changes in the way of teaching the course were basically in the didactics of the program, with the withdrawing of theoretical classes and an increase of the practical classes. It therefore becomes necessary to develop this study with the main goal of evaluating comparatively the results of the students in the theoretical valuations of the course of ACLS provider, between the two teaching modalities.

The study concerns an exploratory study, transversal design, accomplished at the training center of the SOMITI, in Belo Horizonte, MG. The sample was composed of 173 valuations of the pre and post tests, of eight classes of the course, four of each teaching modality. The data are from the data bank of the mentioned training center. The results show about the student profile that most of them were physicians, general practitioners, within 5 years or less of graduation, and act in critical care. About the comparative analysis, there was no difference in the theoretical evaluations between the two teaching modalities, concerning the theoretical knowledge of the students, during the course. We hope that results of this study help in increasing the instructors' knowledge about the students' results on the evaluations, allowing and stimulating considerations about its actions and becoming a reference to the other training and research centers.

P377

Results from inhospital cardiopulmonary resuscitation records in a medical cardiologic ICU

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Introduction New techniques have been used in cardiopulmonary resuscitation (CPR) since the introduction of closed cardiac

massage in 1960. Despite this progress, there has been no significant improvement in survival rates after inhospital cardiac arrest over the past 40 years. In a general hospital, survival rates at discharge, not considering specifically ICU patients, is around 15–20%. Few data are available considering survival in cardiologic care units.

Methods Between April 2004 and December 2004 we recorded and analysed all attempted cardiopulmonary resuscitation in a medical ICU of a teaching cardiologic hospital. The patients were 64 ± 20 years old, 44 (62.8%) male and 26 (37.2%) female. Diagnosis at admission in ICU were: cardiogenic and/or septic shock 37.2%, heart failure (NYHA IV) 20%, acute coronary syndrome 21.4%, acute respiratory failure 10%, others 11.4%. Associated diseases: acute renal failure 68.5%, hypertension 60%, diabetes mellitus 37.2%, COPD 10%, infection 91.5%. Using an Utestein-based template, data were collected immediately after each resuscitation, by physicians who have performed CPR. They were previously certified in acute cardiac life support (ACLS).

Results Seventy cardiopulmonary arrests were recorded in 50 patients. Of these, 49% returned to spontaneous circulation and 4% had hospital discharge. Twelve patients had more than one event. First pulseless rhythm was divided as follows: VF/VT (14.08%), asystole (19.7%), PEA (66.22%). Predictive factors of return to spontaneous circulation in univariate analysis were: time from ICU admission to cardiopulmonary arrest ≤7 days ($P = 0.03$) age <75 years ($P = 0.003$), time of CPR <18 min ($P = 0.0001$). In multivariate analysis, only the time from admission to the ICU to cardiopulmonary arrest ≤7 days was predictive of a return to spontaneous circulation ($P = 0.015$, OR 1.19, CI 95% 0.6–5.9).

Conclusion Survival after CPR in cardiac patients is poor, Considering our population, it is lower than that observed in general hospital patients. These data could help physicians in attempting resuscitation, patients and families in making end-of-life decisions.

P378

Pediatric cardiopulmonary resuscitation in a cardiology hospital

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Background Numerous reports document the efficacy of pediatric inhospital cardiopulmonary resuscitation (CPR). There are few data about pediatric patients with heart diseases.

Methods All inhospital CPRs in children during 12 months at a university hospital of cardiology, were described and evaluated using Utstein reporting guidelines. CPR was defined as chest compression and assisted ventilation or defibrillation provided because of cardiac arrest or severe bradycardia with poor perfusion.

Results A total of 110 attempted resuscitations were performed in 55 children. From these patients 72.2% had return to spontaneous circulation and 21.4% were discharged alive. Most of the children had congenital heart disease (74.5%). Bradycardia with poor perfusion were present in 55.4% as an initial rhythm of the 110 episodes, asystole in 18.2%, electric activity without pulse in 15.4% and ventricular fibrillation or tachycardia without pulse in 10.90%.The most common precipitating causes were hypotension (22.8%), arrythmias (17.3%), metabolic disturbance (17.3%) and hypoxemia (14.2%). Univariate predictive factors correlating with hospital discharge were hypoxemia as the precipitating cause of arrest, duration of resuscitation <10 min and single cardiac arrest. In addition administration of bicarbonate, three or more doses of epinephrine during resuscitation, vasoactive drugs and mechanical ventilation at moment of cardiac arrest were negatively associated with survival. Multivariate stepwise logistic regression analysis identified independent association of survival with duration of resuscitation <10 min (OR 36.5, 95% CI 3.6–366.3) and single arrest (OR 17.1, 95% CI 1.6–181.3).

Conclusion Survival to hospital discharge and predictors of children with heart diseases and cardiac arrest are similar to patients in general pediatric hospitals.

P379

Unidirectional blood flow can be naturally generated by changing intravascular pressure: an extracorporeal model for elucidating the blood flow mechanism in CPR

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Objectives There are two mechanisms for the generation of forward blood flow during extrathoracic cardiac compression for cardiac arrest; direct cardiac compression and thoracic pump. We postulate that the difference of vascular resistance from the arterial to peripheral capillary in tandem and the existence of competent venous valves make it possible for blood to flow forwardly by a simple change of intravascular pressure in a cardiac arrest model.

Methods A mongrel dog was anesthetized with i.v. sodium pentobarbital. The dog was mechanically ventilated. The right femoral artery was cannulated. A double lumen catheter was introduced via the external jugular vein. The cardiac rhythm and heart rate were monitored. Midline thoracotomy was performed. After the infusion of heparin 300 U/kg, KCl 20 mEq was injected intravenously to induce cardiac arrest. A Y-shaped extracorporeal circuit was primed with heparinized normal saline beforehand. Each end of the two branches of the circuit has a 3/8-inch connector, respectively, and the other end was connected with a 50 cm^3 syringe. A connector was introduced at the junction of the SVC and IVC via the right atrium. The aorta was transected above the aortic valve and another 3/8-inch connector was inserted directly into the ascending aorta. Indocyanine green dye was injected via the connector of the right atrium.

Results At the beginning of syringe resuscitation, aortic and vena caval blood was drained slightly during the suction phase and the blood moved to in both directions during the push phase; however, the dye transferred gradually from the vena cavae to arterial side while showing a concomitant to-and-fro movement of its own with the repeated piston movement.

Conclusion We observed that forward blood movement from the aorta to peripheral artery occurred without cardiac valves while changing the intravascular pressure using a syringe pump. This proves that an intravascular pressure change generated by direct cardiac compression or an intrathoracic pump during external cardiac compression can produce systemic blood flow probably both by the innate vascular resistance difference and by the intravenous valvular patency, irrespective of cardiac valve motion.

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P380

Impact of bystander cardiopulmonary and cerebral resuscitation in the prehospital setting on survival rates in the short and long term

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Background The results of CPCR attempts after cardiac arrest (CA) are very poor because of the irreversible brain damage, myocardium damage and other organ damage that may occur within 4 min of no blood flow. Early initiation of CPCR by a bystander is crucial, in order to obtain a low blood flow up to the arrival of the mobile intensive care unit (MICU).
Objective To evaluate the impact of resuscitation by a bystander on the short-term outcome (STO) and long-term outcome (LTO).
Methods A consecutive and prospective study over a period of 5.5 years (1 January 1999–9 July 2004) was conducted. The patients were treated by the MICU of the Academic Hospital of the Vrije Universiteit Brussel (AZ-VUB) onsite and later on in the Emergency Department (ED).
Results In patients who were initially resuscitated by a bystander before arrival of the MICU, ROSC was achieved in 66 (35.29%) cases, while 114 (60.96%) patients were declared dead on the scene. CPCR was continued during transport to the ED in seven (3.74%) patients. When CPCR was initiated by the MICU, ROSC was achieved in 207 (13.81) patients, and 1278 (85.26%) did not achieved ROSC. CPCR was continued during transport to the ED for 14 (0.93%) patients.
One year after resuscitation, 66 (44.07%) of the patients that were initially resuscitated by a bystander and thereby resumed ROSC were still alive, and 33 (55.93%) were declared dead. Out of the patients that were initially resuscitated by the MICU or the first tier and achieved a ROSC, 20 (15.50%) were still alive 1 year after the event and 109 (84.50%) were dead.
Conclusions Bystander CPCR plays a crucial role in the chain of survival. Compared with patients that were initially not resuscitated by a bystander, significant differences in the STO and LTO are observed.

P381

Outcome of cardiopulmonary resuscitation in the ICU in a university hospital

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Introduction Cardiac arrest is the third leading cause of coma, second only to trauma and drug overdose. Over the past two decades several publications have reported the outcome of cardiopulmonary resuscitation (CPR) for inhospital cardiac arrest. Only a sparse amount of data is available concerning the initial CPR success rates and long-term survival in adult ICUs from Germany. Initial CPR success rates range from 16.8% to 44% and long-term survival to discharge from hospital ranges from 3.1% to 16.5%. Although the initial successful resuscitation rate in ICU patients may be high, long-term and hospital discharge rates have been reported to be unsatisfactory.
Objective To evaluate the demographic characteristics of patients who suffered cardiac arrest in our ICUs as well as to identify those factors influencing outcome after resuscitation following cardiac arrest.
Methods We reviewed the records of all patients who underwent CPR in our ICUs at the Georg-August University Hospital Göettingen, Germany from January 1999 to December 2003. The GISI database was used to search for all admissions to these ICUs, and records of patients who had CPR during their stay in the ICUs were retrieved and studied.
Results During the study period, 169 patients underwent CPR. Eighty of the 169 patients with confirmed inhospital arrest survived to hospital discharge, giving a survival to hospital discharge rate of 47.3%. The initial monitored rhythm recorded at the time of arrest was asystole in 99 (58.6%) patients. Ventricular tachycardia/fibrillation was recorded in 59 (34.9%) and pulseless electrical activity in seven (4.1%) patients. Forty-six (54.8% of the survivors), 31 (36.9%) and five (6.0%) patients with initial recorded asystole, VT/VF and PEA rhythms, respectively, survived to hospital discharge. Of the 80 patients that survived to hospital discharge 75 (93.8%) achieved good cerebral recovery (CPC 1 or CPC 2) and were alert and fully oriented on discharge; four patients (5.0%) were severely disabled (CPC 3), while one (1.2%) remained unconscious and was reported dead 5 days after discharge to another local hospital. Illness severity as assessed by the SAPS II score on admission was 38.8 ± 16.0. None of our patients with SAPS II score >40 24 hours after CPR survived to be discharged from the ICU.
Conclusion Our study showed that nearly half the patients that had cardiac arrest in our hospital ICUs had a favourable outcome despite initial rhythms that are traditionally associated with a poor outcome. This confirms that good results are achievable in these groups of patients. The overall survival (47.3%) from CPR is close to that reported internationally. Advancing age, coexisting diseases and early initiation of the resuscitation protocol had significant effects on the outcome of CPR as observed in our study.

P382

Recent circumstances of out-of-hospital CPA in Yokohama, a typical Japanese urban city

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Introduction In Japan, the out-of-hospital emergency medical service (EMS) system has been established by the ambulance service and an emergency life-saving technician (ELST) belonging to the fire department, and the inhospital Emergency Department has been supporting this system. The licence of ELST was established in 1991 and has been enlarging their activity; defibrillation, infusion of Ringer solution, insertion of a laryngeal mask, EGTA, and laryngeal tube. Moreover, now some of them who have received prearranged education can be permitted to perform endotracheal intubation and infusion therapy of epinephrine. Recently television stations frequently deal with ELST, resulting in enlightenment of many citizens on the importance of immediate CPR and defibrillation. In this study, we examined recent circumstances of out-of-hospital CPA in a Japanese typical urban city.
Methods Patients' records of our Emergency Department were reviewed for the past year. In our city, Yokohama (3,700,000 people), the CPA patient is transferred to the nearest emergency department of 11 hospitals, which are selected because of their adequate ability of CPR and cerebral resuscitation for CPA patients. In our department, we usually perform echocardiography and abdominal sonography, chest X-ray examination, blood examination including troponin I or T, and cerebral plane CT or chest CT to determine cause of CPA and to treat this pathological condition.
Results In our Emergency Department, we dealt with 250 CPA patients in the past year, 95 of whom were cardiac aetiology and 155 of whom were noncardiac aetiology. Eleven were SAH and 14 were acute aortic dissection diagnosed by CT or ultrasonography.

In cardiac aetiology patients, 31 were witnessed. Six of them were witnessed by an ELST during transfer and 25 were witnessed by a layperson; 16 were witnessed by patients' families, three by patients' friends, and four by a passenger. Seventeen were witnessed in the patient's home, 13 of whom were witnessed in the patient's private room, two were in the bathroom, and one in the lavatory. Only eight of 25 witnessed CPA patients underwent bystander CPR, who underwent bystander CPR mainly in the patients' homes by the patients' families.
Conclusion In Japan, we often encountered CPA patients with noncardiac aetiology, including SAH or acute aortic dissection. CPA patients were witnessed mainly in their home, particularly in their private room, bathroom, and lavatory. However, only eight CPA patients underwent bystander CPR. We should enlighten citizens (potential patients' families) on the importance of immediate CPR to save CPA patients.

P383

Implementation of the new European Resuscitation Council guidelines regarding epinephrine administration during out-of-hospital cardiopulmonary and cerebral resuscitation, and its effect on the outcome of the patients

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Background Epinephrine has been used in cardiopulmonary and cerebral resuscitation (CPCR) procedures since the end of the nineteenth century. Since the 1960s an epinephrine dose of 1 mg up to 5 mg, every 5 min, was recommended. According to the current international guidelines from the European Resuscitation Council (ERC), only 1 mg every 3–5 min should be administered and hereby discourage administration of high doses of epinephrine.
Objective To investigate the implementation of the new guidelines for CPCR, in the out-of-hospital setting, regarding the administration of the standard dose of 1 mg epinephrine during resuscitation, and its influence on the outcome of the patients.
Methods A consecutive and prospective study over a period of 5.5 years (1 January 1999–9 July 2004) was conducted. The patients were treated by the MICU of the Academic Hospital of the Vrije Universiteit Brussel (AZ-VUB) onsite and later on in the Emergency Department (ED).
Results Correct implementation of the new ERC guidelines regarding epinephrine administration during resuscitation was seen in 564 (58.39%) of 966 patients. In 402 (41.61%) patients an excessive dose of epinephrine (EDE), relative to CPCR duration, was given. From those 564 (58.39%) patients where the guidelines were correctly implemented, 180 (31.91%) achieved ROSC, 337 (59.75%) died on the scene, and 47 (8.33%) were still being resuscitated during their transport to the ED. From the 402 (41.61%) patients where the guidelines were not properly implemented, 90 (22.39%) patients achieved ROSC, while 290 (72.14%) patients were declared dead. In 22 (5.47%) patients, CPCR was continued up to the ED. Evaluation of the LTO in patients that received a guideline-respected dose of epinephrine revealed that: 93 (58.49%) patients were still alive 1 year after resuscitation, and 32 (41.51%) were dead. For those whom received an EDE, relative to CPCR duration, 180 (60.00%) survived and 32 (40.00%) died 1 year after resuscitation.
Conclusions There is a lack of adherence to the current guidelines regarding epinephrine administration during CPCR. Moreover, 1 mg epinephrine each 3–5 min seems to increase the percentage of ROSC, but unfortunately this beneficial effect disappears 1 year after the insult.

P384

Predicting failure to survive cardiopulmonary resuscitation in intensive care: evaluation of two morbidity scores

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Introduction Major advances have been made in providing prompt cardiopulmonary resuscitation (CPR) to cardiac arrest patients within the hospital. As patients undergoing cardiac surgery become older and sicker with concomitant co-morbidities, the quality of immediate and long-term postoperative care as well as resuscitation are likely to become increasingly important. Inappropriate and unsuccessful resuscitation of these patients is associated with a large expenditure of health care resources. CPR is a time-consuming and resource-consuming procedure that was never originally recommended for all patients. Gillon [1] described CPR as 'violent, painful and undignified'. Therefore, the goal of CPR should be to 'reverse premature death not prolong inevitable death' [2].
Objective The aim of this study is to evaluate the usefulness of two morbidity scores – prognosis after resuscitation score (PAR) and modified PAM index (MPI) – in predicting failure to survive following cardiopulmonary resuscitation (CPR) in our ICU.
Methods We reviewed the records of postoperative cardiac adult patients who underwent CPR in our ICU from April 1999 to March 2003 at the Georg-August University Hospital, Göttingen, Germany.
Results During the study period, 169 patients had cardiac arrest for which CPR was instituted. Eighty (53.7%) survived to discharge from the ICU and 71 (47.7%) survived to be discharged from the hospital. The mean time interval until ROSC was re-established and the duration of CPR differed significantly in survivors and nonsurvivors ($P = 0.008$ and $P = 0.0002$, respectively). The PAR score identified 77 patients with a score >7 and the MPI score identified 74 patients with a score >7 none of whom survived to be discharged from the ICU. The sensitivities of the PAR score and MPI for predicting failure to survive following CPR were 86.5% and 83.1%, respectively. The PAR and MPI scores did not incorrectly identify a patient as a nonsurvivor who subsequently survived.
Conclusion The PAR and MPI scores are useful in identifying patients in whom CPR may be unsuccessful and could additionally provide useful information to physicians and patients involved with decisions about do-not-attempt-resuscitation orders.
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P385

Invasive versus conservative waiting strategy in complicated acute pediatric leukemia patients

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Introduction The outcome for children with acute lymphoblastic leukemia (ALL) has improved dramatically with current therapy

resulting in an event-free survival exceeding 75% for most patients over the past four decades. Modern child leukemia treatment requires an interdisciplinary cooperation – PICU interventions demand serious pathological cases with immediate life exposure originated from long-term haematological treatment: (1) patient's clinical status impairment related to aggressive cytostatic therapy (febrile neutropenia, sepsis, pneumonia, respiratory failure, ARDS, hemodynamic instability, MODS, MOF, life-threatening bleeding, neurological alterations in the course of toxic encephalopathy, etc.), (2) postanesthesia intensive care for complications due to invasive procedures (CVC implantations) or vital sign decompensation after anaesthesia.

Objective To assess the benefit of early invasive (transfer from standard hematology to PICU, respiratory and circulation support, invasive arterial blood pressure and central venous pressure [CVP] measurement, continuous hemodynamic monitoring [PICO, NICO], permanent urinary catheter and nasogastric tube insertion) versus a conservative waiting strategy without invasive procedures when complications appear during hematology leukemia treatment.

Design Retrospective analysis, $n = 29$ patients with acute leukaemia admitted to the PICU because of life-threatening complications during their hematological treatment, within the years 2000–2004.

Patients and methods Critically ill patients admitted to the PICU. Twenty-nine children with leukemia, 20 × ALL, 8 × acute myeloid leukaemia, 1 × chronic myeloid leukaemia, average age 8.7 years (from 5 months to 18 years), 21 boys, eight girls. All patients were hospitalized at the PICU 45 times altogether within the period under consideration (2000–2004) regarding life-threatening events: postanesthesia care (complicated CVC implantation – haemothorax, pneumothorax), febrile neutropenia, sepsis, septic shock, respiratory failure, hemodynamic instability, acute neurological deterioration.

Results Twenty-two children (76%) from 29 patients with leukemia admitted to the PICU survived. Seven children (24%) died (6 × MOF and septic shock, 1 × fatal intracerebral hemorrhage) – in three of them (42% mortality rate) it was hesitated for invasive treatment initiation (conservative waiting strategy). The authors detail the monitored parameters, clinical patient's status (PRISM), laboratory findings, and at the conclusion illustrate the casual report of a 15-year-old boy with ALL, MODS and septic shock with good outcome thanks to early invasive treatment and adequate therapy (mechanical ventilation, invasive arterial blood pressure monitoring, CVP monitoring, continuous cardiac output measurement from the PICO).

Conclusion Although pediatric leukemic patients with severe sepsis remain at very high risk, recent findings suggest that their outcomes may be better, as previously reported, using aggressive and early ICU interventions.

P386

Assessing the poisoning cases being monitored in the ICU in terms of causes and mortality

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Introduction The Medline investigations carried out in recent years demonstrate that morbidity and mortality caused by acute poisoning are higher in elderly patients, suicidal attempts and multiple drug intakes [1].

Method We retrospectively studied a total of 121 poisoning cases that were monitored in our ICU between January 2002 and July 2005 in terms of causes and mortality.

Results Of the subjects, 55 were poisoned by organophosphates, 18 by multiple drugs, 18 by tricyclic antidepressant (TCA), and 11 by methanol, four by foods and 15 by various types of poisons. In dead patients the mean age, APACHE II score, and times of mechanic ventilation (TMV) were higher compared with the discharged group and their Glasgow Coma Scores (GCS) at admittance were found significantly reduced from those discharged (Table 1). While 56 patients were directly admitted to our hospital, 65 patients were referred. Although there was no statistical significance in APACHE II scores of those who were referred, their TMV and length of stay in the ICU were found statistically significant. It was determined that the rate of female patients who subjected to multiple medicines and TCA poisoning was higher and they were younger than other groups. Mortality was 21.8% in the organophosphate group, 5.6% in the multiple poisoning group, 0% in the TCA group and 54.5% in the methanol group. APACHE II scores were found significantly higher in the methanol group compared with the other four groups. A considerably prolonged TMV was detected in the organophosphate group than in the multiple drug poisoning and TCA groups. Three of the patients in the multiple drug poisoning group were those who received antidepressive treatment previously. Four of the patients in the organophosphate group had received cardiopulmonary resuscitation where they transferred and three of these patients were lost during observation in our ICU. Three of the patients in the organic phosphate group accidentally took poison (one through inhalation and two through foods) and all other poisoning cases were intentional suicide attempts except the methanol and food poisoning cases.

Table 1 (abstract P386)

	Exitus	Alive	*P* value
Age	38.15 ± 14.01	31.25 ±14.66	0.028
APACHE II score	21.06 ± 10.96	10.54 ±6.51	0.000
Admittance GCS	6.30 ± 4.11	10.64 ±4.09	0.000
TMV	6.37 ± 6.12	2.75 ± 5.0	0.000

Discussion It was established in the epidemiology study of two acute poisoning cases reported in Spain that the suicide attempts related to depressive disorders were predominant in women and the mortality was high despite advanced life support and antidote therapy being provided [2]. In our study, old age, lower GCS at admittance and prolonged admittance time were considered factors affecting mortality in terms of overall poisoning. Interestingly, the majority of the patients in the multiple and TCA poisonings with suicidal intention were younger women who received antidepressive treatment.

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P387

Brazilian ITO model in Latin America: Medical Training and Simulation Laboratory Center at the Heart Institute (InCor)

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This abstract presents experience of the Educational Centre of the MTSL InCor Sao Paulo in training of the various profiles of medical personnel (medical doctors and medical technicians) that are employed in the emergency services of the prehospital and hospital type in Brazil. A period of the last year (2000) when the

Educational Centre was restructured, becoming one of the most active services in the medical sector of the MTSL in Brazil, has been emphasised in particular. The Educational Centre was participating in a number of international projects related to education. Fifty-five courses of the various levels and with different programs – BLS, ALS, ACLS, ACLS-instructor course, EMT-course, EMT-advanced course – were carried out in the mentioned period. Seven thousand six hundred and ten hours of theoretical teaching and practical training were provided for the 3230 candidates who successfully completed training in various programs. First-aid training for the civilian population was also conducted. Two first-aid courses were carried out and successfully achieved by 64 candidates. In this way, 19 hours of theoretical teaching and practical training were realised. In order to make first-aid training popular, 160 children from different institutions were also introduced to CPR-school and first-aid principles. It has been pointed out that a well-equipped and trained team for urgent medical intervention with necessary teamwork is a crucial factor for the successful treatment of an emergency that involves a patient in a life-threatening situation.

P388

Impact of an accreditation process in a surgical ICU

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Background Accreditation has been generally viewed as a desirable process to establish standards and work toward achieving higher quality medical care. The worldwide emphasis on accountability has stimulated dramatic growth in internal quality management programs, external benchmarking with comparative data and accreditation for healthcare facilities. There are few published data about the effects of an accreditation process on ICU performance. The aim of this study was to describe the effects of an accreditation process in a surgical ICU.
Methods In this retrospective cohort study we considered two different periods, the first one (October 2003–September 2004) as the pre-accreditation (PA) period and the second one (October 2004–September 2005) as the accreditation period (A). We obtained demographic data, APACHE II score, ICU-mortality rate, LOS, ICU-acquired infection rate, invasive procedure-related complication rate and number of training hours per staff member. We compared these variables between the PA and A periods using the Wilcoxon test.

Table 1 (abstract P388)

	Mean	SD	*P* value
APACHE II score – PA	7.09	1.48	0.017
APACHE II score – A	8.29	1.18	
LOS (days) – PA	2.51	0.43	0.002
LOS (days) – A	3.89	1.09	
Mortality (%) – PA	6	5	0.158
Mortality (%) – A	11	7	
Infection (%) – PA	2	2	0.091
Infection (%) – A	4	3	
IPCR (%) – PA	1	1	0.161
IPCR (%) – A	2	2	
TH (hours) – PA	0.46	0.25	0.086
TH (hours) – A	2.22	1.92	

Results We included 784 patients in the study: 426 in the PA period and 358 in the A period. As shown in Table 1 although we observed a statistical significant increase in APACHE II score and LOS we were unable to demonstrate any difference in the other variables between the periods. Also we could observe a trend toward increasing training hours per staff member as a possible benefit from an accreditation process.
Conclusions Based on these preliminary data we were unable to demonstrate any benefit from the implementation of accreditation standards in ICU routine daily practice. A trend toward increasing training hours could be observed. Whether an accreditation process has a positive impact on ICU performance is a question that remains to be answered.

P389

Monitoring a high-cost drug in critical care units

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Introduction Recombinant human activated protein C (APC) (Drotrecogin-alfa activated) was licensed for the treatment of severe sepsis following the large randomised controlled trial, PROWESS [1]. Subgroup analysis of PROWESS and the subsequent ADDRESS [2] study have shown that only the sickest patients (at least two organ failures or APACHE II score >25) benefit from APC. Treatment is associated with an increased risk of serious bleeding, and so the use of APC is contraindicated in patients at high risk for this complication. The cost of using APC is high, both financially and in terms of possible adverse effects, thus appropriate patient selection is crucial. Upon European Licensing in 2002, the South East London Critical Care Network (SELCCN) successfully bid for funding to use APC on the understanding that the hospital Trusts would provide regular usage reports.
Objective To collect post-licence surveillance data of APC use in severe sepsis across a network of six ICUs (SELCCN). To certify adherence to agreed prescribing guidelines, and to monitor outcome (mortality), adverse events and financial data, thus ensuring best clinical practice and continued funding.
Methods Guidelines for APC were agreed by the SELCCN. A reporting tool and supporting database reflecting these guidelines was designed and implemented to prospectively collect clinical and financial data. The collated data were reported monthly and progress was discussed at local and network meetings.
Results Data were collected and analysed for 249 patients from November 2002 to June 2005. A total of 87% of patients met the agreed criteria for APC with an average expenditure of €7658 ± €3451 per patient. During treatment, 30 haemorrhagic events were cited with four reported as serious. Of those receiving APC, 126 (51%) where discharged home, 85 (34%) died in the ICU and nine (4%) died as post-ICU patients. Forty per cent of patients with ≥4 organs in failure at the time of APC administration were discharged home. Funding was retrieved in at least one site for all patients who received APC.
Discussion These results demonstrate that it is possible to develop and ensure excellent adherence to consensus guidelines for the use of a high-cost, life-saving drug. A simple reporting tool allowed easy monitoring of selection criteria, patient outcome, and adverse events across the critical care network. The data show favourable patient outcome especially in those with ≥4 organs in failure (40% surviving) when compared with the average survival (19.4%) of a similar group of patients as measured in 91 ICUs

throughout the UK [3]. This process of ongoing monitoring of essential data, including cost, ensured a continuous funding stream for this effective therapy and is the first report of such a process in critical illness.

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P390

Critical care costs per patient-day are inversely related to the annual admission rate

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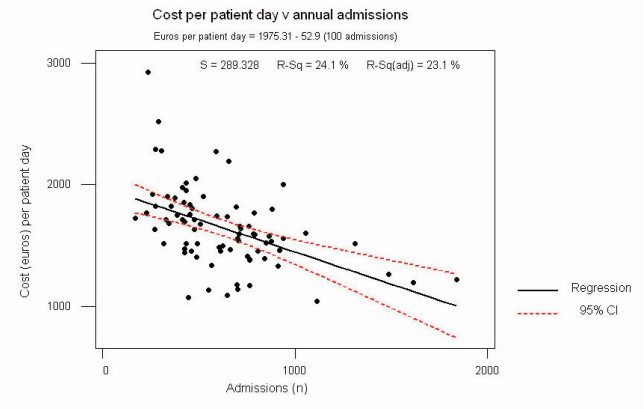
Introduction The Critical Care National Cost Block Programme collects annual cost data for staff, consumables, and clinical support services. We postulated that larger critical care units reduce the overall running costs (independent of capital expenditure) compared with their smaller counterparts.

Methods Data were analysed for the financial year 2003–2004 relating to all 80 critical care units in the Cost Block programme. Regression analysis was performed comparing the cost per patient-day with the unit size. Following this, stepwise regression analysis was used to assess the individual components of cost to identify the elements (medical, nursing, consumables and other) most strongly related to admission number.

Results Figure 1 shows the data relating ICU size (defined as number of admissions per year) with average costs per patient per day. The daily costs per patient were reduced by €53 for every 100 admissions increment. Analysed for the individual components that contribute to the daily cost per patient, we found that nursing costs (€22.3 per 100 admissions increment, $P = 0.019$) and consumables (€14 per 100 admissions increment, $P = 0.003$) had the strongest impact. Medical and other costs had lower impacts (€8.9 and €7.5, respectively).

Conclusion The cost per patient per day is higher for smaller units than that for larger units. There appears to be an economy of scale for larger critical care units relating mainly to a reduction in daily nursing and consumable costs. A previous study examining the data for the financial year 2000–2001 also suggested that there was an association between the cost per patient day and the ICU size [1].

Figure 1 (abstract P390)



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P391

Bedside teaching in intensive care: effect on attitudes and skills of fourth-year medical students

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Introduction A shortfall of intensivists in the future is expected. Therefore increasing interest early in the medical training could increase the number of ICU trainees. In addition many medical students have no clear image of what intensive care is all about. Although an orientation in the ICU is part of many medical school curricula worldwide, little is known on the impact of these programs.

Materials and methods Fourth-year medical students attended a 2-hour bedside teaching course in intensive care where observation, hemodynamics and organ support were the main topics. Nurses and medical staff participated actively in the course. All students ($n = 193$, 135 females) attended the program and 192 students completed pre-course and post-course 5-point Likert questionnaires (scale 1 = strongly disagree to 5 = strongly agree). Data are presented as the mean ± SD. The Mann–Whitney test was used to compare responses before and after the teaching program. $P < 0.05$ was considered statistically significant.

Results Overall attitudes towards the ICU as well as self-reported skills improved significantly following the course. Interest to qualify as an intensivist increased significantly ($P = 0.002$). Also fewer students pictured the ICU as a typical drama-series ICU following the course ($P < 0.001$). In addition the students felt they could better describe the organization and structure of the ICU team following the course (2.9 ± 0.8 vs 4.0 ± 0.6, $P < 0.001$). The self-reported ability to identify and qualify organ failure and hemodynamics improved significantly, i.e. the ability to calculate the mean arterial pressure increased from 2.9 ± 1.1 to 4.3 ± 0.9 ($P < 0.001$). Students reported no emotional/coping problems associated with the visit to severely ill patients. One medical student was involved in acute circulatory arrest of a patient. The majority of the nurses were positive on the involvement in this training program and also the burden to their day-to-day clinical work in relation to the experienced positive effect was limited.

Conclusion A 2-hour ICU orientation in the undergraduate curriculum based on adult learning principles was successful in increasing interest for the profession, improving understanding of the ICU organization as well as improving the ability to recognize vital organ functions and principles of the monitoring of critically ill patients.

P392

Benchmarking procedural competence in paediatric intensive care using cumulative sum analysis: intravenous access, arterial lines and intubation

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Objectives There are no benchmarks for assessing competence for paediatric intensive care (PICU) procedures such as peripheral (PVL), central venous (CVL), and arterial cannulation (ART) and intubation. We evaluated PICU trainee competence using the cumulative sum analysis method (CUSUM) against data published for elective anaesthetic procedures in adults [1,2]. Our objective was thus to document whether the suggested procedural failure rates for adults are applicable in PICU and the number of cases required to achieve procedural competence.

Method We prospectively recorded outcome for procedures (PVL, CVL, ART, intubation) performed in a tertiary PICU by residents ($n = 6$) and fellows ($n = 10$) over a 4-month period. A successful procedure was defined as: PVL = cannulation with two or less punctures at a single site, CVL = cannulation with two or less punctures at a single site in 10 min, ART = cannulation with two or less punctures at one site within 10 min, and intubation = endotracheal tube entry into the trachea on the first attempt with two or less laryngoscopy attempts. Change in site or operator was recorded as failure. Ultrasound was used in 8% of CVL insertions.

The CUSUM method calculates a weighted score for each procedure using predefined acceptable (p0) and unacceptable failure rates (p1). Success is weighted as $s = [\log(1 - p1) / (1 - p0)] / \{[\log(p1 / p0)] + [\log(1 - p1) / (1 - p0)]\}$ and failure as $(1 - s)$. The cumulative sums of these values are plotted on a time chart with an upward slope indicating failure $(1 - s)$ and downward slope success(es) for each group (residents and fellows). Competence is defined as the point where the downward slope crosses the lower control limit using an α and β error of 0.1.

Results Eight hundred and seventy-six procedures were performed on 561 patients (mechanical ventilation 82%, inotropes 27%.) Median (IQR) age 6.3 months (1.1–34), weight 6.4 kg (3.3–13.6) and PIM2 score 2.9 (1.3–7.2). Thirty-four per cent of procedures were performed by residents and 66% by fellows. The number of procedures required to achieve competence for each group is shown in Table 1, with residents not achieving competence for any procedures except PVL insertion. Fellows failed as a group to gain competence for CVL insertion. Figure 1 contains the CUSUM plots for ART insertion by fellows and residents (group plot).

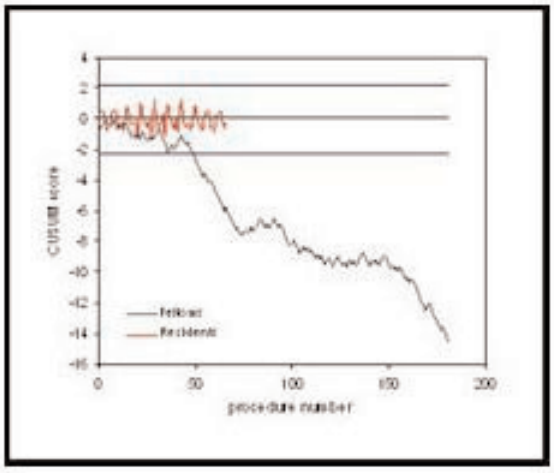
Conclusion The suggested procedural failure rates for adults (PVL 20%, CVL 5%, ART 20% and intubation 5%) are applicable in the PICU setting. Competence was achieved by PICU fellows within 27–36 procedures, except for central line insertion that may be improved by routine use of ultrasound guidance. A 4-month period does not provide PICU residents with sufficient exposure to gain competence for the central venous and arterial cannulation and intubations.

Table 1 (abstract P392)

Procedure	Operator	p1	p0	Failure/ total cases	NFC
PVL [1]	Resident	20%	40%	113/222 (50%)	76
PVL [1]	Fellow	20%	40%	97/241 (40%)	27
CVL [2]	Resident	5%	15%	3/7 (43%)	Failed
CVL [2]	Fellow	5%	15%	35/88 (40%)	Failed
ART [1]	Resident	20%	40%	37/67 (55%)	Failed
ART [1]	Fellow	20%	40%	76/182 (41%)	41
Intubation	Resident	5%	15%	3/16 (19%)	Failed
Intubation	Fellow	5%	15%	15/56 (8.9%)	27

NFC, number for competence.

Figure 1 (abstract P392)



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P393

Iatrogenic complications in the ICU: prospective study during 17 months

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Critical Care 2006, **10(Suppl 1):**P393 (doi: 10.1186/cc4740)

Introduction Iatrogenic complications (IC) are defined as an adverse event that occurs independently of the underlying disease. In fact, in the USA, IC is noted in 4% of hospitalised patients leading to death in 14% of cases.

Objectives To evaluate the incidence and types of IC in ICU, their repercussions on morbidity and mortality rates, and to identify the associated factors of risk.

Materials and methods A prospective study, performed between February 2002 and June 2003. All episodes of IC are recorded. The type, the cause and the repercussions are noted. IC was divided, according to their consequences, into categories: major, moderate and minor.

Results Two hundred and forty-three patients are enrolled with mean age 45 ± 19 years, sex ratio = 1.8, SAPS II = 34 ± 18, LOD = 6.5 ± 3.75, OMEGA score = 126 ± 228. Fifty-four per cent needed mechanical ventilation. Two hundred and fifty episodes of IC occurred in 91 patients. Incidence was 37.5% and a density of incidence of 231/1000-day stay in the ICU. Cardiovascular complications are the most frequent ones, including mainly hypotension and arrhythmia (40.8%). The incidence was judged

major in 67 cases. Risk factors retained are age under 60 years, prognosis indices (SAPS II, APACHE II) and length of stay. The mortality is 45% in the event of IC and 28.75% without this.
Discussion IC are frequent, they are induced by the development of invasive techniques of investigation and monitoring, human error and a high or excessive nursing workload. Their pathogenesis is related to the acute disease and the characteristics of the ICU.
Conclusion To decrease IC incidence, human and material resources must be optimised and the indications of invasive investigations and monitoring must be more rigorous.

P394

Iatrogenic complications in ICU patients

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Introduction and objective Iatrogenic complications in the ICU are inevitable and often lead to medical emergencies. They may affect the clinical course of patients by increasing morbidity and mortality. The aim of this study was to evaluate frequency, types, severity and morbidity of complications associated with medical and nursing practice, to determine possible risk factors and to suggest efficient protective measures for reducing the risk.
Patients and methods Eighty-four adult patients were included in the study over a 12-month period. An iatrogenic complication was defined as an adverse effect that was not associated with the patients' underlying disease. Two ICU physicians who assessed all complications monitored patients during their entire hospitalization and a 6-month follow-up. Drug interactions and their adverse effects were excluded.
Results Ninety-nine iatrogenic complications were recorded in 42 of the 84 admissions. Although 58 (39%) complications were considered as major, none was directly associated with the death of a patient. Major complications included respiratory distress, severe hypotension, pneumothorax, hemothorax, cardiac arrest and bacteremia. Eighty-five per cent of the complications were due to human errors while misused and default material were considered the cause of the rest. Patients with a higher APACHE II score experienced more complications (25 ± 5.9, $P = 0.027$). The subgroup of patients admitted to the ICU with more than two organ failures had also a higher risk for an iatrogenic complication ($P = 0.045$). The age of the patient, excessive nursing workload as well as the number of complications were the most important prognostic factors ($P = 0.022$, $P = 0.015$, $P = 0.056$, respectively) for persistent morbidity. Patients without complications had a 2.89-fold higher possibility of survival compared with those with complications. Days in the ICU and APACHE II score were statistically significantly lower in these patients ($P < 0.0001$).
Conclusions Iatrogenic complications were common and associated with increased morbidity and mortality rates. Human errors accounted for the majority of them, and were often associated with high nursing workload. The elderly and the severely ill patients are at greater risk of presenting a major complication. To increase safety, preventive measures should be taken. Better organization of the daily workload, better training of the medical and nursing staff as well as avoidance of invasive monitoring, wherever this is possible, could contribute to decrease iatrogenic complications.

P395

Quality indicators in critically ill patients

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Introduction Quality indicators are working tools that permit measurement of the medical care provided. They can provide warning signs and identify problems or improvements and departures from standard care.
Objectives The Spanish Society of Intensive Care and Coronary Units (SEMICYUC) developed a Strategic Plan that included the drawing up of quality indicators for key processes in the care of critically ill patients.
Materials and methods Over a 2-year period, the 14 working groups of the SEMICYUC drew up a consensual list of 120 quality indicators. The methodology was coordinated and supervised by the Avedis Donabedian Foundation (FAD). The initial phase was the definition of the process and identification of the most important aspects according to priority criteria. The design phase consisted of the description of the various sections of the indicator in order to ensure its validity and reliability (definition, dimension, justification, formula, explanation of terms, population, type, data sources, standard and commentaries). All these process were based on the best scientific evidence available and expert opinion.
Results A total of 120 quality indicators, covering all areas and dimensions of intensive care medicine, were drawn up. Of these, 20 were considered important enough to recommend their monitoring in all ICUs: (1) Early administration of acetylsalicylic acid (ASA) in acute coronary syndrome. (2) Early reperfusion techniques in acute coronary syndrome with ST elevation. (3) Semirecumbent position in patients with invasive mechanical ventilation. (4) Prevention of thromboembolic disease. (5) Surgical intervention in head trauma with epidural and/or subdural hematoma. (6) Monitoring of intracranial pressure (IPC) in severe head trauma with pathological CAT. (7) Pneumonia associated with mechanical ventilation. (8) Early management of sepsis/septic shock. (9) Early enteral nutrition. (10) Prophylaxis of gastro-intestinal hemorrhage in patients with invasive mechanical ventilation. (11) Adequate sedation. (12) Management of analgesia in nonsedated patients. (13) Inadequate transfusion of blood concentrates. (14) Real donors. (15) Compliance with hand-washing protocol. (16) Information for the families of ICU patients. (17) Therapeutic limitations. (18) Survey of perceived quality at discharge from the ICU. (19) Round-the-clock presence of intensive care specialists in the ICU. (20) Register of adverse effects.
With respect to the type of indicator included: five were structural, 79 were procedural and 36 were concerned with results. The principal quality dimensions evaluated in the indicators were: risk (53); effectiveness (42); adaptation (25); efficiency (10); satisfaction (seven); continuity of care (three) and accessibility (one), although the majority evaluated more than one dimension of quality.
Conclusions This project led to the drawing-up of 120 quality indicators of the key processes in the care of the critically ill patient. Twenty basic indicators were identified that we consider should be monitored in all ICUs, with the other indicators depending on the case mix. According to these indicators, the dimensions monitored with greatest frequency are risk and effectiveness.

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Quality–efficiency square: a new way to look at cost and quality in critical care

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Critical care units are under increasing pressure to account for the large cost of managing complex patients. Ideally, cost-utilisation analysis (€/QALY) [1] should be used to assess treatment; however, this is very difficult in the uncontrolled environment of a working critical care unit with a heterogeneous patient population. Cost/survivor is often used as a cost measure that considers outcome and is easier to measure; however, this is case-mix dependent so comparisons between units are flawed. We aimed to develop a measure of cost efficiency and quality that was independent of factors outside the control of each unit. We postulated that this could be achieved using a cost factor based on patient days weighted for average risk of death (RoD) and annual admission number [2], which along with the SMR would allow construction of a matrix that could assess both cost efficiency and outcome quality (the QES).

Forty-seven units from the UK National Cost Block Programme (2003–2004) were included. Regression analysis was used to create a formula for cost/patient-day based on the admission number and RoD. Residuals representing the deviation from the predicted cost were plotted against the SMR. Units that had both low SMR and low cost (<95% CI) were considered to have high quality and high economy or high quality–efficiency (QE). Those with high SMR and high cost were considered to have low QE. We identified seven units that had high QE and six units that had low QE.

We categorised units by cost/survivor and then assessed the QE categories in these terms. There was only limited correlation between the two methods.

We believe that the QES is a relatively easy measure of both economic efficiency and quality, and may be a useful, powerful and convenient tool to assess critical care units.

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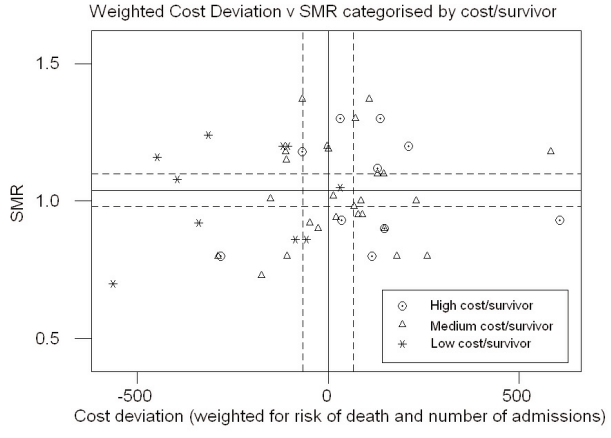
Figure 1 (abstract P396)



P397

Influence of second-generation and third-generation mobile phones on critical care medical equipment

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Introduction The restricted use of cellular phones in patient areas in hospitals seems hard to enforce considering the growth in use and the decrease in size of these devices. The electromagnetic incompatibility of the first-generation mobile phones (i.e. GSM) with medical equipment has been described. Information on the safety of new mobile communication technology (second-generation GPRS and third-generation UMTS) is scarce. A recent paper showed minor interference with GRPS and UMTS suggesting improved safety with new networks [1].

Objective We hypothesized that GPRS and UMTS have adverse influences with clinical relevance on critical care equipment.

Methods Sixty-one medical devices used in the critical care environment were tested (i.e. nine ICU ventilators, 13 critical care monitors, seven syringe and four volumetric pumps, five hemofiltration/dialysis equipment). All were tested during full operation; a simulator was connected if necessary. A signal generator (HP/Agilent E4433B/ESG-D Digital RF) was used to generate the GPRS signal I and II (with different time slot durations both at carrier frequency 900 MHz) and the UMTS signal. Their power level was controlled at 2 W for GRPS and 0.2 W for UMTS, corresponding with maximal transmit performance of cellular phones in daily practice. The distance from the antenna to device during the tests varied from 500 to 0 cm. Incidents were classified according to an adjusted critical care adverse events scale: 'hazardous' (direct physical influence on patient by unintended change in equipment function), 'significant' (influence on monitoring significant level of attention needed with distraction from patient care) or 'light' (influence on monitoring significant level of attention needed without distraction from patient care).

Results A total of 49 incidents were found in 26 devices (43% of all tested devices). Seventeen incidents were classified as 'hazardous', 20 as 'significant' and 12 as 'light'. The hazardous incidents occurred in 26% with GPRS-1, in 6% with GRPS-2 and in 2% with the UMTS network. Hazardous incidents occurred at a median distance of 3.0 (0–300) cm.

Conclusions Despite safety requirements of electronic medical equipment as stated in international standards, ICU devices are still vulnerable for electromagnetic interference by new-generation wireless telecommunication technology. Restricted use of cellular phones in ICUs is still warranted.

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P398

Value of routine daily chest radiography in a non-university ICU: results of a controlled prospective study

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Background A strategy of daily-routine chest radiographs (CXR) is practiced in many ICUs, although its efficacy remains controversial.

The aim of this study was to evaluate the diagnostic and therapeutic efficacy, as well as the costs of the daily-routine CXR, and compare this with CXR that were judged clinically necessary ('on-demand CXR').

Materials and methods In this prospective, blinded, controlled study, daily-routine CXR were obtained from all patients in a mixed surgical–medical ICU in a university-affiliated teaching hospital. CXR were evaluated by trained radiologists (to score for the presence of predefined items such as progressive or new infiltrates, pneumothorax, malposition of the tube/lines); CXR were not accessible for intensivists. In addition to these 'daily-routine CXR', the intensivist ordered 'on-demand CXR' if deemed necessary. In all these cases, a specific form had to be completed with reasons for CXR and suspected abnormalities. Considerable worsening according to predefined criteria on the 'routine CXR', but not clinically recognized or suspected, was communicated daily with the intensivist. From these data, diagnostic efficacy (the number of CXR with significant abnormality/total number of CXR) and therapeutic efficacy (number of CXR leading to an intervention/number of CXR) were calculated. Chi-squared analysis was used to test differences.

Results During 4 months, 1063 CXR in 153 patients were obtained (725 'daily-routine' CXR and 338 'on-demand' CXR). Diagnostic efficacy of 'daily-routine' CXR was 6.3%; diagnostic efficacy of 'on-demand CXR was 21.9% ($P < 0.0001$). Therapeutic efficacy of 'daily-routine CXR' was 2.6%; therapeutic efficacy of 'on-demand' CXR was 21.3% ($P < 0.0001$). The most frequent interventions on the basis of CXR findings were the administration of diuretics (20%) and repositioning of the tube (18%). A potential CXR volume reduction of 36% was observed when the 'routine CXR' strategy would have been replaced by an 'on-demand CXR' approach. This amounts to a potential cost reduction of €82,000 per year.

Conclusion The value of the 'daily-routine CXR' is low. Based on these preliminary data, daily-routine CXR should probably be abandoned for ICU patients.

P399

Minimal number of adverse physiological events during physiotherapy intervention

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Background There has been some controversy as to whether physiotherapy causes adverse physiological changes (APC) that could be harmful to intensive care patients.

Aims and method A multicentre study in six Australian tertiary-level ICUs was performed to investigate the incidence of APC during physiotherapy in critically ill patients over a 3-month period, to benchmark this against studies that have recorded spontaneous APC, and to investigate whether there were any trends in patient category, demographic characteristics, type of intervention, or seniority of physiotherapist.

Results There were 12,800 physiotherapy treatments completed, with 27 treatments resulting in adverse physiological changes (0.22%). This incidence was significantly lower than a previous study of APC (663 events/247 patients over a 24-hour period); that is, the incidence during physiotherapy was lower than during general ICU care. Significant factors were apparent, with a decrease in blood pressure or arrhythmia the major APC noted in patients on medium to high doses of inotropes/vasopressors, having unstable baseline hemodynamic values, previous cardiac co-morbidities, receiving intervention consisting of positive pressure (two-sided Fisher's exact test $P = 0.07$), or right-side lying (two-sided Fisher's exact test $P = 0.006$).

Conclusion This study has demonstrated that the overwhelming majority of physiotherapy treatments in intensive care are safe, but further factors should be investigated in controlled trials.

P400

Three generations of mortality prediction models: accuracy for outcome prediction in the critically ill obstetric patient

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Introduction Mortality prediction models (MPM) [1-3] are generalistic severity of illness scoring systems. No score is computed, and a logistic regression equation directly provides a probability of hospital mortality. Three generations of MPM scores are already available, and assess mortality at admission to the ICU (first hour).

Objective To determine the accuracy of the different MPM systems in the critically ill obstetric patient.

Patients and methods Prospective data collection of the parameters to calculate MPM1-H0 and MPM2-H0 [1,2], and retrospective chart review of one of two additional parameters necessary to calculate MPM3-H0 [3] from the MPM2-H0 score [2]. Study period: January 1996–December 2003. Inclusion criteria: all obstetric patients hospitalized in a multidisciplinary ICU and with a length of stay >1 hour. Exclusion criteria: same as those published in the original references [1,2].

Performances of the three systems were compared, using the area under the receiver–operator characteristic curve (AUROC) to assess the discriminatory power and the Hosmer–Lemeshow (HL) goodness-of-fit test for calibration. Data was computed on R version 2.1. $P < 0.05$ was considered significant.

Results See Table 1.

Table 1 (abstract P400)

	MPM1	MPM2	MPM3
AUROC	0.801	0.853	0.885
HL	0.036	0.156	0.37

Discussion and conclusion There is no significant difference in the performances of MPM2 and MPM3. They are clearly better than the oldest model. The two new parameters included in the MPM3 did not significantly influence the performance of the system. Many reasons could explain these findings: when computing the MPM3 system, addition of a 'zero–factor' term [3] for patients with no risk factors other than age does not improve model performance in our population, because our database is composed of young woman issued from a homogeneous case mix. The fact that the 'Full Code' factor was assessed retrospectively and that we deal with young pregnant patients where very few Do Not Resuscitate orders were given explains that this parameter got little influence. We can conclude that MPM1 is outdated, and MPM3 tends to be better than the previous version without having a statistically significant difference. Adding known prognostic factors not included in MPM systems could have enhanced performances of MPM3 in our particular case mix.

References

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P401

Expanded Multiple Organ Dysfunction score: is it better than the Sequential Organ Failure Syndrome score?

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In our database, the day 1 Sequential Organ Failure Syndrome (SOFA) score performs significantly better than day 1 Multiple Organ Dysfunction score (MODS) in outcome prediction (data not published). The Expanded Multiple Organ Dysfunction score (EMODS) is a simple modification of MODS. It is calculated by summing up MODS with the Organ Support/Failure Score (OS-F). The OS-F is a dichotomous score of 1 or 0, given to each organ support/failure the patient received, namely: mechanical ventilation present at the 24th hour of admission, inotropes for more than 1 hour/day, transfusion and serum creatinine >200 μmol/l. The Maximum score a patient could receive is 4. The above modifications seem necessary for MODS as it does not account for therapeutic interventions.

Objective To compare performances of EMODS with SOFA in outcome prediction.

Design Retrospective analysis of prospectively collected data as part of the APRiMo study [1].

Patients and methods All critically ill obstetric patients admitted to our independent multidisciplinary ICU were included. Exclusion criteria: length of stay <24 hours. Necessary data for calculation of the MODS, SOFA and OS-F Score at the first day of ICU hospitalization were available. Main outcome of interest: vital status at ICU discharge. Performances of EMODS and SOFA were assessed using adequate statistical tests.

Results Six hundred and forty patients were included in the analysis. Mortality rate 13.3%. Mean age 31 ± 6 years. Mean length of stay 5 ± 5 days. Mean MODS 4.3 ± 3.8, mean SOFA score 4.9 ± 4.2, mean EMODS 5.1 ± 4.6. Nonsurvivors vs survivors: mean SOFA score 11.5 ± 4.9 vs 3.9 ± 3 ($P < 0.001$), mean EMODS 12.3 ± 4.9 vs 3.9 ± 3.8 ($P < 0.001$) (Table 1).

Table 1 (abstract P401)

	ROC	Hosmer–Lemeshow
MODS	0.9 ± 0.07	0.004
SOFA	0.913 ± 0.05*	0.287
EMODS	0.922 ± 0.05†	0.290

*$P < 0.05$ MODS vs SOFA; †$P < 0.01$ EMODS vs MODS.

Discussion and conclusion EMODS sensitivity was significantly better than MODS and performed at least as well as the SOFA score. Adding organ support enhanced the performance of MODS, sustaining organ dysfunction/failure assessment with SOFA (which involves mechanical ventilation and use of inotropes) is a better way to evaluate respiratory and hemodynamic dysfunctions. The choice of transfusion as an additional criterion to assess hematologic dysfunction is pertinent in our particular case mix. After computing a logistic regression model with OS-F components, single-component MODS, with vital status as the dependent variable; a serum creatinine level >200 μmol/l gave an OR of 23. This emphasizes again the importance of acute renal failure as a prognostic factor in the ICU, but also rises again the question about the optimal parameter to evaluate renal organ dysfunction.

Reference

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P402

Value of APACHE II score to predict mortality in cardiogenic shock patients of a cardiologic ICU

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Introduction APACHE II score was primarily designed to predict mortality in general patients in ICUs. In patients with specific diseases (such as severe trauma, COPD and acute pancreatitis), however, other score systems were more sensitive

Hypothesis The aim of this study was to establish the value of the APACHE II score in predicting mortality of patients with cardiogenic shock admitted to a cardiologic ICU of a university hospital

Methods This was a retrospective analysis of a prospective cohort observational study of 84 patients with cardiogenic shock admitted to a cardiologic ICU. Clinical and laboratory data to calculate the APACHE II score were recorded on admission. The outcome measure was mortality. Logistic regression was used to estimate the predictive ability of the APACHE II score, and the chi-square test was used to compare the difference between predicted and observed mortality.

Results Patients had a mean age of 54 ± 20 years, 65.5% were male, ICU length of stay was 17.3 ± 20.2 days, mean ejection fraction (EF) was 25 ± 5% and mean APACHE II score was 15 ± 6. Observed mortality was 62% and the corresponding APACHE II prediction was 21.9%. There was a significant difference between observed and predicted mortality ($P < 0.001$).

Conclusions These data show that mortality in cardiogenic shock cannot be predicted by the APACHE II scoring system. In this population new assessment tools should be determined for better outcome prediction.

P403

Use of the SOFA score in an Indian cancer hospital ICU

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Objective To determine the pattern of organ failure in critically ill cancer patients and whether the SOFA score is useful in predicting outcome.

Methods Six hundred and two consecutive admissions (369 males, 233 females) from July 2004 to September 2005 were prospectively studied in a 21-bed ICU-HDU. Two hundred and sixty-three patients were admitted following surgery (Group 1), 209 patients with solid tumours were admitted from the wards (Group 2) and 130 had haematological malignancies, lymphoma or myeloma (Group 3). Mean SAPS II was 36.0 ± 9.4. Length of ICU stay was 5.2 ± 6.6 days. Parameters for calculating the SOFA score were assessed daily until ICU discharge. The total SOFA score on day 1 (SOFA1), the highest SOFA score of the first 3 days (MAX3) and during the ICU stay (MAXSOFA), the change in SOFA score between day 2 and day 1 (DELTA1) and the MEANSOFA (total SOFA score for all days/days in ICU) were calculated. Organ failure was present if the score for any organ was >2 in the first 48 hours.

Results ICU mortality was 33.6% (11%, 36% and 75% for Groups 1, 2 and 3, respectively, $P < 0.000$). Nonsurvivors had higher organ scores and SOFA score on day 1 (6.3 ± 4.1 vs 1.7 ± 2.1, $P < 0.001$) and until day 7. Respiratory (RS) failure was the most common (17.1%), followed by coagulation (11.8%), central

nervous system (CNS) failure (8.8%), cardiovascular (CVS) failure (7.8%), renal and liver failure (3.5% and 2.5%; $P < 0.000$). The incidence of RS, coagulation, CVS and CNS failure on day 1 was very high in Group 3 (40%, 38%, 19% and 16.2%, respectively) and least in Group 1 (5.3%, 1.1%, 1.9% and 3.4%, $P < 0.000$). Patients in Group 3 had significantly higher SOFA1 (6.6 ± 4.0 vs 3.5 ± 3.4 for Group 2 and 1.4 ± 2.0 for Group 1, $P < 0.000$), and scores for all organ systems on day 1. Of the organ failures developing within 48 hours, CVS failure was associated with the highest mortality (86.3%), while RS failure and coagulation failure were associated with mortality of 68.9% and 75.6%, respectively. Group 1 patients had significantly less mortality with RS (30%), CNS (30%) and coagulation (50%) failure compared with the other groups. A total 13.6% of patients with no organ failures within 48 hours died, while patients with one, two, three and >3 organ failures had a mortality of 51.3%, 73.3%, and 92% and 100%, respectively. For patients staying >1 day, the area under the ROC (SE) for SOFA1, DELTA1, MEANSOFA, MAXSOFA and MAX3 were 0.81 (0.02), 0.65 (0.03), 0.91 (0.02), 0.91 (0.02) and 0.87 (0.02), respectively. The univariate ORs (95% CI) were highest (1.9 [1.7–2.1] and 1.6 [1.5–1.7]) for MEANSOFA and MAX3, respectively, and lowest (1.4 [1.2–1.6]) for DELTA1.

Conclusions Patients with haematological malignancies have a higher incidence of coagulation failure and worse outcome with multiple organ failure compared with general ICU patients. The MEANSOFA best discriminates between survivors and nonsurvivors, while SOFA1 and MAX3 were superior to DELTA1.

P404

Evaluation of APACHE II and the ICU cancer mortality model in an Indian cancer hospital ICU

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Introduction The performance of a prognostic score must be validated before it may be used in an ICU, especially where there is a specific patient case mix.

Objective To validate a cancer-specific ICU scoring system – the ICU Cancer Mortality Model (ICMM) [1] – and to compare its performance with that of a general ICU scoring system – APACHE II.

Methods Six hundred and two consecutive admissions (369 males, 233 females, mean age 50.3 ± 14.1 years) from July 2004 to September 2005 were prospectively studied in a 21-bed ICU-HDU. To hundred and sixty-three patients were admitted following surgery (Group 1), 209 with solid tumours were admitted from the wards (Group 2) and 130 had haematological malignancies, lymphoma or myeloma (Group 3). In case of multiple ICU admissions during a single hospital admission, data from the last ICU admission were recorded. Discrimination was determined by computing the area under the receiver–operating characteristic curve (AUC, represented as area ± SE). Calibration was calculated using the Hosmer–Lemeshow goodness-of-fit test.

Results The average APACHE II score was 15.3 ± 9.8, and ICU length of stay (LOS) 5.2 ± 6.6 days. Predicted mortality in hospital was 24.8% by APACHE II and 50.3% by ICMM. Two hundred and eleven patients died in hospital (observed mortality 35.0%), yielding a standardized mortality ratio (SMR) of 1.4 and 0.7, respectively. Both APACHE II and ICMM discriminated well (AUC 0.90 ± 0.013 vs 0.87 ± 0.016, respectively). Both scoring systems calibrated poorly (APACHE II, ^H 59.0, $P < 0.001$, df = 10 and ICMM, ^H 97.6, $P < 0.001$, df = 10). The mean APACHE II score in Group 1 (8.6 ± 5.8) was significantly lower ($P < 0.001$) than in Groups 2 (17.9 ± 8.5) and 3 (24.9 ± 7.9). Mortality was 11%, 39% and 77% in Groups 1, 2 and 3, respectively. The SMR for Group 1 was 1.19 for APACHE II and 0.32 for ICMM; for Group 2, 1.36 and 0.72, respectively; and for Group 3, 1.54 and 1.02. APACHE II showed better discrimination than ICMM in Group 1 (AUC 0.86 ± 0.04 vs 0.79 ± 0.04) and calibrated well for Group 1 (^H = 14.9, df = 10, $P = 0.14$).

Conclusion Both APACHE II and the cancer-specific ICMM discriminated well but were poorly calibrated, and could not be validated for use in our patients. APACHE II worked well for a subgroup consisting of surgical patients with a lower severity of illness, while the ICMM tended to better for patients with hematological malignancy with a high severity of illness and mortality.

Reference

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P405

Severity of disease and infection were related to bad outcomes of elderly patients in a general ICU

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Background Elderly patients (≥70 years old) are progressively more frequently admitted to ICUs. Studies addressed to evaluate short-term and long-term outcomes of the elderly were not conclusive about the effect of age as a predictor of bad outcomes. This study was designed to evaluate our experience in managing elderly patients admitted in our 21-bed medical–surgical ICU.

Objective To evaluate which of the patients' characteristics and interventions were related to outcomes in elderly patients admitted in a general ICU.

Methods A prospective cohort study, including all consecutive patients ($n = 788$) admitted from December 2003 to December 2004. Variables included for analysis were: demographic, diagnosis, severity scores at entrance; intervention issues during ICU stay: TISS28, organ dysfunction, mechanical ventilation, vasoactive medication, procedures, clinical infection and complications; outcomes recorded were: ICU and hospital length of stay, ventilator-days, mortality. Elderly patients' characteristics and outcomes were compared with the less old (<70 years old).

Results The elderly were 426 (54.06%) patients and the less-old group was 362 (45.93%). Characteristics of the elderly compared with the less-old group were: no differences in gender; higher ultimately fatal and fatal underlying disease (8.2% vs 4.4%, $P < 0.02$ and 18.3% vs 14.4%, $P < 0.02$, respectively); higher APACHE II score (15.95 ± 6.35 vs 12.08 ± 6.7, $P < 0.001$); more frequent infection disease at admission (33.1% vs 24.9%, $P < 0.01$) and sepsis (19.0% vs 13%, $P < 0.02$). During the ICU stay there were a higher use of inotropic agents (36.9% vs 29.6%, $P < 0.03$) and no significant differences in the use of sedation, dialysis, insulin, recombinant human activated protein C, surgery and nutritional therapy. There was no difference in SOFA score at ICU discharge between groups (1.58 ± 3.3 vs 1.49 ± 3.9, $P < 0.74$). More important bad outcomes were observed in the elderly group compared with less-old patients: higher mortality rate at ICU (15.7% vs 9.1%, $P < 0.009$); higher mechanical ventilation-days (3.97 ± 12.7 vs 2.45 ± 6.38, $P < 0.001$); higher nosocomial sepsis rates (12.4% vs 8.8%), but not significant ($P < 0.108$). The hospital stay after ICU discharge was higher in the elderly group (11.4 ± 17.3 vs 7.7 ± 11.7 days, $P < 0.002$), as well as hospital discharge rates being lower (69.2% vs 83.4%, $P < 0.001$). Age separately was not significant as a predictive factor of bad outcome (OR 1.8; 95% CI 1.19–2.90, $P < 0.005$) in univariate analysis.

Conclusions Age separately was not predictive of bad outcomes. The sum of ICU therapeutic interventions was not discriminative for outcomes between elderly and less-old patients. Severity of illness and infection at admission were determinant of bad outcomes in the elderly patients.

P406

Comparison of risk prediction models for admissions to UK critical care units following traumatic brain injury

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Introduction Traumatic brain injury is a potentially fatal condition and a common cause of admission to ICUs in the United Kingdom. We describe the case mix and outcomes of head injury patients requiring intensive care and evaluate the ability of five risk prediction models to predict mortality in these patients.
Method Secondary analysis of a high-quality clinical database, the Intensive Care National Audit and Research Centre Case Mix Programme Database, on 374,594 admissions to 171 critical care units in England, Wales and Northern Ireland from 1995 to 2005. Calibration of risk prediction models was assessed by the area under the receiver–operating characteristic curve (AUROC), discrimination by the Hosmer–Lemeshow (H-L) C statistic and the intercept and slope from Cox's calibration regression, and overall fit by Brier's score.
Results A total of 11,021 admissions following traumatic brain injury were identified (3% of all admissions). The mean age was 44 years and 77% were male. Mortality was 23% in the ICU and 33.5% in the hospital. The median (interquartile range [IQR]) length of stay in the ICU was 3.2 (1.1–8.1) days for survivors and 1.6 (0.7–4.0) days for nonsurvivors. Median (IQR) length of stay in hospital was 24 (10–51) days for survivors and 3 (1–9) days for nonsurvivors. SAPS II, MPM II and the ICNARC model discriminated best between survivors and nonsurvivors and were better calibrated than APACHE II and III in 5393 patients eligible for all models (Table 1).

Table 1 (abstract P406)

Model	AUROC	H-L C	Cox intercept, slope	Brier
ICNARC	0.84	24.9	0.17, 1.08	0.147
MPM II	0.81	38.2	0.20, 1.04	0.163
SAPS II	0.81	61.4	0.02, 0.89	0.158
APACHE II	0.74	215	−0.26, 0.66	0.187
APACHE III	0.76	2478	0.50, 0.61	0.194

Conclusion Traumatic brain injury requiring intensive care is associated with a high mortality rate with a short ICU length of stay in nonsurvivors. APACHE II and III have poorer calibration and discrimination than SAPS II, MPM II and the ICNARC model in predicting mortality in these patients.

P407

Using outcome prediction tools in the ICU: performance of APACHE II and SAPS 2 scores in clinical patients

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Background Outcome prediction has become increasingly important over time, either to evaluate quality of care or to make therapeutic decisions. The APACHE II and SAPS 2 scores are widely used tools to assess prognosis among ICU patients. Nevertheless, there are still conflicting data concerning the best instrument to be used in specific groups of patients.
Objective To compare the performance of APACHE II and SAPS 2 in a cohort of clinical patients.
Design A prospective cohort study in a 19-bed ICU in a private hospital.
Patients All clinical patients admitted to the ICU during the period of the study.
Measurements and results There were 527 patients admitted between September and November 2005. Seventy-nine (15%) of them were admitted for clinical reasons, and 56 (70.8%) had simultaneous measurement of the APACHE II and the SAPS 2 scores. The mean APACHE II and SAPS 2 were 20.87 ± 10.27 and 39.09 ± 14.59, respectively. Nine patients died (3.7%). The mean APACHE II and SAPS 2 in the survivors and nonsurvivors were 18.09 ± 7.94 and 35.44 ± 8.86 ($P < 0.0001$), and 35.36 ± 12.33 and 58.56 ± 9.08 ($P < 0.0001$), respectively. The area under the ROC curve (AUC) was 0.960 (95% CI 0.910–1.010) for the APACHE II score, and 0.934 (95% CI 0.869–0.998) for the SAPS 2 score. Using a cutoff value of 51 points for the SAPS 2, sensitivity was 100%, specificity 88.4%, positive predictive value (PPV) 64.3% and negative predictive value (NPV) was 100%. Using a cutoff value of 25 points for the APACHE II, sensitivity was 100%, specificity 91.5%, PPV 69.2% and NPV 100%. The OR for an APACHE score >25 was 3.25 (95% CI 1.44–7.34), and for SAPS 2 >51 was 2.8 (95% CI 1.39–5.66). The association of both scores increases the specificity to 97.9% and PPV to 90%, maintaining the sensitivity and NPV of isolated scores, increasing the OR to 10 (95% CI 1.59–64.20).
Conclusion In this cohort of clinical patients, the association of SAPS 2 and APACHE II scores is a better predictor of mortality than the isolated measurements.

P408

SAPS 2 is a better score than APACHE II to predict mortality in the ICU

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Background The prediction of mortality in the ICU is very important to evaluate the quality of the care for our patients. The two most used scores that are used are the APACHE II and the SAPS 2, but there are conflicting results in the literature regarding which of them is the best predictor tool.
Objective To compare the performance of both scores to predict mortality in a surgical ICU in Brazil.
Design A prospective cohort study in a 19-bed medico-surgical ICU in a private hospital.
Patients All patients admitted to the ICU over a period of 4 months.
Measurements and results Between September and November 2005, 527 patients were admitted in the ICU. Of those, 187 (35.5%) had simultaneous assessment of the APACHE II and the SAPS 2 scores. The mean APACHE II and SAPS 2 scores were 13.47 ± 5.93 and 26.09 ± 13.94, respectively. There were seven deaths (3.7%). The mean APACHE II and SAPS 2 in the survivors and nonsurvivors were 13.24 ± 5.63, 19.29 ± 10.05 ($P = 0.062$), and 25.07 ± 12.73 and 52.43 ± 18.31 ($P = 0.001$), respectively. The area under the ROC curve was 0.887 (95% CI 0.743–1.032) for the SAPS 2. The best cutoff value was 39.5 points, and the sensitivity and specificity were 85.7% and 88.9%, respectively.

The SAPS 2 mean predicted mortalities for patients with score <39.5 and ≥39.5 were 6.31 ± 0.48% and 48.7 ± 7.5%, respectively. However, the observed mortality in the patients with SAPS 2 score <39.5 and ≥39.5 were 0.6% and 23.1%, respectively.
Conclusion In the studied population, SAPS 2 is a better tool to predict mortality than APACHE II. However, the mortality was overestimated by this score.

P409

Comparison of prognostic scores at a pediatric ICU

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Objective The main aim of the pediatric intensive care unit (PICU) is promoting qualified care with the objective of achieving the best results and better prognosis for critically ill children. One means of comparing the quality and efficacy of care provided at a given unit is made by risk adjustment systems. The principal scores that have been developed for the pediatric population are the Pediatric Risk of Mortality (PRISM) and Pediatric Index of Mortality (PIM) scores. Our aim in this study was to compare the commonly used pediatric mortality risk scoring systems and to assess the feasibility of using these scoring systems in developing countries
Methods The cohort study conducted prospectively in an eight-bed tertiary medical PICU in University Children's Hospital from December 2002 to July 2004. The scoring systems compared were PRISM III-12, PRISM III-24 and PIM-2. Observed and expected mortality were compared by the Lemeshow–Hosmer goodness-of-fit $\chi 2$ test. Mortality was also standardized for case mix using the standardized mortality ratio (SMR). Mortality discrimination was quantified by calculation of the area under the receiver–operating characteristic curve.
Results During the study period, 334 patients enrolled to the study. Eighty-four (25.7%) of the 334 patients studied died. Estimated mortality by PRISM III-12 was 38.71 with a standardized mortality rate of 2.17, by PRISM III-24 was 46.99 with a standardized mortality rate of 1.78, and by PIM-2 was 32.4 with a standardized mortality rate of 2.45. The Hosmer–Lemeshow test gave a chi-square of 31.1 ($P < 0.001$) for PRISM III-12, 21.2 ($P < 0.001$) for PRISM-III 24, and 34.6 ($P < 0.001$) for PIM-2. The area under the ROC curve was 0.80 in PRISM III-12, 0.85 in PRISM III-24, and 0.76 for the PIM model. Only 9.3% ($n = 31$) of the patients was admitted electively to PICU. The presence of mechanical ventilation (38% vs 7%, $P < 0.01$) and the existence of chronic organ disease (50% vs 24%, $P < 0.001$) were significantly associated with mortality.
Conclusion The PIM test was less well calibrated overall. PRISM III-24 offers better capacity for discriminating between survivors and nonsurvivors in our country. We observed an underestimation of mortality in every scoring system. The underestimation of mortality may be associated with the existence of high proportion of chronic organ disease in our PICU.

P410

Surgical Procedure Assessment score predicts ICU length of stay in cardiac surgical patients

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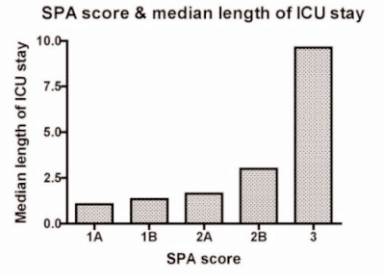
Introduction With a high volume of cardiac surgical patients, effective allocation and prediction of the use of limited ICU beds is essential. We developed the Surgical Procedure Assessment (SPA) score (see Table 1) as a simple preoperative tool to assess ICU needs for cardiac surgical patients. After a pilot study (182 patients), we applied this score to a larger prospective cohort to test its association with ICU length of stay (LOS).

Table 1 (abstract P410)

SPA score	Surgical factor[a]	Patient factor[b]
1A	Low complexity	– comorbidities
1B	Low complexity	+ comorbidities
2A	Moderate complexity	– comorbidities
2B	Moderate complexity	+ comorbidities
3	High complexity	± comorbidities

[a]Low complexity, CABG, MVR or AVR; moderate complexity, heart Tx, CABG and VR; high complexity, VAD, lung Tx. [b]Comorbidities: inotropes, IABP, LVEF < 20%, diabetes, severe systemic disease, lung disease requiring oxygen, ventricular arrhythmias.

Figure 1 (abstract P410)



Methods SPA scores were assigned preoperatively to all patients undergoing cardiac surgery during 2002 at a single center. All patients were admitted to either the cardiothoracic or surgical ICU following surgery and data were collected prospectively during the hospitalization.
Results A total of 1201 patients were enrolled. The mean age was 64 years (SD ± 14.2) and 66% were male. There was an increase in median length of stay for each step increase in the SPA score (1A: 1.1 days; 1B: 1.3 days; 2A: 1.6 days, 2B: 3.0 days, 3: 9.6 days), which was statistically significant ($P < 0.01$ Cuzick's nonparametric test for trend) (see Fig. 1).
Conclusion There is a strong correlation between the preoperatively assigned SPA score and ICU LOS for patients undergoing cardiac surgery. This simple, easily assigned score may provide an efficient method for improving cardiac surgery scheduling and allocation of ICU resources.
Reference
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P411

Is SOFA score a mortality predictor in surgical patients admitted to the postoperative acute care unit?

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Objective To assess the mortality predictive value of an organ failure score (SOFA) compared with other three risk scores (POSSUM, ASA, and SAPS II) in surgical patients admitted to a postoperative acute care unit (PACU).

Methods Prospective collection of demographic, clinical and laboratory data of 330 consecutive patients admitted to the postoperative care unit following elective and emergency surgical procedure, for a 6-month period. The ASA score was assessed preoperatively, the POSSUM score was calculated preoperatively and postoperatively, and the SAPS II and SOFA score were computed for the first 24 hours postoperatively. The outcome measure was inhospital mortality. Receiver–operating characteristic (ROC) curve analysis was used to estimate the predictive ability for inhospital mortality of the various scoring systems.
Results Among the 330 patients admitted to the PACU, 14 were transferred to the ICU after an interval of time varying from 24 hours to 9 days. The median length of stay in the PACU was 3 (1–17) days. The area under the ROC curve (AUROC) was 0.78 for SOFA score, 0.63 for POSSUM, 0.57 for ASA, and 0.67 for SAPS II. The cutoff values were 7 for SOFA, 47 for POSSUM, 3 for ASA and 21 for SAPS II scores. The observed mortality rate was 3.6%, while expected mortality rates according to POSSUM, ASA and SAPS II scores were 6.8%, 6.2% and 5.4%, respectively.
Conclusions Our study suggests that SOFA score might be useful to predict outcome in the PACU surgical patients. The POSSUM, ASA and SAPS II scores overestimate inhospital mortality rates for surgical patients admitted to the PACU. The use of organ failure scores might improve the power of predictive scores in these patients.

P412

Stability and Workload Index for Transfer score predicts unplanned medical ICU patient readmission

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Introduction Unplanned readmission to the medical intensive care unit (MICU) is associated with worse outcome. Unfortunately, the ability to predict which patients are likely to deteriorate after MICU dismissal is limited. We developed and tested a numerical index that measures and quantitates suitability for patient transfer from a critical care unit to a general services care environment (Stability and Workload Index for Transfer [SWIFT] score).
Methods We identified consecutive patients admitted to a tertiary care MICU from May 2004 to May 2005. The primary outcome was unplanned readmission to the MICU or unexpected death on the floor precluding ICU readmission. Utilizing a nursing workload database, an APACHE III database, a computerized medical record and a hospital laboratory database, we extracted information related to patient functional status, severity of illness and the demand for specific nursing interventions. Multivariate logistic regression was used to determine the association between specific risk factors and MICU readmission.
Results We evaluated 1131 patients during 1242 hospital admissions, 100 of whom were readmitted to the MICU and five died unexpectedly on the floor. Elements of the SWIFT score include: ICU length of stay, ICU admission source, day of discharge Glasgow Coma Scale, PaO_2/FIO_2 ratio, and the nursing demand for complex respiratory care. The SWIFT score predicted ICU readmission more precisely (ROC curve AUC 0.75) than the day of discharge APACHE III score (AUC 0.62) or day of discharge APACHE III predicted hospital mortality (AUC 0.66).
Conclusions The initial SWIFT score work has delineated a universally available set of parameters that acceptably correlate with risk of MICU readmission. If validated in an independent sample, the SWIFT score may improve the precision of MICU patient transfer decisions.

P413

Modified early warning system scoring and critical care readmission

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Introduction Modified early warning systems (MEWS) have been developed in an attempt to address suboptimal patient management prior to critical care admission [1]. The use of MEWS scoring as a predictor of critical care readmission has not been described previously.
Patients and methods We have reviewed MEWS scores from all critical care discharges, from a 17-bed mixed medical/surgical critical care unit in a university teaching hospital, assessed by our outreach service from November 2004 to June 2005. Two hundred and thirty-eight patients were reviewed, with MEWS scoring being performed routinely at critical care discharge and at outreach review 24 hours later.
Results Of the 238 patients reviewed, 197 underwent uneventful critical care discharge and did not require further admissions. Forty-one patients required readmission to critical care due to a deterioration of their presenting problem. The two groups of patients were well matched with respect to age, sex, medical/surgical split and admission Acute Physiology and Chronic Health Evaluation II score. The was no difference between the groups with respect to MEWS score at critical care discharge. MEWS score on outreach review, 24 hours after critical care discharge, was significantly higher in those patients requiring critical care readmission (Table 1).

Table 1 (abstract P413)

Readmission?	Discharge MEWS (SD)	Outreach MEWS (SD)
No ($n = 197$)	0.8 (1.2)*	0.7(1.3)**
Yes ($n = 41$)	0.9 (1.1)*	3.5 (3.0)**

*$P = 0.4$ MWU test; **$P < 0.001$ MWU test.

Conclusion MEWS scoring at critical care discharge does not predict critical care readmission. MEWS scoring by the Critical Care Outreach Team 24 hours after discharge, however, appears to predict the need for critical care readmission.
Reference
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P414

Can we distinguish patients at risk of deterioration?

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Track and trigger scores such as the Modified Early Warning System (MEWS) score are currently used in many hospitals throughout the United Kingdom. Calculating the scores for only those patients judged to be 'at risk' may potentially miss patients who actually are at risk.
We carried out a survey in our hospital looking at which patients were having their MEWS scores calculated, and therefore judged to be at risk of deterioration, and compared their MEWS scores and outcome (inpatient mortality) with those who were not having a formal scoring system carried out. For those patients not being scored we carried out the appropriate observations to enable a MEWS score to be calculated.

Table 1 (abstract P414)

MEWS score	Recorded: number	Recorded: mortality	Not recorded: number	Not recorded: mortality
0	13 (15%)	1/12 (8.3%)	62 (20.8%)	1/62 (1.6%)
1	48 (55.2%)	3/46 (6.5%)	136 (45.6%)	18/133 (14.2%)
2	9 (10.3%)	0/9 (0%)	61 (20.5%)	6/60 (10%)
3	9 (10.3%)	4/9 (44%)	27 (9.1%)	2/23 (8.7%)
4	4 (4.6%)	2/4 (50%)	6 (2%)	2/6 (33%)
>4	4 (4.6%)	3/4 (75%)	6 (2%)	2/5 (40%)

We reviewed 389 patients; four patients were on care of the dying pathways and were excluded. Of the remaining 385, 89 (23%) had a MEWS score calculated. The difference in mortality was calculated using a chi-square test. Table 1 shows our results.
Mortality figures were available for 373 patients. Overall mortality for those patients having MEWS calculated was 13/84 (15.5%), while for the other group mortality was 31/289 (10.7%) (NS).
From these data it would appear that we are not able to predict which patients are at risk of dying and many patients not scored were sicker than expected. It may therefore be prudent to calculate MEWS scores for all patients who are having observations carried out, which may enable us to identify those patients who are beginning to deteriorate, and institute measures to prevent this.

P415

Evaluation of available data on physiological track and trigger warning systems

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Background Physiological track and trigger warning systems (TTs) use periodic observation of vital signs (tracking) with predetermined criteria (trigger) for requesting attendance of a senior clinician or critical care outreach team (CCOT). There has been a proliferation of such systems in recent years, but with little formal evaluation. There is no clear evidence identifying an ideal system for timely recognition of critically ill patients.
Objective To assess the ability of different TTs to predict patient outcomes within and across hospitals, in different age groups, wards and specialties. To identify the best TT for timely recognition of critical illness.
Methods Cohort study of data from 31 acute NHS hospitals in England and Wales. Participants varied by data source; predominantly all patients seen by CCOT or all patients on selected wards. Patient outcome was a composite of death, admission to critical care, 'do not attempt resuscitation' or cardiopulmonary resuscitation. Primary assessment was by sensitivity and positive predictive value, secondary assessment by specificity and negative predictive value.
Results Fifteen datasets met predefined quality criteria and were included. Sensitivity and positive predictive value were low with median (quartiles) values of 43.3 (25.4, 69.2) and 36.7 (29.3, 43.8), respectively. Specificity and negative predictive value were generally acceptable, with median (quartiles) values of 89.5 (64.2, 95.7) and 94.3 (89.5, 97.0), respectively. Within hospitals there were differences in the discrimination of TTs in relation to age, ward and specialty, but these were not consistent across hospitals.
Conclusion We were unable to establish the best existing TT or develop a new high-quality TT for timely recognition of critical illness due to wide variation in the datasets. Sensitivity of existing TTs is very low, meaning that a high number of patients requiring intervention are likely to be missed if clinicians rely solely on these systems for identifying deteriorating patients. The low sensitivity may be due, in part, to sudden deterioration and infrequent measurement of vital signs. It is probable that using a TT improves identification of critical illness but it should be used as an adjunct to clinical judgment. The challenge is to increase the sensitivity of TTs while maintaining acceptable specificity.

P416

Abstract withdrawn

P417

Patients with liver transplantation readmitted to the ICU: a 15-year retrospective study

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Objective To evaluate risk factors and outcomes in patients with liver transplantation who were readmitted to our ICU after liver transplantation during their hospital stay.
Design A 15-year retrospective study.
Patients A total of 152 (102 male and 50 female) patients admitted to our ICU after liver transplantation over a 15-year period (1990–2004).
Results Of the 129 patients who survived the first ICU stay after liver transplantation, 28 patients (17 male and 11 female) (21.7%) were readmitted. The mean age was 44 ± 14.3 years, SAPS II score of first ICU admission and readmission were, respectively, 37 ± 7.1 (predicted mortality 39.4%) and 41.3 ± 10.8 (predicted mortality 47.6%). SAPS II score for non-readmitted (NREAD) ICU patients was 32.9 ± 5.8 (predicted mortality 31.7%). The recipient age was similar between readmitted (READ) and NREAD patients. Child–Pugh class C was 71% for NREAD and 82.2% for READ patients. The time between extubation and ICU discharge was 1.4 ± 0.7 days. Early readmission (<48 hours after ICU discharge) occurred in 25% of READ patients. Causes of early readmission were acute respiratory failure (ARF) 42.8%, cardiac disorders 28.5% and gastrointestinal (GI) surgical complications 28.5%. Causes of late readmission (days between first ICU admission and readmission was 17.8 ± 13.8) were ARF 43.3%, cardiac disorders 6.7%, GI surgical complications 36.6%, sepsis 6.7%, CNS complications 6.7%. First ICU stay was 5.1 ± 6.1 days for READ patients and 3.8 ± 3.3 days for NREAD. Readmission ICU stay was 6.25 ± 5.9 days. ICU mortality for READ patients was 42.8%. Three-month mortality was 68% for NREAD patients and 76.8% for READ patients.
Conclusion The results of this study provide evidence that READ patients appeared to be sicker than NREAD and they had longer length of first ICU stay. Cardiopulmonary complications were the main cause of early or late readmission, and the ICU and 3-month mortality was higher for patients readmitted to the ICU after liver transplantation.
Reference
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P418

Patients readmitted to the ICU during the same hospitalization: a 2-year study

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Objective To determine risk factors and outcomes in critically ill patients who were readmitted to the ICU during their hospital stay.
Setting A general ICU of a tertiary community hospital.
Patients and methods We retrospectively analysed ICU readmissions between 1 January 2003 and 31 December 2004. The data analysed included patients' clinical characteristics, APACHE II, SOFA score, TISS-28, length of ICU stay, ICU and hospital mortality.
Results During the study period, 735 patients were admitted to the ICU. Among patients who survived (467 patients), 42 patients (27 male, 15 female) (9.03%) were readmitted. The mean age was 53 ± 17.7 years. The prevalent cause of readmission was respiratory and cardiovascular complications (63.61%) followed by sepsis (12.22%), surgical problems (11.74%), neurological disorders (7.34%) and miscellaneous (5.09%). Patients whose neurological and respiratory disorders were the main admission reasons in the ICU had the highest readmission rate. APACHE II on first admission was estimated for non-readmitted patients (NREAD) (21 ± 7.5) and for readmitted patients (READ) (24 ± 6.6) (predicted mortality was 37%, and 47%, respectively), while initially admitted READ patients required less need of organ support than at the time of readmission (SOFA score was 8.0 ± 3.3 and 9.5 ± 3.5 respectively). Patients needed more therapeutic procedure at readmission than at their first ICU admission (TISS-28 on first ICU admission was 31 ± 5.4 and at readmission was 35.3 ± 5.6). The ICU mortality in READ patients was 42.7% and their hospital mortality was 65.7% (NREAD hospital mortality was 52.8%). The time between extubation to ICU discharge was 1.42 days (±0.79), the median interval between first ICU discharge and readmission was 3.97 days (12 hours–14 days), while 11 patients (26.19%) were in need of the ICU less than 48 hours after discharge.
Conclusion Patients with neurological and respiratory disorders were at greatest risk of requiring ICU readmission. Respiratory and cardiovascular complications were the major reasons for readmission. The readmitted patients appeared to be sicker and they had a higher risk of hospital death than non-readmitted patients. Probably, if an intermediate ICU was available in our hospital, the readmission rate in ICU would be visibly lower.
Reference
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P419

Trend in the severity of illness and hospital mortality rates of ICU patients over a 10-year period

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Critical Care 2006, **10(Suppl 1):**P419 (doi: 10.1186/cc4766)

Objective To describe the trend in the severity of illness and hospital mortality rate of patients admitted to the ICU over a 10-year period.
Methods This retrospective study involves the analysis of a prospectively collected APACHE III database of patients admitted to the ICUs of a tertiary medical center from 1995 to 2004. We created a customized logistic regression model for predicting hospital mortality and calculated the severity of illness and the standardized mortality ratio (SMR) for each year of the 10-year study period.
Results Excluding patients who did not authorize their medical records to be reviewed for research and readmissions, 46,618 admissions were included in the study. The mean (SD) first ICU day APACHE III score was 47.2 (25.5). The overall hospital mortality rate was 9.7%. The area under the curve (95% CI) for the customized model was 0.871 (0.866–0.876) and the Hosmer–Lemeshow statistics was 30. The average (95% CI) predicted and observed mortality rates and SMR for each year of the study period are presented in Table 1.

Table 1 (abstract P419)

Year	Predicted death [% (95% CI)]	Observed death [% (95% CI)]	SMR (95% CI)
1995	5.9 (5.6–6.3)	6.8 (6.0–7.8)	1.16(1.01–1.32)
1996	6.6 (6.3–6.9)	7.2 (6.5–7.9)	1.09(0.98–1.20)
1997	7.0 (6.7–7.3)	7.8 (7.1–8.5)	1.11(1.01–1.22)
1998	8.3 (7.9–8.6)	9.2(8.5–10.0)	1.11(1.01–1.21)
1999	9.0 (8.6–9.4)	10.7(9.9–11.7)	1.19(1.09–1.30)
2000	10.8(10.3–11.2)	10.8(9.9–11.8)	1.00(0.91–1.10)
2001	12.4(11.9–12.9)	12.7(11.8–13.7)	1.02(0.94–1.11)
2002	12.9(12.4–13.5)	12.7(11.4–13.4)	0.96(0.88–1.04)
2003	12.8(12.3–13.3)	11.2(10.4–12.2)	0.88(0.81–0.95)
2004	12.1(11.7–12.7)	8.8 (8.0–9.7)	0.73(0.66–0.80)

Conclusions Despite the increase in the severity of illness, the adjusted mortality rate of patients admitted to the ICU has declined recently.

P420

ICU patients requiring mechanical ventilation: incidence, mortality, characteristics and mortality risk factors

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Introduction Acute respiratory failure (ARF) is a frequent cause of admission to ICUs and usually necessitates mechanical ventilation (MV). Knowledge about the incidence, mortality, and risk factors associated with patients that require MV is essential to improve outcomes.
Objectives To determine the characteristics, risk factors prior and/or during MV, and general and specific mortality rates in patients under MV in a general university ICU in southern Brazil.
Methods A prospective cohort of 400 adult patients admitted to the ICU who needed MV for at least 24 hours, between March 2004 and April 2005. Data were collected daily, for up to 28 days. The age, gender, APACHE II score, medical or surgical patients, causes for the requirement of MV, organ dysfunction/failure developed prior to MV and during MV, ventilatory parameters,

duration of MV, modes of MV, tracheostomy and duration of weaning were some variables studied. Univariable and multivariable analysis were performed.
Results The incidence of MV was 18.5%; the overall and specific mortality rates were 9.4% and 57.0%, respectively. The mean (±SD) age was 67.4 ± 8.6 years; 51% were males; the mean APACHE II was 29.1 ± 23.9; the mean duration of MV was 10.4 ± 7.4 days. A multivariable analysis indicated that age ($P < 0.001$), MV duration ($P = 0.02$), vasoactive drug use ($P = 0.01$), acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) ($P = 0.002$) and renal failure ($P = 0.05$ – borderline) occurring during the MV period were independently associated with death.
Conclusions The risk factors associated with mortality in 28 days (age, MV duration, vasoactive drug use, ALI/ARDS, and renal failure during MV) are similar to some literature studies. The overall and specific mortality rates were higher. Final conclusions will require evaluation of the mortality rates of specific pathologies, planned when our sample size will be increased. The identification of these factors may allow early interventions to improve therapeutic strategies.
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P421

Chronic pain after surviving sepsis

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Critical Care 2006, **10(Suppl 1):**P421 (doi: 10.1186/cc4768)

Introduction In Germany about 90,000 patients survive sepsis per year. Few data are available indicating quality of life and chronic pain states of sepsis long-term survivors [1].
Methods One hundred and fifty-two patients were approached who survived severe sepsis or septic shock (ACCP/SCCM) on our ICU. In order to obtain specific information about chronic pain states, these patients received the SF 36 as well as the Brief Pain Inventory (BPI) questionnaire, an instrument asking for different aspects of pain intensity and pain-associated functional interference. Data are presented as the mean ± SD. The norm scores of the SF 36 on subtest levels were compared with the scores of our sample. For statistical analysis *t* tests have been used. $P < 0.05$ was considered statistically significant.
Results Sixty-four patients, 43 males and 21 females, returned the questionnaires. The mean age was 62 ± 15 years. SF 36 items concerning bodily pain occurred in septic survivors significantly more frequently compared with the healthy normal population (49.4 ± 29.9; norm: 79.1 ± 27.4; $P < 0.0001$). In most of the BPI items, patients scored over 3 on an 11-step numeric rating scale (0 = no pain, 10 = worst possible pain). This limit is thought to differentiate between low pain on one side and the need for treatment on the other. For example, 44% of the patients reported a maximal NRS value of 0–3, but 56% a maximal value of 4–10 (mean: 4.1 ± 3.4). Mean values of pain-associated functional interference ratings were (0 = no interference, 10 = worst possible interference): general activity: 4.2 ± 3.1; mood: 3.4 ± 3.0; walking ability: 4.5 ± 3.5; work: 5.1 ± 3.5; relationship: 3.1 ± 3.1; sleep: 3.7 ± 3.0; enjoyment of life: 3.7 ± 3.1.
Discussion Differences in quality of life were previously evaluated in adult survivors of critical illness investigating general ICU populations compared with healthy controls [1]. We focused on chronic pain states in patients who survived severe sepsis or septic shock. Here, we found highly significant differences in the pain-associated domain of SF 36 between survivors of severe sepsis or septic shock compared with the German healthy population. Furthermore, the interference due to pain was revealed to be high in septic survivors. Underlying reasons remain unclear and need to be evaluated. One potential contributing factor may be the proinflammatory cytokine response in sepsis that has been shown to increase pain in experimental settings.
Conclusion In conclusion, we could reveal that quality of life in long-term survivors of severe sepsis or septic shock was impaired in comparison with the German healthy population. For the first time, we demonstrated additionally a higher incidence of pain in these patients.
Reference
1. Dowdy DW, *et al.*: **Quality of life in adult survivors of critical illness: a systematic review of the literature.** *Intensive Care Med* 2005, **31:**611-620.

P422

Significance of the qualified psychotherapeutic care in the PTSR development

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Critical Care 2006, **10(Suppl 1):**P422 (doi: 10.1186/cc4769)

Introduction Kuzbass is the largest industrial region of the mines, heavy metallurgy and transport industry, which governs the high level of traumatism increase, twice as large as the national level. Treatment of patients with severe trauma was directed to the physical state in most cases. The psychogenic factor is not spared by attention. It is known that instantly or in a short time period after the physical trauma there are the different psychic disorders connected with stress in most people.
Objective The analysis of the factors' role in the complex study of the endured traumas' consequences (head injuries, fractures of the locomotor system, burns), occurring in extreme situations. The problem's actuality is conditioned by the necessity for social psychological adaptation of the patients.
Materials and methods We examined the patient group with different traumas occurring in extreme conditions. The patients suffered from the sleep disorders, anxiety, affective and other psychopathologic disorders apart from the main pathology. All patients received psychological care from relatives, medical staff, and social organizations. However, during all periods of hospitalization psychotherapy was included in the rehabilitation complex program only in some of the patients. Furthermore, we observed dynamically two patients groups. The psychotherapy specialist worked in the first group, whereas in the complex treatment of the second group psychotherapy was not included.
Results Most patients of the first group lose many symptoms of the psychic disorders. The second group demonstrated various dynamics. We observed a reduction of the psychopathological disorders in one part of the patients, and their development with formation of the PTSR signs, adaptation disorders and specific phobias in other part. Some members of the patients' families had nerve psychic disorders.
Conclusions Analysis showed that the psychological support of nonspecialists is important but it is not adequate in the different traumas occurring in extreme cases. The circumstances of the trauma require qualified psychotherapeutic care not only to the patient, but also to the members of his/her family.

P423

Long-term outcome and quality of life of patients treated in surgical intensive care: a comparison between sepsis and trauma

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Objective To determine long-term survival and quality of life of patients treated in the SICU due to sepsis or trauma.
Design An observational study in an 11-bed closed SICU at a 860-bed general hospital during a 1-year period (January 2003–December 2003).
Patients and methods Patients were divided into two groups according to admission diagnoses: group 1, sepsis or group 2, trauma (polytrauma, multiple trauma, head injury, spinal injury). Quality of life was assessed after 2 years following intensive care admission using the EuroQol 5D (EQ-5D) questionnaire.
Results A total of 164 patients (66 trauma patients and 98 patients with sepsis) were included in the study. Trauma patients were younger compared with patients with sepsis (53 ± 21 years vs 64 ± 13 years, $P < 0.001$). There was no statistical significant difference between both groups in APACHE II score and length of stay in the SICU. Trauma patients were hospitalized longer in the general ward (35 ± 44 days vs 17 ± 24 days, $P < 001$).
SICU survival, hospital survival and 2-year survival were lower in the sepsis group compared with the trauma group (60% vs 74%, 42% vs 62% and 33% vs 57%, respectively, $P < 0.05$). Long-term mortality of the sepsis and trauma groups were higher compared with the age-matched healthy population (nine times vs six times, respectively).
There was no statistically significant difference in quality of life in all five dimensions of EQ-5D between groups: almost 70% of patients had pains, 62% mobility problems, 50% signs of depression.
Conclusion Patients with sepsis treated in the SICU have higher short-term and long-term mortality compared with trauma patients. However, quality of life is reduced to the same level in both groups.

P424

Outcome following severe burn injuries in Belgium

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Background Mortality in burn patients can be predicted by three risk factors: age ≥ 60 years, total burned surface area (TBSA) ≥ 40%, and presence of inhalation injury. According to the formula of Ryan [1], patients with zero, one, two or three of the above risk factors, have a mortality rate of 0.3%, 3%, 33% and 90%.
Objective Evaluation of the predictive value of the risk factors as proposed by Ryan in Belgian burn patients.
Methods We retrospectively analysed all patients admitted between 1999 and 2004 to the six Belgian burn units.
Results During the study period 6227 patients were admitted. The annual incidence rate of severe burn injuries admitted to the burn unit was 10.11 per 100,000 inhabitants. The median age was 34 years (IQR: 16.0–48.0). The median TBSA was 5% (IQR: 2.0–15.0). Inhalation injury was present in 574 patients (9.2%).

Table 1 (abstract P424)

Number of risk factors	Mortality
Zero	24/4768 (0.5%)
One (AGE)	57/707 (8.1%)
One (TBSA)	19/144 (13.2%)
One (inhalation)	26/281 (9.3%)
Two (AGE + TBSA)	20/34 (58.8%)
Two (AGE + inhalation)	28/73 (38.4%)
Two (TBSA + inhalation)	77/182 (42.3%)
Three (AGE + TBSA + inhalation)	33/38 (86.8%)
Total	284/6227 (4.6%)

Overall mortality was 4.6%. When zero, one, two or three risk factors were present, mortality was respectively 0.5%, 9%, 43% and 87%. Table 1 presents outcome for the different combinations of risk factors.
Conclusion The incidence rate of severe burn injury in Belgium was low. The risk factors proposed by Ryan were also indicative for outcome. However, some of these three risk factors were more important for outcome than others. Also, the combination of different risk factors influenced outcome considerably.
Reference
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P425

Factors associated with mortality in severe burn patients

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Critical Care 2006, **10(Suppl 1):**P425 (doi: 10.1186/cc4772)

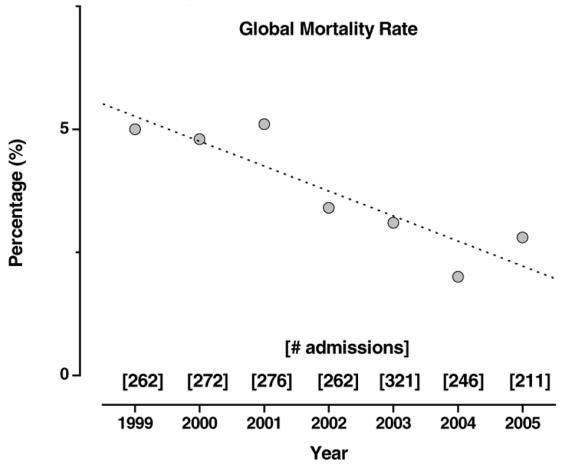
Objective To estimate mortality and the factors associated with mortality in severe burn patients.
Methods We included burn patients older than 18 years admitted to the burns ICU from Hospital Universitario de Getafe from May 1992 to November 2005. The following variables were collected: age, gender, mechanism of burn, total and deep burn surface, inhalation injury and need of mechanical ventilation. To estimate the factors associated with mortality we split the population into two randomized cohorts: model cohort (including 80%) and validation cohort (20%). We performed a backward stepwise logistic

Table 1 (abstract P425)

	OR (95% CI)
Age	
<35 years	1
36–60 years	2.48 (1.23–4.95)
61–80 years	7.28 (3.30–16.08)
>81 years	30.86 (11.33–84.05)
Deep burned surface	
<10%	1
11–20%	2.71(1.14–6.41)
21–40%	9.06 (4.35–18.87)
>41%	39.05(17.35–87.90)
Inhalation	1.91(1.05–3.46)
Mechanical ventilation	14.89(4.89–45.34)

regression entering the variables with $P < 0.05$ in the univariate analysis. The Hosmer–Lemeshow goodness of fit was used to evaluate the calibration. Discrimination was tested by measuring the area under the receiver–operating characteristic (aROC) curve.
Results In the period of study 1014 patients were admitted. The mean age was 46 years (SD 20), 25% was female. The mean deep burn surface was 14% (SD 19%). Inhalation injury was diagnosed in 33%. Mechanical ventilation was required in 44%. Median length of stay in the unit was 9 days (interquartile range: 2, 24). Overall mortality was 15%. Factors associated with mortality are presented in Table 1. The obtained model had a satisfactory calibration (Hosmer–Lemeshow goodness of fit $\chi^2 = 10.49$; $P = 0.10$) and an excellent discrimination (aROC: 0.94; 95% CI: 0.90–0.98; $P < 0.001$).
Conclusions In our cohort of burn patients we observed a mortality of 15%. Factors associated with mortality were: age, deep burn surface, inhalation injury and mechanical ventilation.

Figure 2 (abstract P426)



P426

Mortality in the Brussels burn unit: a 7-year longitudinal study

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Background Logistic regression techniques evidence that the Baux Score, the Edlich Burn Score, and the Zawacki Score highly correlate with burn patient survival [1]. All these scoring systems put significant weight on the size of burns and the patient's age. The Baux Score is a summation of these two variables. The presence of inhalation injury has also been recognized as another risk factor [2].
Objective The mortality rate of the patients hospitalized in our unit was studied for the past 7 years (1999–30 November 2005).
Results For the period a total of 1887 patients were entered into the cohort, corresponding to a yearly average of 270 ± 36 patients. Yearly cohorts were compared for age, total burn surface area (TBSA) and incidence of inhalation injury, and were found to be matched for all three parameters (Fig. 1). The mean age range was 34–39 years, TBSA ranged between 9.9% and 12.3%, inhalation incidence between 6% and 11%. The overall mortality rate decreased during the time period considered (from 4.8% to 2.8%, $r^2 = 0.69$) (Fig. 2).
Conclusion The global mortality rate in the whole cohort compares favourably with the Ryan study [2]: 4.1% (67/1665) vs 3.7% (70/1887) in this study. It should be emphasized that there is an improving trend over the 7 years, and that this improvement was mainly achieved among the most severe burns (Baux Score >100) (Fig. 3). This also highlights the need for a burn registry to objectively measure the quality in burn treatment.

Figure 3 (abstract P426)

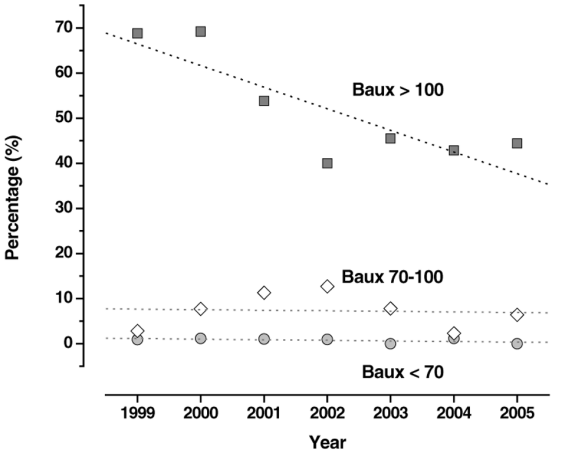
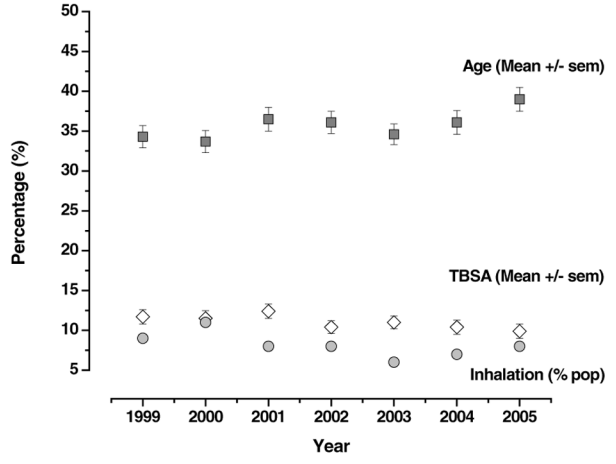


Figure 1 (abstract P426)



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P427

Quality of life before, during and following intensive care treatment: a long term follow-up study

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Introduction Patients recovering from critical illness may show persisting organ dysfunction that could impair functional status (physical, social, emotional function) with an associated reduced health-related quality of life (HRQOL). The purpose of this study was to describe the impact of critical illness and intensive care (ICU) treatment on HRQOL of ICU survivors and to compare their HRQOL with ICU nonsurvivors and an age-matched normal Dutch population.
Patients and methods A long-term prospective study in ICU patients admitted to the ICU for >48 hours. Patients or proxies completed the Short Form 36 (SF-36) in the first 48 hours of admission, to assess HRQOL in the pre-ICU period. Patients completed the SF-36 at ICU discharge, hospital discharge, and 3 and 6 months after ICU discharge.
Results Of the 451 included intensive care patients, 252 could be evaluated 6 months after ICU discharge (40 were lost to follow-up, 159 died). A multidimensional drop in SF-36 scores (all $P < 0.001$) was observed during the ICU stay, with a gradual improvement near to normal functioning at 6 months after ICU discharge. Nevertheless, at 6 months after ICU discharge, physical functioning, general health and social functioning were still decreased ($P < 0.05$) as compared with baseline values, while all dimensions scores except bodily pain remained lower than in a comparative normal population (all $P < 0.05$). Pre-admission SF-36 scores of ICU survivors were higher compared with ICU nonsurvivors for seven of the eight dimensions (all $P < 0.001$; except role-emotional $P < 0.05$). Moreover, pre-admission HRQOL in ICU patients was already lower than in a normal population.
Conclusion This study demonstrates that critical illness has a strong impact on HRQOL. A sharp multidimensional decline is followed by gradual recovery towards normal functioning. HRQOL recovery was, however, incomplete in physical functioning, general health and social functioning, and in comparison with the normal population.

P428

How are you feeling 6 months after your ICU discharge?

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Introduction Staying in an ICU is a distressing event that can influence quality of life (QOL). We compared the QOL of patients 1 month before hospitalization and 6 months later.
Methods The study included all adult patients who stayed for more than 24 hours in a mixed, 31-bed, medico-surgical ICU of a university hospital, between 3 June and 13 November 2004. During their ICU stay, we questioned patients or their relatives about their QOL (EuroQOL-5D) 1 month before hospital admission, and collected all their data. Six months after ICU discharge, we questioned the surviving patients again, by telephone or by letter, about their QOL at that time and their memories about the ICU stay.
Results Six months after ICU discharge, 68% of respondents perceived the general state of their health to be the same as or better than it had been before hospitalization ($P < 0.001$). The global EuroQOL-5D 6 months after ICU discharge was somewhat lower (i.e. QOL somewhat better) than before hospitalization, although this was not significant ($P = 0.12$). Each component of the EuroQOL-5D (mobility, autonomy, usual activities, pain/discomfort, anxiety/depression) was the same as or better after ICU discharge than before hospitalization in the majority of the respondents ($P < 0.001$). If necessary, 92% of patients said they would return to the ICU, 5% would not return and 3% did not know ($P < 0.001$). The most common disturbing memory was loss of orientation in time (36%) and the item perceived as most important was fear of dying, with a grade of 8 on a scale from 0 to 10.
Conclusion In our experience, the general state of patients' health and their quality of life 6 months after hospitalization in an ICU was the same as or better than 1 month before, in the majority of respondents. Most patients would agree to be readmitted to the ICU if necessary. Loss of orientation in time was the most commonly reported disturbing memory and fear of dying was the most important item.

P429

Differences in ICU admissions for the elderly between the United States and the United Kingdom

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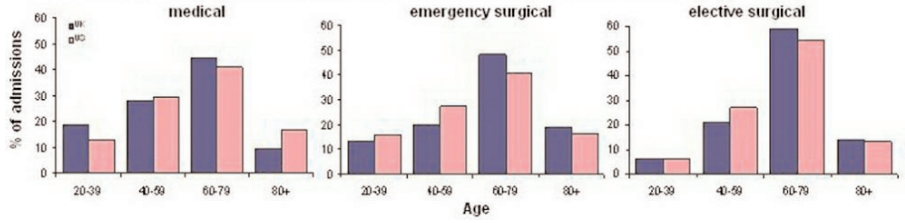
Background Conventional wisdom holds that ICUs in the United States are more likely to admit very elderly patients than ICUs in many other developed countries. However, adequately representative datasets upon which this hypothesis could be tested have been lacking. We therefore compared patient age distributions in a very large dataset of US and UK ICU patients.
Methods We analyzed a dataset of ICU admissions to 352 adult general medical, surgical and medical–surgical ICUs in the United Kingdom and the United States from 1997 to 2004. The dataset was constructed from the UK Case Mix Programme Database (Intensive Care National Audit & Research Centre, UK) and the US Project IMPACT database (Cerner, USA). Both databases include ICUs from a broad mix of hospitals from their respective countries. All variables used in the final dataset were validated as being defined and collected similarly in both countries and patients less than 20 years old were excluded.
Results The cohort consisted of 635,630 admissions, of which 315,118 (49.6%) were admissions to 172 ICUs in the United Kingdom (excluding Scotland) and 320,512 (50.4%) were admissions to 180 ICUs in the United States. While the UK population is slightly older than the US (median age 39.0 vs 36.3), the median age of admissions to the ICU was 65 years in both countries (interquartile range: UK 51–75 years; US 50–76 years). Medical admissions represented 53.1% of all admissions in the United Kingdom, and 62.9% in the United States. The United States admitted more elderly medical ICU patients (16.8% vs 9.4% of cases 80+ years old) (see Fig. 1). For emergency surgery admissions, a smaller percentage were age 40–60 in the United Kingdom (20.0% vs 27.1% in the US), and a greater percentage were age 60–80 (48.1% vs 41.0% in the US); the age distributions of elective surgery admissions was very similar in the two countries.

Figure 1 (abstract P429)



Comparison of the age of adult admissions to intensive care in the UK and USA.

Conclusion The overall age distribution of ICU admissions is similar between the United States and the United Kingdom, but the United States admits many more very elderly patients with acute medical conditions. Although this finding could be due to differences in sampling of ICUs, it most probably represents differences in admissions decisions in the two countries.

P430

Intensive care capacity in Denmark

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Since most admissions to intensive care are acute, patient flow in the ICU can hardly be controlled. Furthermore, ICU beds are costly. Consequently, a shortage of ICU beds is a common occurrence. However, there is a lack of precise figures describing the magnitude of this problem. We therefore conducted a survey to investigate the available ICU resources in Denmark. The survey consisted of two parts. The first part was a questionnaire sent to the directors of all ICUs in Denmark. This questionnaire described the staffing and resources of the ICUs and the perceived magnitude of the 'ICU full' problem. In the second part, bed availability and occupancy in all Danish ICUs was measured twice daily in two separate weeks. Furthermore all transfer of patients due to lack of resources (beds) was recorded.
The total number of ICU beds was 386 during workdays and 354 during weekends, corresponding to 2.1% and 2.0% of the total number of hospital beds in Denmark. As Denmark has a population of around 5,500,000, this is about 7 (6.4) ICU beds/100,000 inhabitants. With 49 ICUs in Denmark there were 1386 measuring points in the second part of the investigation. In 418 instances (30%) the ICUs were reported to be full, and during these 2 weeks there was a total of 32 patients who were transferred to other ICUs because of bed shortage, corresponding to 834 transferrals per year.

P431

Mortality as a measure of lack of ICU availability

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Background Patients who need intensive care but are not admitted to the ICU have a poor outcome, while demand for ICU beds exceeds supply. Patients dying outside the ICU might include those for whom ICU care has been refused, and as a result have had a poor outcome. Examination of patients dying outside the ICU could therefore reveal the extent to which ICU refusal is associated with subsequent mortality, and for which patients.
Hypotheses That a request for ICU admission has been made for a significant proportion of patients dying in non-ICU admission areas, and that access to ICU care for fatally ill patients is not equal for all hospital departments.
Methods Over a 6-month period, demographic data were collected on all patients who died in the Hadassah Hebrew University Medical Center, Jerusalem, both in and out of the ICU. For those dying outside the ICU, the treating physicians were interviewed regarding do-not-resuscitate (DNR) status, requests for ICU admission, or the reasons why ICU admission was not requested.
Results Overall 366 patients died during the study, 244 (67%) outside ICUs and 122 (33%) within ICUs. Of the patients dying outside the ICU, a request for ICU admission was made and refused for only 18/244 (7%) patients. Of these, six (33%) were assigned a DNR order. Among the 226 patients for whom ICU was not requested, 71 (31%) were not DNR. The ICU was not requested for the following 106 reasons (more than one possible per patient): poor prognosis (42 [40%]), patient died suddenly or found dead in bed (33 [31%]), no indication (12 [11%]), severity of underlying disorders (9 [8%]), advanced age (4 [4%]) and others (6 [6%]). The treating physicians believed that ICU care could have been beneficial for 20/71 (18%) of these patients.
Among non-DNR patients dying outside the ICU, 67/71 (94%) were from medical wards and the remaining four (6%) patients from surgical wards, as compared with 69/122 (57%) medical and 53/122 (43%) surgical patients among those dying in the ICU ($P < 0.0001$). The mean age of the patients dying outside the ICU was 70 ± 18 years vs 63 ± 20 years for those dying in ICUs ($P = 0.0153$).
Conclusion ICU care is requested for only a minority of patients dying on hospital wards, even when patients are not defined as DNR, and when the treating physicians believe that this care might be beneficial. Few surgical patients die outside the ICU (as compared with medical patients), while patients dying in ICUs are younger.

P432

Is the benefit of a post-ICU follow-up service dependent on the risk of death pre-ICU discharge?

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Introduction The introduction of a post-ICU follow-up service has been shown to reduce post-ICU deaths [1]. However, follow-up may be less effective in patients at high risk of death at ICU

discharge and would then lead to a selection of deaths with more risk factors after the introduction of a post-ICU follow-up service.

Methods A retrospective database survey was performed. All deaths in the year before follow-up were compared with all deaths after a follow-up service was established. Known risk factors predicting post-ICU death were compared between both groups of deaths: age, sex, APACHE scores, LOD scores at discharge, source and type of admission and co-morbidity. Source of admission was classified as ward vs nonward and type of admission as acute surgical vs other. Co-morbidity was classified as present or absent according to the APACHE system classification of chronic illness. Differences between means of continuous variables were tested by Student *t* test. Differences between proportions were tested by the method as described by Armitage [2]. $P < 0.05$ was considered statistically significant.

Results Twenty-seven deaths were identified in each period. A total of 16 complete datasets were available for analysis. There was a trend towards lower mortality after establishment of a follow-up service (8.76% vs 10.26%). Patients who died after establishment of a follow-up service had undergone significantly more acute surgery and showed a trend towards higher APACHE and LOD scores as well as a higher prevalence of co-morbidity.

Table 1 (abstract P432)

	Pre follow-up	Post follow-up	*P* value
Age (years)	76.6	75.8	0.43
Male sex (%)	71.4	55.6	0.26
APACHE	32	36.7	0.31
LOD	2.29	3.9	0.12
Night discharge (%)	28.6	11.1	0.19
Source: ward (%)	57.1	44.4	0.31
Acute surgical (%)	0	33.3	0.05
Co-morbidity (%)	14.3	22.2	0.35

Conclusion The effectiveness of a post-ICU follow-up service may be less, the higher the risk of death pre-ICU discharge.

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P433

Manganese and hepatic encephalopathy: a prospective study

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Critical Care 2006, **10(Suppl 1):**P433 (doi: 10.1186/cc4780)

Introduction We hypothesized that the manganese (Mn) concentration in the blood in cases of acute liver failure (ALF) and acute-on-chronic liver failure (ACLF) is associated with the Mn concentration in the liver tissue and cerebral globus pallidum and could be a marker of hepatic encephalopathy.

Methods Mn blood tests were performed for 129 patients (54 patients of control group, 29 with ALF and 46 with ACLF) admitted to the ICU from October 2003 to July 2005, and pathological samples of liver and brain tissues were analyzed from 34 dead patients whose relatives gave their consent for this procedure (10 of control, 11 of ALF and 13 of ACLF). The Mn concentration in the vein blood and organs was analyzed by graphite furnace atomic absorption spectroscopy.

Results The Mn concentration in the blood was significantly different ($P < 0.04$) in ALF (0.76 ± 0.06) and ACLF (1.04 ± 0.1) groups without significant difference between these two groups and the control group. The Mn concentration in the liver tissue was significantly different between all groups of patients ($P < 0.026$): the biggest one in ACLF patients (7.58 ± 1.0), and the smallest one in ALF patients (4.17 ± 0,7). The Mn concentration in the cerebral globus pallidum was also significantly different between all groups of patients ($P < 0.03$): the highest one in ACLF patients (4.17 ± 0.34), and the lowest one in ALF patients (1.71 ± 0.2). No statistically significant correlation was found between Mn concentrations in the tissues ($P \geq 0.075$) either in ALF or in ACLF groups of patients.

Conclusion The Mn concentration in the blood was not confirmed as a marker of hepatic encephalopathy in cases of acute and acute-on-chronic liver failure.

P434

High thoracic epidural improves postoperative cardiac outcome in ischemic patients undergoing major abdominal surgery

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Background Postoperative cardiac morbidity (PCM) continues to pose considerable risks to surgical patients. High thoracic epidural analgesia (HTEA), with its selective blockade of cardiac sympathetic innervation, has been used for treatment of medically or surgically refractory angina pectoris. However, its use in patients with coronary artery disease (CAD) undergoing noncardiac surgery has not been adequately investigated.

Objective To investigate the effect of HTEA on PCM in patients with established CAD undergoing major abdominal surgery as opposed to a comparable analgesic technique: low thoracic epidural analgesia (LTEA).

Method After approval, 30 patients with CAD undergoing major abdominal surgery were included. Before general anesthesia, they were randomly allocated to receive HTEA or LTEA for both intraoperative and postoperative pain relief. In addition to haemodynamic measurements, PCM was investigated by comparing the preoperative ECG, echocardiography and troponin I

Table 1 (abstract P434)

	Group I = 15	Group II = 15	*P* value
Sex: male/female	10 (66)/5 (33)	9 (60)/6 (40)	NS
Age (years)	56.6 (0.8)	56.7 (0.8)	NS
Weight (kg)	73.5 (1.9)	76.5 (2.1)	NS
Goldman risk	5.7 (0.6)	6.3 (0.8)	NS
Operative time	3.8 (0.2)	3.5 (0.3)	NS

Table 2 (abstract P434)

	Group I = 15	Group II = 15	*P* value
Ischemia			
By echocardiography	2 (13.3%)	8 (53.3%)	<0.05
By ECG	0 (0%)	5 (33.3%)	<0.01
Infarction			
By echocardiography	0 (0%)	2 (13.3%)	NS
By ECG	0 (0%)	1 (6.7%)	NS
By tropinin I	0 (0%)	2 (13.3%)	NS

with the postoperative ones done on the first, third and seventh days. Data are expressed as the mean (SE).
Results Cardiac morbidity was only diagnosed in 13.3% of patients in the HTEA group (Group I). In the LTEA group (Group II), 53.3% were found to have new ischemic changes and 13.3% developed postoperative MI. There were no reported cases of cardiac mortality. The absolute risk reduction was 53.3% and the NNT was 2.
Conclusion HTEA in patients with CAD undergoing noncardiac surgery has resulted in a reduced postoperative cardiac morbidity. It may be worthwhile establishing this technique, unless contra-indicated, in such patients.

P435

Addition of propofol, midazolam, or haloperidol to sufentanil for intravenous sedation in the ICU using the bispectral index

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Objective Inadequate sedative techniques may adversely affect morbidity and mortality in the ICU, and the search for the ideal sedative agent continues. Combinations of hypnotics and opiates have become commonly used for sedation. In our study, we aimed to assess whether the addition of propofol, midazolam, or haloperidol infusion decreased or not the sufentanil requirements using the bispectral index (BIS).
Materials and methods The study was planned in 60 ICU patients. All patients received 0.5 mg/kg sufentanil i.v. bolus. Immediately after, Group S received 0.25 mg/kg sufentanil infusion, Group SP received sufentanil infusion + propofol 25 mg/kg/min infusion, Group SM received sufentanil infusion + midazolam 0.04 mg/kg/hour infusion, and Group SH received sufentanil infusion + haloperidol 3 mg/kg/hour infusion for 6 hours. Average BIS values were kept in the range of 61–80 by decreasing or increasing sufentanil levels in all groups, and hourly sufentanil consumption was determined. Hemodynamic, biochemical parameters, and arterial blood gases were determined at baseline, and were repeated in study hours.
Results There was no significant difference in hemodynamic and biochemical parameters and arterial blood gases among the groups. Propofol, midazolam, and haloperidol infusion, when added to sufentanil infusion, decreased the consumption of sufentanil in all the measured times ($P < 0.001$).
Conclusion We aimed to determine the effect of propofol, midazolam, or haloperidol infusion when added to sufentanil infusion in a short period of time, and found that propofol, midazolam, or haloperidol infusion decreased sufentanil requirements in ICU patients.

P436

Remifentanil dosage in critically ill patients is independent of organ dysfunction

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Introduction Continuous analgo-sedation of ICU patients with established opioids is difficult due to unfavorable pharmacokinetics, especially in patients with major organ dysfunctions. Remifentanil (RF) is more suitable for these patients because of its short half-life independent of the duration of the preceding infusion and organ functions. No large observational study has investigated the influence of multiple organ dysfunctions and old age on the dosage and duration of RF infusion in critically ill patients.
Methods Set in a general surgical ICU of a university hospital. Within 28 months, 876 postoperative patients requiring ventilation received analgo-sedation with a constant low-dose propofol infusion (1.5 mg/kg/hour) and a variable continuous RF infusion to a target Ramsay Sedation Score 2–3, until either ventilatory withdrawal was initiated or sedation regimen was changed after 48 hours. The hourly dosage and total duration of RF infusion, and the SOFA score were documented. Potential predictors for RF dosage were evaluated by univariate and subsequent stepwise multiple regression analysis. Significance was set at $P < 0.05$.
Results The median (±IQR) SOFA score was 7 ± 4, infusion duration 16 ± 12 hours, age 70 ± 29 years, mean (±SD) RF dosage 87 ± 44 ng/kg/min. Neither the total SOFA score or any single composite organ dysfunction influenced the dosage of RF infusion (Table 1). However, older patients needed considerably smaller RF dosages. Patients with multiple organ dysfunction had prolonged infusion duration, but no change in dosage. After discontinuation of RF infusion, all patients were awake and extubated within 1–2 hours.

Table 1 (abstract P436)

	SOFA score	Renal dysfunction	Liver dysfunction	Age
RF dosage	$P = 0.59$	$P = 0.11$	$P = 0.12$	$P = 0.0002$
Infusion duration	$P < 0.001$	$P = 0.40$	$P = 0.001$	$P = 0.22$

Conclusions In critically ill ventilated postoperative patients, even multiple severe organ dysfunctions do not alter the dosage of continuous RF infusion. Due to predictable pharmacokinetic properties and reliably short extubation times, RF may be the most adaptable and safest choice for these patients. Actual dosages necessary to provide appropriate analgo-sedation are lower and therefore less costly than expected, especially in older patients. Further studies to evaluate a cost–benefit ratio and to afford dosage recommendations for RF analgo-sedation in ICU patients are warranted.

P437

Remifentanil versus sufentanyl narco-sedation in a surgical and medical critical care unit with prevention of narcotic-induced hyperalgesia: a randomized double blind study

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Critical Care 2006, **10(Suppl 1):**P437 (doi: 10.1186/cc4784)

Background The authors hypothesized that the efficacy of a remifentanil-based regimen (R) with prevention of narcotic-induced hyperalgesia (NIH) [1] by magnesium sulphate (MS), ketamine (K) or clonidine (C) was greater than that of a conventional sufentanyl-based regimen (S).
Methods One hundred patients were randomly allocated to receive a blinded infusion of either R at a rate of 0.15 μg/kg/min (±0.10 μg/kg/min) (G1: $n = 50$) or S at 0.35 μg/kg/min (±0.15 μg/kg/min) (G2: $n = 50$). The opioid infusion was titrated, in the first intent, to achieve optimal sedation as defined by a Sedation Agitation Scale (SAS) of 4. NIH in G1 was realised by infusion of MS (0.008 mg/kg/hour), K (0–8 μg/kg/min) or C (0–0.01 μg/kg/min) depending on hemodynamic stability. A tramadol open-label (0.25 mg/kg/hour) infusion was started if additional analgesia was required. Sedation was performed in all patients with a propofol infusion (0–6 mg/kg/min). The SAS was maintained between 3

and 4. For statistical analysis a Shapiro–Wilk test, Wilcox test and a Student *t* test were used.

Results The mean percentage hours of optimal sedation was significantly longer in the R group (108.3 ± 26.3 = 5.5 days) than in the S group (86.5 ± 6.5). This was achieved with less frequent infusion rate adjustments (0.34 ± 0.25 changes/hour) than in the S group (0.42 ± 0.22 changes/hour). The mean durations of mechanical ventilation were comparable in both groups (76 ± 14 hours SD). The extubation time were significantly longer in the S group (22.1 ± 4.4 hours, 75 ± 5 min) than in the R group (4.1 ± 2.0 hours, 10 ± 6 min), respectively ($P < 0.001$). The total mean hospitalisation time in the ICU was reduced by 48 ± 8 hours in G1 compared with G2 ($P < 0.005$). The R mean infusion rate was 0.12 ± 0.9 μg/kg/min, whereas the S mean infusion rate was 0.38 ± 0.14 μg/kg/min. More subjects in the S group (32 of 50) than in the R group (6 of 50) required tramadol ($P < 0.001$). The mean EVA at the end of the ICU stay was for G1: 1 ± 1 and for G2: 2 ± 3 ($P < 0.005$). The incidence of adverse events was low and comparable across the two treatment groups. The global hospitalisation cost shows a 26% reduction for patients in G1 despite a raise of 8% when R is used compared with S.

Conclusions A remifentanil-based regimen was more effective in the provision of optimal analgesia sedation than a standard sufentanyl-based regimen. The remifentanil-based regimen allowed a more rapid emergence from sedation and facilitated earlier extubation, and so diminished total ICU hospitalisation time and cost. The prevention of NIH allows an optimal narco-sedative level without increased doses of remifentanyl and lower needs for analgesics at the end of ICU hospitalisation.

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P438

Sufentanil versus fentanyl in intraoperative and postoperative periods in pediatric patients

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In our study we compared sufentanil vs fentanyl in children undergoing Lich–Gregoir antireflux plasty. The aim of this study was to evaluate and compare the hemodynamic parameters during anesthesia as well as the time of extubation of both opioid analgesics.

Patients were included in two groups of 20 patients: group I, sufentanil and group II, fentanyl (mean age 5.42 ± 3.25 years; mean body weight 15.87 ± 4.02 kg). All were premedicated with midazolam 0.2 mg/kg intranasally, 10 min before induction of anesthesia. Anesthesia was induced with sufentanil 0.5 μg/kg (group I) or fentanyl 2 μg/kg (group II) and propofol 3–4 mg/kg, followed by vecuronium 0.1 mg/kg. Anesthesia was maintained using isofluorane in oxygen and nitrous oxide. In group I sufentanil was administered in the dose of 1 μg/kg intravenously prior to skin incision. In group II fentanyl was administered in the dose of 1 μg/kg intravenously at the same time. Hemodynamic parameters such as systolic and diastolic blood pressures and heart rate were recorded.

Following induction of anesthesia and tracheal intubation, hemodynamic parameters in group I did not increase. During intubation patients in group II showed an increase of measured hemodynamic parameters. The average time before postoperative tracheal extubation was 62.20 ± 15.55 min in the sufentanil group and 75.27 ± 10.20 min in the fentanyl group, which was statistically significant. In the ICU pain and overall satisfaction were assessed with a 10-point visual scale. There was no difference in the requirements for pain relief.

Our study showed that sufentanil versus fentanyl in an appropriate dose does not change hemodynamic parameters during anesthesia induction. Postoperative requirements for pain relief were the same in both opioid analgesics.

P439

Sparing analgesic effect using pregabaline in postsurgical trauma patients in the ICU

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Introduction Pregabaline (Lyrica®), a γ-aminobutyric acid analogue, reduces neuropathic pain more than placebo does and is well tolerated [1]. We wanted to determine the possible sparing effect over piritramide demands when pregabaline was given as soon as acute pain occurred in postsurgical trauma patients.

Methods Thirty-three polytrauma patients needing orthopaedic surgery were admitted to our ICU during a 10-month period of time. On average, enteral feeding could be given 2 days after surgery and the prospective double-blind randomized study began thereafter. Two groups were defined: the control group (Gc: $n = 21$) receiving placebo every day via nasogastric tube, and the second group (Gp: $n = 22$) receiving pregabaline using the same route (T1: days 1–2, 75 mg/12 hours; T2: days 3–7, 150 mg/12 hours; T3: days 8–35, 300 mg/12 hours). Every patient received intravenously perfusalgan (1 g/6 hours) and piritramide via an infusion pump for patient-controlled analgesia (bolus 2 mg/10 min with a maximal dose of 12 mg/hour) when the Visual Analogue Scale was over 4. Piritramide consumption (Pc: total bolus delivery) was noted every day in every group. This study was approved by the Ethics Committee of the Centre Hospitalier Kirchberg and informed consent was obtained for each patient via family members. For statistical analysis a Shapiro–Wilk test, Wilcox test and a Student *t* test were used.

Results Demographic data were comparable in both groups in terms of age (38 ± 19 years), gender (32% female in Gc vs 35% in Gp) and injuries (ISS: 18 ± 8). The total mean hospitalisation time in ICU was similar in both groups (Gc: 25 ± 6 days; Gp: 22 ± 10 days). In Gp two patients died at days 11 and 16 from septic complications, in Gc three patients died at days 8, 19 and 22 from septic shock, lung emboly and multiple organ failure. The average Pc values at T1 do not differ significantly between groups (Gc: 36 ± 2; Gp 33 ± 2). At T2 significant differences appeared showing a decrease in Pc by 22% in Gc (28 ± 2) and by 42% in Gp (19 ± 1) ($P < 0.005$). At T3 a more significant decrease of 78% in Pc was observed in Gp (4 ± 4) and of 46% in Gc (15 ± 6) ($P < 0.002$). No neurological adverse effects were described in Gp.

Conclusion In this study, pregabaline was used for the first time as a preventive analgesic drug and showed its importance by sparing piritramide consumption in postsurgical trauma patients. Pain control became more efficient by diminishing stress and thus co-morbidity factors. This could effectively reduce the future occurrence of chronic pain, cost and thus improve quality of life upon discharge from the hospital.

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P440

Assessment of sedation in patients with pressure-controlled ventilation: tidal-volume variance, sedation scores or bispectral index?

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Background Mechanical ventilation is nonphysiological and usually requires sedation. The assessment of sedation is not standardised. Until now, clinical criteria and several scores are used to assess sedation (Ramsay Score [RS], Cook and Palma Score [CPS], Cohen and Kelly Score [CKS], Chamorro Score [CS], linear Sedation Score [LSS] and RASS). Time-consuming apparative methods such as EEG are not routinely used. The bispectral index (BIS) is promising, but not routinely available. Biologically, variability of ventilation parameters is a well-known phenomenon; however, it is not used to assess sedation. It was therefore the aim of our study to investigate the correlation of tidal-volume variance (TVV) and the aforementioned sedation scores.
Materials and methods In 80 patients of an internal ICU with MOF, pressure-controlled ventilation and continuous sedation, RS, CPS, CKS, CS and LSS were independently documented by physician (P), nurse (N) and investigator (I; not working in the ICU). Subsequently 200 consecutive tidal volumes were documented. TVV was calculated and compared with the aforementioned sedation scores. Additionally TVV was compared with the BIS. Ventilation was according to ARDSnet recommendations, Siemens Servo 900C or Servo300, Trigger –2 cmH_2O. Statistics: SPSS software, Spearman correlation.
Results Patient characteristics (mean ± SD): age 57.4 ± 15.4 years, 28 female, 52 male, APACHE II score 28.2 ± 6.6; number of organ failures 4.0 ± 1.12; preceding ICU period 8.5 ± 9.3 days; continuous sedation with midazolam 31.2 ± 34.2 mg/hour, fentanyl 0.12 ± 0.08 mg/hour, propofol 45.6 ± 105.2 mg/hour; sedation assessment according to RS 5.65 ± 0.63, CPS 5.15 ± 1.67, CKS 0.65 ± 0.69, CS 9.34 ± 2.13 und LSS 1.78 ± 1.69, RASS –4.50 ± 1.27, FiO_2 0.52 ± 0.17, PEEP 8.2 ± 2.4 cmH_2O, ventilatory frequency 20.5 ± 4.8/min, pressure control 16.8 ± 4.4 cmH_2O, tidal volume 540 ± 115 ml, TVV 2525.6 ± 11,366 ml (minimum 1.52; maximum 91,586).
Despite the limited number of patients there was a significant correlation of TVV and the sedation scores (coefficient of correlation of TVV compared with the sedation scores of P, N and I, respectively: $*P < 0.05$; $**P \leq 0.01$, NS = not significant): CKS: 0.32**; 0.408**; 0.396**; CS: 0.212^{NS}; 0.371**; 0.394**; LSS: 0.345**; 0.407**; 0.423**; CPS: 0.413**; 0.363**; 0.388**; RS: -0.2^{NS}; -0.20^{NS}; –0.261*; RASS: 0.23*; 0.188; 0.289**. Additionally, TVV significantly correlated with BIS values (41.3 ± 18.8; Spearman coefficient 0.461**).
Conclusions Calculating TVV is a simple and cheap tool for sedation assessment in patients with pressure-controlled ventilation.

P441

Risk factors for unplanned extubations in critically ill patients, using PRISMA analysis

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Introduction Unplanned extubations (UEs) occur in 4.2–14% of critically ill patients on mechanical ventilation. UE is defined as premature removal of endotracheal tube. UEs are associated with increased morbidity, mortality and utilisation of resources. We collected data from patients who extubated themselves during a 6-month period. The aim of the study was to assess risk factors for UE using the Prevention and Recovery Information System for Monitoring and Analysis (PRISMA) method. The method is used in the chemical and steel industry, and nowadays in health care. The goal of this method is to build a quantitative database of incidents and process deviations from which conclusions may be drawn to suggest preventive measures. Incidents are described by means of causal trees to identify root causes.
Method In a 28-bed surgical, thoracic surgical and medical ICU 24/7 all UEs were directly reported by telephone to the main investigator. By means of a structured interview, data on the specific circumstances of the UE were obtained from the nurse and doctor involved. By exploring the situational characteristics of a UE by interviewing medical and nursing staff, we developed in collaboration with professionals in Patient Safety Systems a causal tree consisting of three main contributing actions: inadequate treatment agitation, patient nonacceptance of tube, and no prevention of UE. Each UE was analysed by two investigators independently to identify which of the main actions contributed. Combinations of causes were subsequently identified, leading to identification of root causes.
Results Twenty-five patients were enrolled with 640 ventilation periods and 2962 ventilation days. This yielded an incidence of 3.9% and 0.8 UEs per 100 ventilation days. The mean age was 58.2 ± 17.0. Male–female ratio was 2.1. The mean APACHE score was 16.6 ± 5.0. At the time of UE, the mean Ramsay sedation score was 1.88 ± 0.7 and the weaning–nonweaning ratio 1.8. Reintubation was needed in 48% of the cases.
In 32% of the patients, inadequate treatment agitation led to UE. In the case of patient nonacceptance of tube (56%), 57% patients were in delirium and 43% were fully conscious left unnecessary intubated. In 83% this delay in extubation despite good clinical condition was due to suboptimal management. In 16%, the decision to extubate the patient was not executed because of the night hour. No prevention of the actual extubation was in 64% related to no detection that occurred because personnel was busy elsewhere (80%) and/or not expecting the extubation (94%). No expectation coincided with false assessment of adequacy of the fixation technique (92%).
Conclusion Incident analysis by the PRISMA method is a feasible method to identify contributing factors to UE. Optimalisation of agitation treatment and extubation protocols, and increased awareness of high-risk conditions, could prevent UEs.

P442

Novel measure for EEG/EMG responsiveness may indicate the level of sedation in ICU patients

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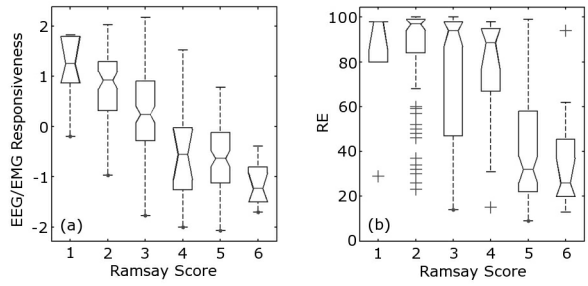
Introduction The level of sedation in ICU patients is difficult to assess, and relies on clinical assessments such as the Ramsay score. These tests discriminate deep sedation poorly. We evaluated a novel measure, EEG/EMG responsiveness, and compared it with Ramsay scores. EEG/EMG responsiveness was calculated by applying an algorithm that detects abrupt changes in the measured EEG signal indicative of a patient's arousal or activation. The results were compared with those obtained using the EEG entropy.

Figure 1 (abstract P442)



Methods Thirty consenting general ICU patients with non-neurologic primary ICU diagnosis were investigated for a maximum of 72 hours. The Response Entropy (RE) and State Entropy (SE) values as well as the EEG signals from which the EEG/EMG responsiveness was calculated were recorded from forehead electrodes using the Entropy™ Module (GE Healthcare). When possible, the Ramsay score was evaluated every 30 min by a single trained observer, amounting to a total of 370 assessments.

Results Figure 1a,b shows the distributions of the EEG/EMG responsiveness and RE values for the six Ramsay levels. The box diagrams indicate the median and quartile values. The obtained prediction probability $P_K = 0.86$ for EEG/EMG responsiveness to distinguish deep Ramsay levels 4–6 from levels 1–3 was significantly higher than the corresponding P_K values 0.80 and 0.79 for RE and SE ($P < 0.05$). In the subgroup of 18 patients judged clinically to have no acute brain disorders, the P_K values for EEG/EMG responsiveness, RE, and SE (0.91, 0.85, and 0.84) were significantly higher ($P < 0.001$) than those in the remaining subgroup of 12 patients with encephalopathy (0.78, 0.73, and 0.75).

Conclusion The novel measure of EEG/EMG responsiveness shows promise as an indicator for the level of sedation.

P443

Delirium impact in a chronic ventilatory care unit

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Background Delirium is a common but underdiagnosed and treated problem in the ICU. It has been associated with poor hospital outcomes, including increased morbidity and mortality, prolonged length of stay and functional decline. Recently published clinical practice guidelines from the Society of Critical Care Medicine recommended monitoring for the presence of delirium in all mechanically ventilated patients.

Objectives To compare the usual clinical assessment for delirium and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), to describe its characteristics in chronically ventilated patients and to evaluate the incidence, associated clinical conditions, use of antipsychotic drugs and late mortality.

Patients and methods A prospective observational study where delirium was evaluated on a daily basis and followed by a group of physicians and a nurse, previously trained. Thirty-five consecutive patients were admitted to the Ventilatory Care Unit (VCU) during a period of 9 mouths. Thirteen tracheotomized, mechanically ventilated, awake and cooperative subjects were included in the study protocol. Three of them returned to the VCU after discharge and were re-included, resulting in a total of 16 patients studied. The CAM-ICU tool was applied 5 days a week at same time in the afternoon and its data was compared with the physicians' and nurse's evaluation. The results are expressed as the mean ± SD. For statistical analysis we used the chi-square test for evaluated difference of proportion, and considered statistical significance as $P < 0.05$.

Results Five females and 11 males were studied. The mean age of the study population was 66.46 ± 14.98 and the mean APACHE II score 18 ± 4.6. Delirium occurred in seven patients (43.8%) during the VCU stay and the CAM-ICU tool detected 68% of it. The mean onset was 11.17 ± 8.91 days and the mean duration was 1.62 ± 0.94 days. New infection was associated with delirium in 30.7% of cases; however, using the CAM-ICU tool this association increased to 56% ($P = 0.16$). Comparing the mean titulated C reactive protein (CRP-t) level and insulin dose used in patients diagnosed with delirium (D group) and no delirium (ND group) was not significant (Table 1). Sensorial deficit was not present in any patient without delirium. Mortality after 30 days was not significant between both groups. Olanzapin and bromazepan were the most prescripted drugs.

Table 1 (abstract P443)

	D group	ND group	*P* value
CRP-t	9.6 ± 5.5	7.5 ± 3.5	0.37
Insulin	46.4 ± 29.7	40.3 ± 33.5	0.76

Conclusion The incidence of delirium in this study was less than expected. CAM-ICU demonstrated inferior sensibility than that described in the literature. We could not demonstrate any difference between groups. The main limitation of this study was the low number of patients enrolled.

P444

The shot-time protective effect of hypoxic preconditioning on ischemia/reperfusion brain

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Objective To observe that hypoxic preconditioning (HP) plays a protective role on ischemia/reperfusion (I/R) brain within a short period. This experiment proved that HP can protect I/R brain by abating death and apoptosis of cells in the hippocampus; furthermore, HP also improved cognition at the fifth day after I/R.

Method Male Sprague–Dawley rats (250–300 g) were used in this experiment. Rats were divided into four groups randomly – sham group, control group (I/R), A group and B group – 16 rats in each group.

Ischemia was induced by withdrawal of 6–10 ml blood from the jugular catheter so as to reduce the mean arterial blood pressure to 25–30 mmHg. The carotids were then occluded with aneutysm clips, and was confirmed by the presence of an isoelectric electroencephalogram. To terminate ischemia, shed blood was reinfused, and the aneutysm clips were removed.

HP refers to rats exposed to 8% O_2 for 3 hours before I/R. The sham group was without HP nor I/R, the control group received I/R without HP. The A group and B group endured I/R with HP before 1 day and 2 days, respectively.

The rats underwent a behavioral test (water maze, Passive Avoidance Task) on the fifth day after I/R followed by histopathology and TUNEL analysis. Histopathology and TUNEL

analysis were performed for death and apoptosis of hippocampus cells, respectively.
All values are expressed as means ± SEM in experiments. Statistical analysis was assessed by one-way ANOVA. $P < 0.05$ was considered significant to reject the null hypothesis.
Results Histopathology showed that I/R resulted in tissue loss and necrosis in the CA1 and CA3 regions, death cells in the control group increased compared with the sham group, $P < 0.01$.The numbers of necrosis cells in CA1 and CA3 of the A group and B group all were significantly lower than the control group, $P < 0.01$. Moreover there were less death cells in the B group than in the A group $P < 0.05$, but there was no difference between the CA1 and CA3 regions. In the TUNEL staining assay, the apoptotic cells were stained brown. The number of TUNEL-positive cells was higher in the sham group than in the control group, $P < 0.01$. The number of apoptotic cells in the control group is more than in the A and B groups ($P < 0.01$), the degree of apoptosis was less in the B group compared with the A group, $P < 0.05$. There was no difference between CA1 and CA3 regions in all groups. The water maze and Passive Avoidance Task showed that the learning and memory ability of rats in the control group was injured after I/R, contrasting with the sham group $P < 0.05$. HP can improve cognition; learning and remembering ability in the A group and B group was significantly better than the control group, $P < 0.05$, especially in the B group. The movement test also offered similar result as these
That I/R can injure the brain has been confirmed by many authors; furthermore, I/R can also impair learning and memory ability. HP was discovered to be a protective method against I/R injury recently. In our experiment, HP can relieve necrosis and apoptosis of the hippocampus CA1 and CA3 regions. Moreover HP improved cognition and movement at day 5 after I/R obviously. From these results it was discovered that HP applied 2 days before I/R can produce more effective function than at 1 day before I/R. In a word, HP can improve cognition a short time after the brain receives I/R, and it is possible that HP played this role by deceasing necrosis and apoptosis cells in CA1 and CA3 of the hippocampus.

P445

Influence of intracellular astrocyte acidification on the behavior of cell volume and intracellular sodium

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Objective In the time course of stroke or traumatic brain injury, astrocytes become acidotic and swollen. The question remains whether acidosis influences intracellular sodium concentrations and the astrocyte volume.
Methods In cultured human astrocytoma cells, the effect of sodium propionate (NP) or ischemic medium (IM) on the cellular volume and intracellular hydrogen or sodium was documented by videomicroscopy and monitoring of the fluorescence of BCECF and SBFI, respectively. To quantify the participation of a Na^+/H^+ exchanger, a specific inhibitor (ethyl isopropyl amiloride [EIPA]) was added.
Results Addition of NP resulted in an immediate intracellular acidosis, which only partially recovered after washout, and an immediate rise in intracellular sodium. NP introduced an increase of cell diameter to 120 ± 2%, followed by a reactive volume decrease within 15 min. EIPA was able to partially inhibit intracellular acidification (5 μM EIPA), and to abrogate cell swelling (10 μM EIPA). Comparable results were found with IM.
Conclusion Intracellular astrocyte pH increase found during life-threatening brain conditions influence astrocyte swelling. Na^+/H^+ exchangers participate in these pathways.

P446

Neuroprotective effects and mechanisms of fentanyl preconditioning against brain ischemia

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Introduction Fentanyl is an artificial agonist of opioids, and belongs to the μ-opioid receptor agonists. During cardiopulmonary bypass (CPB), a large dose of fentanyl was administered (usually achieved 50–100 μg/kg, loading dose exceeded 50 μg/kg, maintenance dose was 20–30 μg/min). Since the advent of CPB, cerebral complications from overt stroke to subtle cognitive dysfunction after CPB for cardiac surgery have been well documented; the postoperative incidence of dysfunction of cognition exceeded 20–70%. The etiology of these injuries are probably associated with cerebral microemboli, global or regional ischemia, inflammation, cerebral temperature modulation and metabolic abnormality. There are disputes about the effects of large doses of μ-opioid receptor agonist; furthermore, evidence about the effect of large doses of fentanyl on brain injury during CPB have not been reported. Some researchers documented that μ-opioid receptor agonists (including morphine or fentanyl) had neuroprotective effects, and predominantly by the activation of δ1 opioid agonist. While reports that μ-opioid receptor agonists have no neuroprotective effect, even causing brain injury can also been seen.
Objective There have been some disputes about the clinical application of μ-opioid receptor agonists, and it is paramount to explore the effects and mechanisms of fentanyl on brain ischemia.
Methods In this study, we investigated the effects of fentanyl on cerebral ischemia during the perioperative period, and the mechanisms of neuroprotective effects modulated by subtype opioid receptors or the molecular signaling pathway were explored. This study consisted of three models: moderate hypothermia cardiopulmomary bypass in the rat, brain slices with oxygen-glucose deprivation (OGD), and PC12 cell lines with OGD. Immunohistochemistry, terminal deoxynucleotidyl transferase dUTP-bition nick end labeling (TUNEL) staining, electron microscopy, RT-PCR, western blot, TTC staining, LDH release, Flow CytoMeter and Hoechst33258 staining were used.
Results This protective effect of fentanyl preconditioning is U-shaped as demonstrated in the dose–response curves. It was found that micromolar concentrations of fentanyl are antiapoptotic, whereas with increasing concentrations fentanyl lacks apparent protective effects. Clinical concentrations of fentanyl preconditioning have neuroprotective effects against cerebral ischemia injury, and antiapoptosis is one of the underlying mechanisms. In detail, we demonstrated that moderate hypothermic cardiopulmonary bypass in the rat can induce hippocampal c-fos, bcl-2 and bax mRNA expressions and protein expressions, increase neuronal apoptosis, and worsen histology injury detected by electron microscope. F50 (fentanyl: LD = 50 μg/kg, MD = 2 μg/kg/min) or F800 (fentanyl: LD = 800 μg/kg, MD = 32 μg/kg/min) can attenuate brain ischemia injury induced by CPB, especially in the dose of 50 μg/kg. Furthermore, the same results were demonstrated in brain slices or PC12 cells with OGD injury. Either 50 ng/ml or 500 ng/ml fentanyl (the peak concentration or plateau concentration, respectively, of fentanyl

with loading dose 50 μg/kg) decreases neuronal apoptosis and inhibits the release of LDH so it can attenuate brain slice injury, Moreover, fentanyl preconditioning can strengthen the protein expression of Bcl-2 while Bax protein expression was inhibited. Compared with fentanyl 500 ng/ml, fentanyl 50 ng/ml played a stronger role in brain slices or PC12 cells with OGD injury.
In addition, we determined that δ-opioid receptors are unique and have a specific role in neuroprotection against OGD injury by activating the MAPK pathway, specifically through δ1-opioid receptors. In detail, fentanyl preconditioning had a protective effect on brain slices with OGD injury. The effect was mainly mediated by the δ1 subtype opioid receptor because the role of fentanyl preconditioning was blocked or attenuated by naloxone (a nonselective opioid receptor antagonist), naltrindole (nonselective δ-opioid receptor antagonist) and BNTX δ1-opioid receptor antagonist), respectively. However, naltriben (δ2-opioid receptor antagonist), β-funaltrexamine (μ-receptor antagonist) or norbinaltorphimine (κ-opioid receptor antagonist) cannot inhibit the protective effect of fentanyl preconditioning. Phosphorylated ERK1/2 was upregulated by fentanyl preconditioning. BNTX or U0126 can block the ERK1/2 phosphorylation induced by fentanyl preconditioning, while the neuroprotective effect of fentanyl preconditioning was also abolished.
Conclusions Collectively, we found that fentanyl preconditioning played a role in neuronal protection against hypoxic ischemia, attenuated ischemia injury and inhibited apoptosis of neurons. δ-opioid receptors were unique and had a specific role in neuroprotection against OGD injury by activating the MAPK pathway, mainly through δ1-opioid receptors. μ-opioid receptor agonist can be safely applied to brain ischemia during CPB.

P447

Antiapoptotic action of delta opioid peptide [D-Ala2,D-Leu5]enkephalin against oxygen-glucose deprivation in brain slices

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Background The delta opioid peptide [D-Ala2,D-Leu5]enkephalin (DADLE) has been shown to play a role in neuronal protection against hypoxic ischemia. However, the cellular mechanisms of these actions of DADLE on neurons are not totally clear. Being an *in-vitro* model of brain ischemia, oxygen-glucose deprivation (OGD) injury in rat brain slices has the advantages of both *in-vivo* and *in-vitro* models, and therefore can imitate damages induced by brain I/R injury in intact animals. In the present study, we examined the protective mechanism(s) of DADLE against apoptosis using a rat brain slice model. In addition, we determined whether δ-opioid receptors are unique and have a specific role in neuroprotection against OGD injury by activating the MAPK pathway, specifically through δ2-opioid receptors.
Methods The brain slices were injured by OGD, and then incubated with different concentrations of DADLE. Selective δ2-opioid antagonist or selective inhibitor of ERK kinase was co-incubated with or without DADLE. The effects of DADLE against apoptosis in neurons were measured by the following biochemical and morphological assays: the LDH release, RT-PCR, western blot, and TUNEL staining.
Results This protective effect of DADLE is U-shaped as demonstrated in the dose–response curves. It was found that micromolar concentrations of DADLE are antiapoptotic, whereas micromolar concentrations of DADLE lack apparent protective effects. The protective effect of DADLE can be attenuated by a selective δ2-opioid antagonist. The treatment of cells with PD98059, a selective inhibitor of ERK kinase (MEK), blocked both the protective effect of DADLE and the ERK phosphorylation induced by DADLE.
Conclusions Our results suggest, therefore, that endogenous opioid peptides may, at low concentrations, promote cell survival via the MEK–ERK pathway, perhaps through δ2-opioid receptors.

P448

Role of optic nerve ultrasonography in the diagnosis of elevated intracranial pressure

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Objective In the evaluation of the emergency patients with elevated intracranial pressure (EICP) due to traumatic or nontraumatic causes, optic nerve ultrasonography (ONUS) has been researched in terms of convenience and utility.
Method Patients who visited the University of Selcuk, Meram Medical Faculty, Department of Emergency Medicine with traumatic or nontraumatic EICP were put through the study. Among these patients, 28 patients with EICP in their cranial computed tomography (CCT) and a control group of 26 patients with no disease had the vertical and horizontal diameters of the optic nerves of both of their eyes measured by ultrasonography. The measurements were done by wetting the closed eyelids and using the 7.5-MHz linear probe placed in a bag that was full of gel. In the statistical research carried out between these two groups (*t* test), it was found that $P < 0.001$. Also, the concordance among all the measurements made in the study was examined within the frame of the 'Concordance Correlation Coefficient' formula. Five of the six values found were over 0.90, and one of them just below 0.90; these results were a sign of support for concordance among the measurements.
Results In the study, the horizontal and vertical diameter measurements of both ONs of the 54 patients were done and then averaged. The mean ON diameter for the 28 patients in the study group was found as 6.4 ± 0.7 mm, and the mean ON diameter for the control group was 4.6 ± 0.3 mm. The ON diameter of all the control group was evaluated as normal, whereas the ON diameter of all the patients with brain edema in their CCT was raised.
Conclusion In detecting and following up the EICP cases such as cerebrovascular accident and trauma, ONUS is a method that is quite practical, risk free, of low cost, convenient and also reliable if done by experts. For the unconscious patients with no diagnosis, ONUS would be very helpful in eliminating an EICP cause and in leading these patients to CCT. In the case of EICP, the first finding is the dilation in the ON diameter, and with this feature it may be more useful, perhaps not in diagnosing, but in detecting EICP, than CCT. In the cases where CCT is not available, the use of ONUS would help lead the diagnosis and treatment of the patients.

P449

Traumatic subarachnoid haemorrhage in the ICU

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Objective A retrospective observational study to establish the traumatic subarachnoid haemorrhage (tSAH) ratio in all traumatic brain injury (TBI), the overall prognosis, and to determine whether the quantity and distribution of blood in subarachnoid space influences prognosis.

Materials and methods Over a period of 1.5 years, 98 patients were admitted diagnosed with TBI. Fifty-two (53.06%) had tSAH. The Greene classification was used to determine the degree of bleeding. We differentiated between patients with tSAH diffused in the convexity, in basal cisterns and those with bleeding in both (mixed pattern). We recorded the sex, age, Glasgow Coma Scale (GCS) and Glasgow Outcome Scale (GOS) at the time of discharge from acute hospitalisation. For the statistical analysis three groups of TBI were considered, according to the GCS: slight (GCS 13–15), moderate (GCS 3–7) and severe (GCS 3–7). Analysis was carried out to determine whether there were any positive or negative factors related to tSAH (paying particular attention to blood distribution). The relationship between age, Greene classification, GCS and GOS were evaluated by multiple logistic regression and chi-square test.

Results The prognosis of the patients with tSAH was worse (Table 1). Chi-square = 5.21 $P = 0.022$. The follow-up study was carried out until discharge from acute hospitalisation: 21 patients (40.38%) had a good prognosis and 30 (57.69%) had an unfavourable prognosis. The overall mortality was 21 (46.15%). There is no statistically significant relationship between tSAH distribution and the GCS on admission, but there is relationship between tSAH distribution and the GOS. A logistic regression model to evaluate the contribution of the GCS, degree of Greene classification and age with the GOS shows these results (Table 2).

Table 1 (abstract P449)

	tSAH	No tSAH
GOS 4–5	22	31
GOS 1–3	30	15

Table 2 (abstract P449)

	Odds ratio	95% CI
Age	1.36	0.65–2.86
Greene	1.14	0.80–1.63
GCS	1.09	0.82–1.45

Conclusion TSAH is a negative prognosis factor: the degree of tSAH is significantly related to the clinical condition on admission and the prognosis of the patient. The presence of tSAH in the cisterns and convexity (mixed pattern) indicates a worse prognosis. It is most frequently located in the convexity and basal cisterns.

P450

Survey of cerebral perfusion pressure measurement: location of the arterial transducer in the patient managed at 30° elevation

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Introduction In 2003 the Brain Trauma Foundation (BTF) published an update notice to its guidelines on the management of severe head injury in adults, focusing on cerebral perfusion pressure (CPP), this being the physiologic variable that drives cerebral blood flow. Guidance suggests that CPP should be maintained at a minimum of 60 mmHg.

Clinical practice in the United Kingdom may involve nursing the severely head-injured patient at an angle of 30°, although there is no consensus as to whether patients should be nursed flat or with their head up to 30°.

The location of the arterial transducer will influence the measured MAP and hence the CPP (CPP = MAP – ICP). This survey was conducted to establish current practice in measuring MAP, and to ascertain when nursing a patient at 30° whether the arterial transducer was referenced to the level of the external auditory meatus or the left atrium.

Methods A telephone survey was conducted of the 28 UK neuroscience ICUs. The nurse in charge was identified and asked, 'When measuring CPP on neurosurgical patients nursed at 30°, is the arterial transducer placed at the level of the head or the heart?'

Results The results suggest differing practice within the United Kingdom. Twenty units positioned the transducer at the level of the left atrium while six units used the level of the external auditory meatus. One unit sited the transducer at the wrist (no extension line used), and in one unit the practice varied depending upon which consultant was on duty. Variation in practice was evident between dedicated neurosurgical as well as general ICUs.

Discussion At 30° above the horizontal, the hydrostatic effect may reduce MAP in the head by up to 10 mmHg. The associated fall in ICP has been shown to be around 3 mmHg. The measured CPP would therefore be 7 mmHg lower if the transducer is at the level of the head as compared with the heart. This discrepancy is of fundamental importance as McGraw's model directly relates outcome to the measured CPP. The BTF recommends a minimum target CPP of 60 mmHg but makes no allowance for posture. In the clinical setting when nursing a patient at 30° with the arterial transducer at the level of the heart, a target CPP of 60 mmHg may result in CPP within the great vessels of the head below the BTF recommendation.

Without a common approach it is difficult to discuss the ideal target CPP. Location of the arterial transducer needs to be clarified as it may result in an outcome difference dependent upon practice, and multicentre trials require a standardised approach. Until this is addressed authors should state the level at which the arterial transducer is referenced in the measurement of CPP.

P451

Impact of severe polytrauma on severe brain injured patients

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Introduction We retrospectively investigated the impact of polytrauma (ISS > 16) on a population of severe brain injured (SBI) patients (GCS < 8).

Patients and methods Thirty consecutive patients with SBI and polytrauma (Group I) were matched with 30 patients with SBI (Group II) treated during the same period. The matching criteria were age +4 years, gender, APACHE II +1, and same GCS. The ICU mortality, length of ICU stay (LOS), duration of intubation, mechanical ventilation (MV), sedation and analgesia were assessed. Patient characteristics (age, gender), severity of illness (APACHE II, GCS), serum Na^+ and glucose, systolic blood pressure (SBP), heart rate (HR) and core temperature were recorded on admission to the ICU. Statistical analysis was performed with the Mann–Whitney U test and statistical significance was considered as $P < 0.05$.

Results See Tables 1 and 2. Significant differences were found between the two groups in LOS, duration of intubation, time with analgesia treatment, admission SBP and temperature. The time on mechanical ventilation, sedation interval and ICU mortality did not differ between the two groups, as indicated in Table 2.

Table 1 (abstract P451)

	Group I	Group II	*P* value
Age	40.8 ± 19.3	42.7 ± 20.6	0.6
Gender (male:female)	26:5	25:5	0.8
APACHE II	18.1 ± 7.2	17.2 ± 6.2	0.4
GCS	5.6 ± 2.4	5.6 ± 2.2	0.9
Glucose	144.9 ± 33.5	146.3 ± 37.6	0.8
Na^+	139.9 ± 5.9	140.7 ± 5.9	0.5
HR	103.7 ± 20.6	99.4 ± 17.1	0.4

Table 2 (abstract P451)

	Group I	Group II	*P* value
LOS (days)	25.3 ± 18.9	16.0 ± 9.4	0.03
MV (days)	17.6 ± 7.6	11.4 ± 6.9	0.6
Intubation (days	21.5 ± 18.8	13.6 ± 9.3	0.05
Mortality	8 (26.6%)	5 (16.6%)	0.9
Sedation (days)	16.4 ± 10.4	10.2 ± 6.3	0.3
Analgesia (days)	19.3 ± 1.1	11.7 ± 0.9	0.08
SBP (mmHg)	90.4 ± 13.7	92 ± 20.7	0.04
Temperature	36.7 ± 1.15	37.3 ± 1.0	0.04

Conclusions Patients with SBI and polytrauma had a lower admission SBP and temperature, a longer ICU stay, more intubation and sedation days without differences in ventilation days and ICU mortality.

P452

Cerebral hemodynamics in young patients after ischemic stroke

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The actuality of the problem is conditioned by the high death rate and invalidism of working-age persons, which is a severe burden for society.

Our aim was the analysis of the cerebral hemodynamics in young patients during an acute period of ischemic stroke (IS).

We examined 17 patients (nine men and eight women) with IS, their mean age was 44.2 ± 4.9 years. None of these patients was observed apropos cerebral vascular disease before IS. Brain CT scans of all patients demonstrated the symptoms of ischemic stroke as the decreased density foci in the basin of the middle cerebral artery.

To study cerebral hemodynamics, all patients underwent duplex scanning of the neck and brain vessels using the scanner ACUSON 128XP/10c (USA) according to the standard method.

Only one patient (6.4%) had no changes during the US examination of the vessels. Six patients (35.3%) demonstrated small thickening of more than 1.1 mm of the 'intima-media' complex in the carotid artery in the absence of plaque formation, 30–40% asymmetry of the blood flow velocity in the medial cerebral arteries, and peripheral resistance indexes increased in the medial cerebral arteries or in the vertebrobasilar basin. In 11.5% of cases the symptoms of atherosclerotic change of the carotid arteries were more evident, but they were hemodynamically insignificant. There were small plaques in the bifurcation zone of the internal carotid arteries and S-shape tortuosity of the orifices of the internal carotid arteries. Almost one-half of the patients had evident signs of atherosclerosis. Occlusion and significant stenosis were observed in two patients with moderate changes at the extracranial level in one of the medial cerebral arteries. The atherosclerotic changes were evident in other patients (six persons, 35.3%); moreover, one-half of the patients had significant stenosis revealed in the carotid and in the vertebral arteries. Two patients had occlusion in one of the internal carotid arteries and one patient had significant stenosis only in the vertebrobasilar basin.

In spite of the young age of the patients, they all therefore had quite evident changes of the cerebral hemodynamics in the background of the different degrees of atherosclerotic signs. The ultrasonic markers of early-stage atherosclerosis in the increased arterial tonus were revealed in one-third of patients. More than one-half of the patients after IS had the evident atherosclerotic changes of the cerebral vessels. In spite of the presence of the arterial occlusion in some patients, the clinical manifestation was absent before the stroke.

P453

Multiparametric monitoring in patients with traumatic brain injury: association with outcome

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Objective To investigate the association between multiple monitoring parameters and the outcome in patients with severe brain trauma.

Patients and methods Thirty-one patients with a mean age of 43 ± 18 years were included in this prospective study. All of them had suffered serious traumatic brain damage (GCS ≤ 8 or GCS < 10 accompanied by a mass lesion in the initial CT scan). Their outcome was evaluated with the GOS in 6 months and they were divided according to that into two subgroups (favorable vs unfavorable outcome). During their ICU hospitalization, these patients were under brain function monitoring, consisting of three intracranial catheters: two for continuous monitoring of ICP and $ptiO_2$, and a third microdialysis catheter for the measurement of glucose, lactate, pyruvate and glycerol in the interstitial fluid of the brain. The microdialysis samples were collected every 2 hours and were automatically analyzed. The monitoring period lasted for up to 10 days.

Results From the patients included, 15 (48.39%) had bad outcome (GOS = 1, 2, 3) and the remaining 16 (51.61%) good outcome (GOS = 4, 5). The group of patients with the good outcome had lower lactate/pyruvate ratio and glycerol values, compared with the group with the bad outcome ($P < 0.001$ and $P = 0.044$, respectively). This difference also existed when the maximum values of these parameters were evaluated ($P = 0.03$ and $P = 0.011$, respectively). Furthermore, mean L/P values >25 correlated with unfavorable outcome ($P = 0.002$). No relationship between glucose and 6-month outcome was found. From all other measurements, only mean CPP values correlated with outcome ($P = 0.036$). Mean ICP values were only marginally significant between the two subgroups. We could also demonstrate some correlations between the studying parameters: mean glucose values with mean pyruvate and mean L/P values ($P = 0.001$ and $P = 0.048$), maximum glycerol values with minimum lactate and maximum L/P values ($P = 0.001$ and $P = 0.019$) and maximum ICP values with minimum $ptiO_2$ values (0.021). Additionally, the presence of L/P ratio >40 was associated with glucose levels less than 0.5 ($P = 0.001$), and $ptiO_2$ values <5 mmHg presented a borderline correlation with glucose values <0.25 mg/dl ($P = 0.058$).

Conclusion Microdialysis, $ptiO_2$ and ICP/CPP monitoring, when used together, may be a useful tool in the ICU setting, allowing continuous evaluation of brain damage and thus prognosis in patients with traumatic brain damage.

P454

Should we perform ocular fundus in patients with severe brain trauma?

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Introduction The high incidence of intracraneal lesions of patients with brain trauma (BT) is well known. The aim of this study is to assess the incidence of an extracraneal injury: retinal haemorrhage (RH) in patients after BT.
Methods A prospective study was performed during 6 months in a 15-bed medical–surgical ICU. RH was diagnosed by an ophthalmologist in the first 4 days after admission to the ICU. Age, personal history, ISS, RTS, SAPS, SOFA score, APACHE score, lactate levels and GCS were recorded on arrival at the ICU. Cerebral edema, brain CT findings, days under mechanical ventilation and need for neurosurgery at any time were also recorded. The statistical analysis was performed using the SPSS 11.0 program.
Results Nineteen patients were included in the study (18 males), age 56 ± 22.56 years. Five RH were described in this group, all males. The mechanism of traumatism was fall in 80% and traffic accident in 20% in the RH group; in contrast, fall in 35.7% and traffic accident in 42.9% in the nonretinal haemorrhage group (NRH). There were no differences between groups in age, ISS, RTS, APACHE score, SAPS, SOFA score, lactate levels and days under mechanical ventilation. Eighty per cent of the patients with RH were alcoholic, and 21.4% of the NRH. The GCS at admission in the ICU was 3 in 60% of the patients with RH and 35.7% in the NRH group. Sixty per cent of the patients with RH required neurosurgery; in contrast, 7.1% in the NHR group. Eighty per cent of the patients with RH developed cerebral edema during their stay in the ICU, while this was 50% in the NRH group. Sixty per cent of the patients with RH had frontal contusion in the CT and 14.3% in the NRH group. Twenty per cent of the patients with RH had epidural haematoma; in contrast, 7.1% in the NRH. Sixty per cent of the patients with RH had epidural haematoma; in contrast, 14.2% in the NRH. All patients with RH were discharged. Two of the patients with RH had unilateral blindness at discharge from ICU.
Conclusions Although it is not possible to draw inferences with so small a number of patients, future prospective studies are warranted to corroborate our findings. RH is a quite common finding in our study (26%). All these patients are male with an antecedent of alcoholism. There was more severe head injury in this group. GCS at arrival is lower. This group have more incidence of frontal contusion, epidural or subdural haematoma, cerebral edema and required more neurosurgical interventions.

P455

New stereological method for the assessment (prediction) of prognosis in patients with epidural haematoma: the volume fraction of haematoma to the total brain volume

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Objective Epidural haematoma (EH) is a very serious clinical event that is seen in almost 2% of the emergency head trauma patients, and it needs immediate diagnosis and treatment. The relation of EH prognosis with older age, additional intracranial pathologies, Glasgow Coma Scale (GCS) and the duration between the trauma and the surgical attempt has been illustrated in various studies. And the studies regarding the effect of the epidural hematoma volume (EHV) on prognosis are not sufficient.
In this study, different from the previous ones, the ratio of EHV over the total brain volume (TBV) has been estimated with a new method and the relation of this ratio with the prognosis has been investigated.
Method In this study, 59 EH patients (46 male, 13 female, average age: 21 years) who attended the emergency clinic have been included. Patients with additional intracranial pathologies have been excluded. The age, GCS and the additional system pathology of the patients and the results of their computed cranial tomography (CCT) were recorded. The EHV and TBV ratio was estimated with a stereological method, and the midline shift amounts have also been determined. From the aspect of clinical results, patients have been classified into three groups as complete recovery (43 patients), disability (eight patients) and exitus (eight patients). The ratio of the EHV and TBV of the groups has been compared within the aspects of GCS, age, shift amount and clinical results.
Results When the ratio of EHV with TBV was compared with clinical results, there was found a statistical sense in the relationship between the groups ($P = 0.007$). Similarly, there has been found a sense from the statistical aspect between these rates and the shift amount and GCS ($P < 0.001$, $P < 0.001$, respectively). However, no difference could be found between the groups in terms of the relationship of EHV ratio over TBV with the age factor ($P = 0.2$).
Conclusion The ratio of EHV mathematically calculated with a new method could be an important sign in determining EH prognosis. This method needs to be supported by more clinical and experimental studies in a wider and deeper range.

P456

Clinical significance of prolonged QTc dispersion in spontaneous intracranial hemorrhage

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Introduction QTc dispersion is a new important prognostic factor for many disease. We have analyzed the admission EKGs of 53 patients with spontaneous intracranial hemorrhage (ICH) for their QTc dispersion. This study is performed to investigate the prognostic characteristics of QTc dispersion in patients with ICH.
Methods On presentation, we measured the QTc dispersion of the ECG and Glasgow Coma Scale (GCS) of patients. The QTc dispersion is the difference in the QT duration of the longest minus the shortest rate-corrected QT interval. Computer tomography of the brain was performed in order to determine the site of the ICH, the presence of intraventricular hemorrhage (IVH) and the amount of ICH. We attempted to determine the relationship between initial factors, including QTc dispersion and findings of computer tomography, as well as the Glasgow Outcome Scale (GOS) at discharge as the final prognosis.
Results Patients exhibited a poor prognosis if they had a lower GCS score on admission, larger volume of hemorrhage and accompanying IVH at computer tomography scan of brain, and increased QTc dispersion on univariate analyses. Although the mean QTc dispersion in the group that showed a favorable outcome was 70.6 ± 29.6 ms, and 63.8 ± 24.2 ms in the group of GOS 1 and 76.8 ± 26.4 ms in the group of GOS 2, the mean QTc dispersion in the group that had an unfavorable outcome was

117.6 ± 36.1 ms; 108.8 ± 29.6 ms in the group of GOS 3, 120.7 ± 1.3 ms in the group of GOS 4 and 141.8 ± 53.4 ms in the group of GOS 5. The difference in the QTc dispersion according to patient outcome was statistically significant.
Conclusion The QTc dispersion in the initial EKG might be a significant factor that could be useful for prediction of outcome in spontaneous ICH patients along with the GOS at discharge. Our results therefore suggest that the QTc dispersion should be included for prognosis and treatment of patients with ICH.

P457

Electrocardiographic changes in patients with acute stroke in the prehospital setting and their prognostic importance

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Introduction Electrocardiographic (ECG) changes can be observed in patients with acute stroke without primary heart disease. The aim of the study was to determine whether ischaemic ECG changes and arrythmia are related to prognosis in this population of patients.
Patients and methods This prospective observational cohort study consisted of 309 patients (168 male and 141 female, age 68.7 ± 31.5 years) with first stroke presenting to prehospital emergency physicians in the field during 6 years (March 1999–February 2005). Among all patients, 258 had ischaemic stroke (IS) and 51 had haemorrhagic stroke (HS). Patients with transient ischaemic attack were excluded from the study. Six-month mortality was analysed by means of ischaemia-like ECG changes (ST segment, inverted T wave, abnormal U wave), and arrythmia.
Results The members of the IS group were significantly older than those in HS group (73 ± 30 vs 52 ± 23 years; $P < 0.05$). The frequency of the ECG changes observed in patients with IS was 69% (178/258) while in patients with HS it was 31% (16/51; $P < 0.05$). In the IS group 81 patients (31%) had ischaemia-like changes and 96 (37%) had arrythmia. The HS group had significantly less ECG changes (15% had ischaemia-like changes and 11% had arrythmia; $P < 0.05$). The HS group had significantly more patients with bradycardia than the IS group (24% vs 4%; $P < 0.05$). The 6-month mortality rate in patients with ECG changes was 29% (56/194) whereas it was 16% (18/115) in those with normal ECG. In multivariate analyses the 6-month mortality in patients with IS was predicted by atrial fibrillation (OR 2.2, 95% CI 1.5–3.7) and ischaemia-like ECG changes (OR 2.1, 95% CI 0.9–3.8). In patients with HS, sinus bradycardia predicted poor outcome (OR 3.9; 95% CI 1.4–9.8).
Conclusion ECG abnormalities are frequent in acute stroke and may predict 6-month mortality. The observations of this study suggest differences between the IS and HS group. The ECG evaluation of patients with acute stroke must be started at the field. Whether the ECG changes are the result of some generalized atherosclerosis that promotes acute stroke, or the magnitude and perhaps location of brain infarction promotes ECG changes in the reverse direction, remains the question.

P458

Decompressive (hemi)craniectomy for refractory intracranial hypertension after traumatic brain injury

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Introduction Sedation, administration of mannitol or hypertonic saline, mild hyperventilation, moderate hypothermia and high-dose barbiturate therapy are all strategies in the treatment of intracranial hypertension in traumatic brain injury (TBI). Intracranial pressure (ICP) >20 mmHg not responding to conservative strategies caries a bad prognosis, mortality exceeding 80%. A final option in refractory intracranial hypertension might be decompressive (hemi)craniectomy.
Methods A retrospective analysis of the outcome of 11 patients with TBI undergoing decompressive (hemi)craniectomy for increased ICP not responding to conservative treatment between July 2001 and April 2005. Outcome was measured on the Glasgow Outcome Scale (GOS). Other parameters considered were: pupil reaction, initial Glasgow Coma Scale after resuscitation (IGCS) and preoperative ICP.
Results Eleven patients (five male, six female; mean age 20.6 years, range 2–42 years) underwent decompressive craniotomy when ICP could not be managed sufficiently by nonsurgical treatment. All patients suffered from blunt, nonpenetrating head injury, all but one had isolated TBI, and one was a multitrauma patient. Unilateral or bilateral absent pupil reaction at admission was seen in five patients. Two of these five patients had recurrent episodes with absent pupil reactions and died.
The mean IGCS was 8. In the patients that died the IGCS was 5 (range 4–6, median Motor score 2). The IGCS in survivors was 9 (range 3–15, median Motor score 4).
The mean injury–craniotomy interval was 72.4 hours (range 0–10 days). In six patients surgery was performed within 48 hours after injury. The mean ICP before surgery was 30.6 mmHg. Most times the ICP measurement device was removed at surgery. In three patients the ICP was measured after decompression and showed immediate decrease in ICP (mean 10.7 mmHg).
Favourable outcome (GOS 4 + 5) was achieved in eight patients (72.7%). Three patients (28.3%) died (GOS 1). None of the patients had severe disability (GOS 2 + 3).
Conclusion This retrospective survey supports the use of decompressive craniotomy in the management of TBI patients with intractable high ICP. The number of patients studied is to small to discriminate predictors of good outcome. Recurrent or persistent absence of pupil reflexes indicates a poor neurological outcome.

P459

Outcome of decompressive craniectomy for large middle cerebral artery territory infarctions: a retrospective review

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Introduction The mortality from large space-occupying infarctions involving the middle cerebral artery (MCA) has been reported as 55–80% despite maximal medical treatment, including barbiturate coma, mannitol and hyperventilation. Patients are typically alert on admission to hospital but deteriorate within 1–3 days from severe brain swelling leading to raised intracranial pressure (ICP), brain herniation and death. Decompressive craniectomy (DC) has been reported to improve survival and functional outcomes following large MCA infarctions.
Methods We conducted a retrospective chart review of all DCs for large MCA infarctions performed at our institution from March 2000 to February 2005. The neurological status was evaluated using the Glasgow Coma Scale (GCS) and functional outcome was evaluated using the Glasgow Outcome Score (GOS) and Modified Rankin Scale (MRS).
Results All values are expressed as the median (range) or mean ± SD. There were 16 patients studied, nine males and seven

females, aged 56.9 ± 8.2 years. Three patients had left-sided MCA infarctions while the rest were right-sided. Three patients had additional infarctions involving the anterior or posterior cerebral artery territories. The GCS was 13 (10–15) at hospital admission and 7 (4–13) at the time of surgery. The time between stroke onset and decompressive surgery was 47.5 ± 29.9 hours, with six patients showing signs of uncal herniation at the time of surgery. One patient had surgery 120 hrs after symptom onset due to late hemorrhagic conversion in the infarct. Fourteen patients received ICP monitoring in the postoperative period. All patients received mannitol while nine patients needed one or more of the following for control of raised ICP: barbiturate coma, hyperventilation and hypothermia. The median duration of mechanical ventilation was 9 (3–11) days, with tracheostomy performed in eight patients. The ICU and hospital mortality rate was 12.5% (2/16) and 31.3% (5/16), respectively. The median GCS of survivors at ICU discharge was 10 (4–11), and 12 (11–15) at hospital discharge. The ICU and hospital lengths of stay were 10 (4–14) and 28 (7–60) days, respectively. At a mean follow-up period of 13 months, 82% (9/11) of survivors were cognitive with a GOS of 3 (2–3) and MRS of 4 (3–5).

Conclusion DCs performed for large MCA infarctions with clinical deterioration resulted in lower mortality compared with rates reported elsewhere for maximal medical treatment. Most survivors regained cognition but required help with walking and activities of daily living.

P460

Magnetic resonance imaging defines structural brain injury acquired during critical illness

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Introduction Patients with non-neurological critical illness commonly develop cerebral dysfunction, which may take the form of delirium, coma, and long-term cognitive impairment. Delirium in the ICU is associated with increased mortality and prolonged mechanical ventilation and hospital stay, and is commonly attributed to metabolic derangements. Tests such as brain computed tomography (CT) and cerebrospinal fluid analysis are frequently nondiagnostic. We hypothesized that brain magnetic resonance imaging (MRI) is a valuable tool in the diagnosis of delirium and coma acquired in the ICU.

Methods Patients who underwent brain MRI for the evaluation of delirium or coma while in the adult medical or surgical ICUs were identified through an institutional database. Subjects with brain disorders diagnosed before their admission to the ICU and those admitted to the neurological ICU were excluded. Patients were classified into two groups according to whether or not MRI identified an acute pathological process.

Results Over a 2-year period, 158 critically ill patients underwent brain MRI, among whom 96 were being evaluated for unexplained delirium or coma. In this group, MRI revealed an acutely evolving structural abnormality in 45 patients (47%), including cerebral infarction in 33, intracerebral hemorrhage in seven, posterior reversible leukoencephalopathy in three, and meningitis in two. Demographic characteristics, admission diagnoses, SAPS II, cardiovascular risk factors, and prevalence of sepsis, acute lung injury, acute renal failure, and acute hepatic failure were not significantly different between patients with and without acute changes on MRI. The ICU length of stay and mortality were also the same in both groups. MRI results led to a modification in presumptive diagnosis in 46 patients (48%), and altered the management plan in 17 (18%). No adverse events were noted in relation to MRI and patient transfer to the radiology suite. When compared with MRI, the sensitivity, specificity, positive predictive value and negative predictive value of CT for detecting acute cerebral changes were 44%, 57%, 42% and 48%, respectively.

Conclusions In ICU patients with delirium or coma, brain MRI reveals an underlying acute structural abnormality in nearly one-half of cases, while the diagnostic impact of CT appears more limited. Occult brain injury may contribute significantly to the pathogenesis of cerebral dysfunction acquired during critical illness.

P461

Critical illness polyneuropathy: incidence and risk factors

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Background Critical illness polyneuropathy (CIP) is an axional peripheral neuropathy. CIP is increasingly diagnosed in ICU patients. The prevalence of CIP, however, is essentially unknown, as are the risk factors of CIP. The aim of this study was to assess the incidence of CIP and to define potential risk factors for CIP.

Methods A database analysis was performed on 1450 patients admitted to the ICU of a tertiary care hospital between March 1998 and December 2003. Diagnosis of CIP was based on clinical judgement confirmed by electrophysiologic evaluation. Clinical, laboratory and haemodynamic variables were analysed for risk prediction of CIP.

Results The overall CIP incidence was 3.3% (48 out of 1450 patients) with a continuous increase in the annual CIP rate (1.4% in 1998 to 5.5% in 2003). CIP patients had higher APACHE II (17 ± 9 vs 21 ± 8; $P = 0.002$) and SAPS II scores (44 ± 22 vs 53 ± 16; $P = 0.01$), a higher incidence of mechanical ventilation (1000/1402 vs 48/48; $P = 0.0001$) and renal support (266/1402 vs 22/48; $P = 0.0001$), as well as a longer duration of mechanical ventilation (median 4 vs 30 days; $P = 0.0001$), renal support (median 4 vs 11 days; $P = 0.0001$) and ICU stay (median 5 vs 36 days; $P = 0.0001$). Furthermore a higher bicarbonate on admission was noted. In the multivariate analysis, only high bicarbonate on admission ($P = 0.0002$) and renal support ($P = 0.0001$) were independent risk factors for the development of CIP. Evaluating factors associated with CIP (as a cause or as a consequence), high bicarbonate ($P = 0.0016$), duration of ICU stay ($P = 0.0001$) and duration of renal support ($P = 0.043$) were independently associated with CIP.

Conclusion CIP is diagnosed in approximately 5% of ICU patients. The incidence of CIP is rising, as are the ICU stay and severity of disease. Development of CIP was associated with severity of disease and ICU length of stay.

P462

Therapeutic cooling in cardiac arrest of noncardiac origin

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On the basis of previous published data, the Interliaison Committee on Resuscitation has advised that unconscious adults with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 33°C during 24 hours when the initial rhythm was ventricular fibrillation (VF) and the cause of the cardiac arrest is of cardiac origin. We postulate that other rhythms might beneficiate from cooling as well as cardiac arrest of noncardiac origin. We therefore started a

prospective study, and we compare the effect of cooling on long-term outcome in patients resuscitated after cardiac arrest of noncardiac origin or having rhythms other than VF.

Twenty-eight patients were included, 14 of them were subjected to hypothermia after achieving return of spontaneous circulation (ROSC) (hypothermia group), the remaining other 14 patients were subjected to normothermia (normothermia group). The cause of cardiac arrest was near asphyxia after strangulation or secondary to choking. Other patients had asystole or pulseless electrical activity (PEA) at the first rhythm assessment.

The postresuscitation phase was similar in both groups. In the hypothermia group, the cooling was initiated either by surface or intravenous cooling. The patient was cooled to 33°C as soon as possible in the Emergency Department, and the temperature was maintained for 24 hours. The re-warming phase was slowly started 24 hours later by increasing the body temperature by 1°C each 4 hours. No difference in complications was observed in the both groups. Good neurological outcome was highly significant in the hypothermia group (Table 1).

Table 1 (abstract P462)

Characteristic	Hypothermia group	Normothermia group
Number of patients	14	14
Median age (years [range])	58 (11–81)	74 (59–91)
Type of cardiac arrest		
Asystole	7	12
PEA	2	2
VF	5	0
Sex	7M/7F	9M/5F
Witnessed collapse	10	6
Bystander - CPR	9	2
Median interval collapse to ROSC (min [range])	24 (10–35)	33 (25–50)
Median tympanic temperature at admission (°C)	36 (32.5–37.7)	35.5 (33.7–36.7)
Outcome		
CPC 1–2	8	1
CPC 3–4	1	1
CPC 5	2	2
Death of other origin than cerebral	3	1

In conclusion, cooling seems to improve the neurological outcome after cardiac arrest even in rhythms other than VF and cardiac arrest of noncardiac origin. Surprisingly cooling also mitigates the brain damage associated with asphyxial cardiac arrest in humans.

P463

Hypothermia after cardiac arrest: impact on myocardial injury

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Introduction The Hypothermia after Cardiac Arrest (HACA) trial assessed whether mild therapeutic hypothermia improved the rate of good neurological recovery in patients successfully resuscitated from ventricular fibrillation cardiac arrest of presumed cardiac origin. Animal data suggest protection of ischemic myocardium with reduced temperature. We evaluated for a subset of patients of the HACA trial the impact of mild therapeutic hypothermia on myocardial injury.

Methods Post-hoc analysis of data of the HACA multicenter trial for patients included at our study center. Patients after ventricular fibrillation cardiac arrest were randomly assigned to mild therapeutic hypothermia of 32–34°C over 24 hours or to conventional treatment. For the present analysis we analysed the effect on plasma levels of CK and CKMB as a measure of infarct size.

Results Fifty-five patients underwent cooling and 56 patients received standard treatment after successful resuscitation. The analysis was performed according to the intention-to-treat principle. The areas under the curve (AUC) within 24 hours for CK were 28,786 U/l × 24 hours (IQR 5646–44,998) in the cooling group and 20,373 U/l × 24 hours (IQR 8211–30,801) for controls ($P = 0.40$). For CK-MB the AUC was 1690 U/l × 24 hours (IQR 724–3330) in the cooling group and 1187 U/l × 24 hours (IQR 490–2469) for controls ($P = 0.18$).

Conclusion In our sample cooling after successful resuscitation for ventricular fibrillation cardiac arrest did not influence infarct size as estimated by CK and CK-MB levels.

P464

Neuron-specific enolase and protein S-100 B as prognostic parameters for children with head injury

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Introduction Neuron-specific enolase (NSE) (glycolytic enzyme in neurons and neuroendocrine cells) and protein S-100 B (calcium^{2+}-binding protein in astroglial and Schwann cells) are established neurobiochemical markers that can be used for evaluating the severity of organic brain damage. The examination of these parameters in serum was used to show the practical relevance in correlation with further examination criteria (Glasgow Coma Scale [GCS], outcome, hospital treatment and ventilation time).

Patients and methods Thirty-nine boys and 16 girls aged 8 ± 4.7 years (range 2 months–16 years) suffering from light to severe head injury (49.1% traffic accident, 38.2% falls, 3.6% child abuse, 3.6% riding accidents, 5.5% other accidents) were included in the study. The examinations of NSE (reference <12 µg/l) and protein S-100 B from the serum were performed using the Liason® Analyser from Byk Sangtec and reagents from Diasorin. Both markers were identified using an immunoluminometric assay (sandwich test). For 52 patients NSE was measured and for 30 patients protein S-100 B was additionally detected after a maximum of 12 hours after the trauma. The correlative behaviour of both parameters towards each other, towards the sex of the patients, the GCS groups (group 1: 4–8 points, group 2: 9–12 points, group 3: >12 points), the hospital treatment time, the ventilation hours and the outcome were tested towards significance (Mann–Whitney test).

Results Significant correlations for NSE and protein S-100 B were seen for the outcome of patients with head injury. NSE ($P < 0.01$) and protein S-100 B ($P < 0.05$) were significantly higher when rehabilitation was necessary or death occurred. Children in need of ventilation had significantly higher NSE ($P < 0.01$). Protein S-100 B did not behave comparably. Comparing the sex of the patients and the GCS groups, no correlation of the parameters were found. A total of 68.1% of the patients were dismissed home, 20% were transferred to a rehabilitation facility, 12.7% were transferred to another hospital and 5.5% of the patients died.

Conclusions NSE and protein S-100 B are closely correlated with the severity of traumatic head injuries in childhood and young adolescence. They should thus find more attention as prognostic parameters in the intensive medical treatment of children.

P465

Correlation of systemic protein S100β levels with postoperative indicators of neurological damage in supratentorial meningioma surgery

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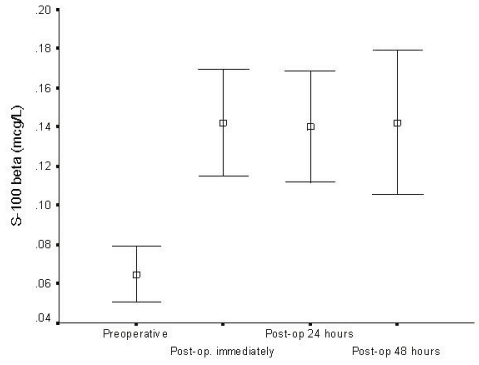
Background Elevated plasma levels of S100β, an astrocyte-derived protein, correlate with neurological deterioration after cardiac surgery [1] and with poor survival following hypoxia [2] and neurotrauma [3] but remain unexplored during elective meningioma surgery. We hypothesized that S100β levels correlate with this tumor's preoperative characteristics and with perioperative neurological injury despite its supratentorial location and non-neural origin.
Methods All patients admitted for meningioma surgery (1 January 2004–31 October 2004) underwent prospective perioperative clinical/radiographic (CT, MRI) neurological evaluation. S100β levels were drawn upon admission and at 2, 24 and 48 hours post-operatively and correlated with clinical/radiological characteristics.
Results Included were 52 patients aged 58.5 ± 13 years (median 60, range 30–80 years), mostly female (40/52). Preoperative mini-mental scores averaged 26.6 ± 6.8 (median 29.5, minimum 11). Several meningiomas were recurrent (14/52) and/or had been irradiated (16/52). MRI demonstrated a mass effect in 35/52 patients. Average tumor and edema volumes were 35.29 ± 29.39 cm^2 and 24.83 ± 32.39 cm^2, respectively. Surgery was usually performed via pterional/frontal approaches and averaged 5 hours. Post-operative CT demonstrated infarct in three patients and bleeding (average volume 1.13 ± 4.19 cm^2, median 0, maximum 29.68 cm^2) in 22 patients. Preoperative S100β levels did not correlate with tumor characteristics. S100β levels rose postoperatively and remained elevated (Fig. 1). Greater elevations of S100β were associated with poor quality of the surgical plane at 2 hours (P = 0.01), deterioration in the postoperative mini-mental score at 2 hours (P = 0.008) and at 24 hours (P = 0.017), and postoperative bleeding at 24 hours (P = 0.046) and 48 hours (P = 0.034).
Conclusions Systemic S100β levels perform poorly as a tumor marker for patients with meningioma but provide early prediction of postoperative neurological injury following meningioma surgery.

Figure 1 (abstract P465)



Systemic S100β levels (presented as average μg/l with 95% confidence intervals); preoperative, immediately postoperative, 24 and 48 hours after surgery.

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P466

Serum neuron-specific enolase as an early predictor of outcome after inhospital cardiac arrest

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Introduction Cardiac arrest is a state of severe cerebral perfusion deficit. Patients recovering from a cardiopulmonary resuscitation are at great risk of subsequent death or incapacitating neurologic injury, including a persistent vegetative state. An early definition of neurologic prognosis for these patients has ethic and economic implications.
Objectives To investigate the prognostic value of serum neuron-specific enolase (NSE) in predicting outcome in patients after a cardiac arrest.
Methods Forty-five patients resuscitated from inhospital cardiac arrest were prospectively studied from June 2003 to January 2005. Blood samples were collected once in each patient, between 12 and 36 hours after the arrest, for NSE measurements. Outcome was evaluated using the Glasgow Outcome Scale (GOS) 6 months after the event. The Mann–Whitney U test was used to compare patients with unfavourable outcome (Group 1, GOS 1, 2) with patients with favourable outcome (Group 2, GOS 3, 4, 5).
Results Age and sex were not different between groups. Cardiac causes were responsible for 37.2% of the cardiopulmonary resuscitations. All nonbystander arrests occurred in Group 1. Asystole was the most common arrest rhythm, more frequently seen in Group 1 (P = 0.046). The mean score on the Glasgow Coma Scale was 6.1 ± 3 in Group 1 and 12.1 ± 3 in Group 2 (P < 0.001). The mean time to NSE sampling was 20.2 ± 8.3 in Group 1 and 28.4 ± 8.7 in Group 2 (P = 0.013). Two patients were excluded from analysis because of hemolysis. At 6 months, good outcome was achieved in nine patients (19.6%), 30 patients (69.8%) died and four patients (9.3%) evolved to a persistent vegetative state. The 34 patients (81.4%) with unfavourable outcome (GOS 1, 2) had significantly higher NSE levels than those with a favourable outcome (median NSE 44.24 ng/ml, range 8.1–370 vs 25.26 ng/ml, range 9.28–55.41; P = 0.034).
Conclusion Outcome after a cardiac arrest is mostly determined by the degree of hypoxic brain damage, and the serum NSE level is a valuable early adjunctive parameter for assessing outcome in these patients.

P467

Prognostic markers of the outcome in severe head injuries

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Introduction Neuronal-specific enolase (NSE) is a subunit of the enolase group specific for the central neural system, found in the

neurons and the neuroendocrine tissue of the brain. NSE is released as a result of leakage across the injured neuronal membrane; elevations of serum NSE are due to neuronal injury and increased permeability of the blood–brain barrier. Protein S-100 (especially the B subunit) is a calcium binding protein found in high concentrations specifically in neurogliar and Schwann cells. Procalcitonin (PCT) is the precursor of calcitonin and under normal conditions it is not detected in the plasma (0–0.5 ng/ml). PCT is elevated in microbial sepsis and trauma.

Objective To investigate the validity of outcome prediction after severe head injury using the serum levels of protein S-100 B, of NSE and of PCT.

Materials and methods Over a period of 24 months (2003–2004) 42 patients with severe head injury older than 18 years treated in the ICU of KAT General Hospital, intubated and mechanically ventilated, were prospectively included in the study. The study protocol was approved by the local ethics committee. Informed consent was obtained from the next of kin of all patients. The patients were 20 men and 12 women, without other injuries, mean age 34 years and mean admission GCS 6. None of the patients had spinal cord injury or any other previous neurological disease. Venous blood samples were taken on admission (first day) and consecutively on the second and third days. The immunoluminometric assay was used for the specimens. We tried to correlate the S-100 B, NSE and PCT serum concentrations with the CT scan intracerebral pathology as well as with the age, gender and ICU outcome.

Results All patients on admission had elevated S-100 B and NSE serum concentrations but PCT was very little increased. There were a gradual reduction from the first towards the third day of ICU stay. The first day the mean values of S-100B were 3.74 μg/l and the third day they were 1.8 μg/l ($P < 0.001$). The first day the mean values of NSE were 21.7μg/l and the third day they were 18.2 μg/l ($P < 0.05$). The first day the mean values of PCT were 1.38 ng/ml and the third day they were 0.49 ng/ml (P = NS). Protein S-100B levels and NSE were higher in patients who died ($P < 0.001$). There was no strong correlation between the initial serum S-100 B and NSE values, the CT scan findings, the GCS on admission, the age of patients and the gender.

Conclusion The protein S-100 B and NSE are biochemical markers that seem to be elevated during the first days after injury in patients with severe head trauma. They could be used as markers of the severity of the injury and with great probability as prognostic markers of patient outcome. On the contrary, the PCT levels seem to have no prognostic value in isolated severe head trauma, although the PCT seems to increase in polytrauma patients.

P468

End-of-life practices in Brazilian pediatric ICUs of three different regions

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Objectives To evaluate the frequency and types of end-of-life practices in five Brazilian pediatric intensive care units (PICU): Porto Alegre (two), São Paulo (one) and Salvador (two).

Methods We conducted a cross-sectional and multicenter study based on a retrospective chart review including every death occurring between January 2003 and December 2004 in five Brazilian PICU of university-affiliated and tertiary hospitals located in Porto Alegre (two), São Paulo (one) and Salvador (two). Two fellows of each service filled a standardized protocol, searching for information regarding: demographic aspects, cause of death, frequency of cardiopulmonary resuscitation register plans, and medical practices in the 48 hours before death. The data were compared using the Student *t* test, ANOVA, chi-square and RR.

Results A total of 332 death patients were identified in this period and 37 cases of brain death were excluded (11.1%). The mortality is similar in the five PICU. Only 120 (36.1%) patients had not been reanimated, with a statistical difference ($P < 0.05$) between the five PICU. Sixty-seven (55.8%) charts of non-reanimated patients had a register of an end-of-life plan made by the assisting team: 41 cases of life support limitation and 26 do-not-resuscitate orders, without differences between the five PICU ($P = 0.2$). There were no cases of withdrawing ventilatory support or a significant increase in sedatives and analgesics doses in the 48 hours preceding death.

Conclusions Despite the increasing number of children who are not reanimated in the end of life in Brazilian PICU, we observed that withdrawing life-sustaining treatment preceding death is still insignificant. Moreover, we observed different medical practices in the five hospitals that can be a consequence of cultural, religious or even personal behaviors of each medical team in the three different Brazilian regions.

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P469

Alveolar epithelial function is better preserved in lungs from nonheart-beating donors compared with heart-beating donors

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Objective Intact function of the alveolar epithelium is of critical importance to resolve reperfusion edema after lung transplantation. The mechanism, known as alveolar liquid clearance (ALC), can be stimulated by β-adrenergic agents such as terbutaline. ALC in lung grafts and the effect of terbutaline was evaluated in an isolated reperfusion model comparing donor lung injury following brain death in the heart-beating donor (HBD) versus 1 hour of warm ischemia in the nonheart-beating donor (NHBD).

Methods Pigs were divided into six groups ($n = 3$/group). In HBD and HBD-T, brain death was induced by intracranial balloon inflation. In control animals, CONT and CONT-T, the balloon was not inflated. In NHBD and NHBD-T, cardiac arrest was induced by myocardial fibrillation. After 5 hours of mechanical ventilation, lungs in HBD, HBD-T, CONT and CONT-T were flushed. In NHBD and NHBD-T, unflushed grafts were explanted after 1 hour of warm ischemia and 4 hour of *in-situ* topical cooling. Grafts in all groups were evaluated for 2 hours in an isolated ventilation and reperfusion model. At the start of reperfusion, 100 ml iso-oncotic albumin solution was instilled in all lungs and mixed with 10^{-3} M

terbutaline in HBD-T, CONT-T and NHBD-T to stimulate ALC. The ALC (percentage of alveolar fluid resorbed per hour) was calculated by comparing the initial and final protein concentrations in the instillate with the formula: 100 × (1 – initial protein / final protein) / 2.
Results See Table 1.

Table 1 (abstract P469)

	CONT	HBD	NHBD	CONT-T	HBD-T	NHBD-T
ALC (%/hour)	17 ± 1.7	8 ± 1.0*	16 ± 0.4	21 ± 8	14 ± 1.1	17 ± 0.9
% increase in ALC				20	43	6.4

Data presented as mean ± SEM. *$P < 0.05$ compared with NHBD and CONT.

Conclusions ALC during isolated reperfusion is decreased following brain death in HBD but not in NHBD. The effect of terbutaline on ALC was mostly apparent in HBD. These data further support the use of NHBD in lung transplantation. Terbutaline may be a promising tool to stimulate epithelial function in lungs from HBD and to resolve ischemia-reperfusion injury.

P470

Older age, female sex, and increased IL-6 decrease the organ yield from cadaveric donors

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Introduction A variety of factors are believed to impact the number of organs explanted for transplantation in cadaveric organ donors, including age, stability of the patient and existing co-morbidities. Brain-death-induced systemic inflammation could also adversely affect the number of organs explanted for transplantation. Hence, in this observational study we sought to examine the various factors including the inflammatory response that occur in cadaveric organ donors and to determine their relative impact on organ explantation.
Methods We enrolled 30 cadaveric organ donors in this prospective observational, two-center study. After obtaining informed consent, we collected clinical information including demographics, cause of death and donor management details. We measured plasma IL-6 levels at baseline and hourly for the first 4 hours after brain death and immediately before organ explantation. We analyzed the association between the number of organs explanted and clinical, demographic and immunologic variables by univariate and multivariable regression. Finally, we repeated our analysis on donors younger than 50 years of age.
Results The number of organs explanted from patients ranged from 0 to 7, with an average of about three organs per patient. In multivariable analysis, older age and female sex were the only variables significantly associated with less than three organs explanted (age: OR = 0.89, 95% CI 0.81–0.96, $P = 0.003$; female sex: OR = 0.13, 95% CI 0.02–0.76, $P = 0.024$). In subgroup analysis, we found that in donors aged younger than 50 years ($n = 17$), female sex still had a significant negative impact on organs explanted ($P = 0.0002$), but age was no longer significant. However, in the younger than 50 age group the mean plasma IL-6 concentration was also negatively associated with the number of organs explanted ($P = 0.001$).
Conclusion Age, as expected, appears to be the primary factor impacting the number of organs explanted from cadaveric organ donors. Surprisingly, female sex is associated with a decreased number of organs explanted. In donors younger than 50 years of age, female sex and mean plasma IL-6 concentrations significantly impacted the number of organs explanted.

P471

Is bispectral index monitoring an alternative method for diagnosis of brain death?

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Introduction EEG and cerebral angiography is usually mandatory beside clinical examination for the diagnosis of brain death. In recent years, for head trauma patients correlation was found between the Glasgow Coma Scale (GCS) and the bispectral index (BIS) that was dependent on the analysis of EEG. We studied whether BIS monitoring is an alternative method or not.
Materials and methods Thirteen patients received in the ICU with deep coma between February 2004 and September 2004 were included in the study. GCS was ≤5 for all patients during ICU admittance. The reasons for coma were intracranial hemorrhagia, head trauma, cerebral anoxia. After the clinical diagnosis of brain death was made, all patients underwent EEG monitoring. Clinical inspection and EEG were made twice for 24 hours, BIS monitoring was performed for 2 hours after the detection of brain death.
Results BIS values were 0 for 12 patients and 5 for one patient. Bioelectric silence was detected in all EEGs of all patients.
Discussion BIS, which depends on bispectral analysis of EEG parameters, is used in the ICU for evaluation of sedation level. A meaningful correlation between neurologic status GCS and BIS has been reported for coma patients without sedation. Our findings are in line with these studies. BIS seems to be an alternative method for diagnosis of brain death with the advantage of easy application. However, EMG activity and cardiovascular hyperpulsatility may cause artifacts and false BIS evaluations. We believe that more studies are necessary for routine application of this new method.

P472

Brain death in children: a cross-section study enrolling five Brazilian pediatric ICUs

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Objectives Studies of brain death and organ donation in children are scarce. The objective is to evaluate the incidence of brain death (BD) as well the guidelines and protocols used for confirming BD in five Brazilian PICUs: Porto Alegre, São Paulo and Salvador.
Methods We conducted a cross-sectional and multicenter study based on a retrospective chart review including every death occurring between January 2003 and December 2004 in five Brazilian PICUs of university-affiliated and tertiary hospitals located in Porto Alegre (two), São Paulo (one) and Salvador (two). Two fellows of each service filled a standardized protocol, searching information regarding: demographic aspects, the death cause, the diagnosis of BD and related protocols (or guidelines), and subsequent management. The data were compared using the Student *t* test, ANOVA, chi-square and RR.
Results A total of 332 death patients were identified in this period and 37 of them (11.1%) were defined as BD. There was a different rate between the five PICUs (18.2%, 10.1%, 14.7%, 4.8% and

5.0%; $P < 0.05$). The median age was 50.5 months without statistical difference related to gender. In 81% of the cases the clinical diagnosis of BD was confirmed through cerebral blood flow examinations (ultrasonography/scintigraphy) or EEG. The interval between the diagnosis of BD and the interruption of vital support as well the incidence of withdrawal vital support after the diagnosis BD showed statistical difference ($P < 0.01$) between the five PICUs. Only six (17.6%) children with BD were organ donors.

Conclusions Despite Resolution 1.480/97 of the Federal Advice of Medicine published in August 1997 that in a clear and objective way defines the criteria that must be adopted to establish the diagnostic of brain death in Brazil, many services still have tremendous difficulty adopting it. These difficulties were well demonstrated when observing the number of patients that remain with vital support after BD was established and the modest number of organ donors in Brazil.

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