ERS International Congress 2023: highlights from the Respiratory Intensive Care Assembly

Clara Bianquis[1], Sebastian Leiva Agüero[2], Chloé Cantero[3], Alejandro Golfe Bonmatí[4], Jessica González[5,6], Xinxin Hu[7,8], Thomas Lacoste-Palasset[9,10], Alana Livesey[11], Raquel Guillamat Prats[12], Grgur Salai[13], Dominic L. Sykes[14], Sile Toland[15], Cristiano van Zeller[16], Pedro Viegas[17], Ana Luisa Vieira[18], Stavroula Zaneli[19], Christian Karagiannidis[20] and Christoph Fisser[21]

[1]Sorbonne Université, UMRS1158 Neurophysiologie Respiratoire Expérimentale et Clinique, Paris, France. [2]Academic unit of the University Institute of Health Science H.A. Barceló Foundation, La Rioja, Argentina. [3]APHP, Groupe Hospitalier Universitaire APHP-Sorbonne Université, Site Pitié-Salpêtrière, Service de Pneumologie, Paris, France. [4]Pulmonology Department, General University Hospital of Castellón, Castellón, Spain. [5]Translational Research in Respiratory Medicine, University Hospital Arnau de Vilanova and Santa Maria, IRBLleida, Lleida, Spain. [6]CIBER of Respiratory Diseases (CIBERES), Institute of Health Carlos III, Madrid, Spain. [7]St Vincent's Health Network Sydney, Sydney, Australia. [8]University of Sydney, Sydney, Australia. [9]Assistance Publique Hôpitaux de Paris, Service de Pneumologie et Soins Intensifs Respiratoires, Centre de Référence de l'Hypertension Pulmonaire, Hôpital Bicêtre, Le Kremlin Bicêtre, France. [10]Université Paris–Saclay, Faculté de Médecine, Le Kremlin Bicêtre, France. [11]University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK. [12]Institute Germans Trias i Pujol, Badalona, Spain. [13]Department of Pulmonology, University Hospital Dubrava, Zagreb, Croatia. [14]Respiratory Research Group, Hull York Medical School, Hull, UK. [15]Department of Medicine, Letterkenny University Hospital, Donegal, Ireland. [16]Department of Respiratory Medicine, King's College Hospital NHS Foundation Trust, London, UK. [17]Departamento de Pneumonologia, Centro Hospitalar de Vila Nova de Gaia/Espinho, Oporto, Portugal. [18]Pulmonology Department, Hospital de Braga, Braga, Portugal. [19]1st Respiratory Department, Medical School, National and Kapodistrian University of Athens, "Sotiria" Chest Hospital, Athens, Greece. [20]Department of Pneumology and Critical Care Medicine, ARDS and ECMO Centre, Cologne-Merheim Hospital, Kliniken der Stadt Köln gGmbH, Witten/Herdecke University Hospital, Cologne, Germany. [21]Department of Internal Medicine II, University Medical Centre Regensburg, Regensburg, Germany.

Corresponding author: Christoph Fisser (christoph.fisser@ukr.de)

Shareable abstract (@ERSpublications)
The latest updates in respiratory intensive care, in particular ARDS and mechanical ventilation, presented at #ERSCongress 2023 in Milan, are summarised by the early career members of @ERSAssembly2 (Respiratory Intensive Care) https://bit.ly/3GvBzFy

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Abstract

Early career members of Assembly 2 (Respiratory Intensive Care) attended the 2023 European Respiratory Society International Congress in Milan, Italy. The conference covered acute and chronic respiratory failure. Sessions of interest to our assembly members and to those interested in respiratory critical care are summarised in this article and include the latest updates in respiratory intensive care, in particular acute respiratory distress syndrome and mechanical ventilation.

Introduction

Respiratory failure is the principal cause of intensive care admission and leads to chronic impairment. Early career members of the European Respiratory Society (ERS) Assembly 2 (Respiratory Intensive Care) here summarise the latest updates in respiratory intensive care that were presented by international experts at the ERS International Congress 2023 in Milan, Italy.

This work builds on information provided during the ERS Congress 2022 [1] and from the Respiratory Failure and Mechanical Ventilation Conference 2022 [2].

The sessions covered advances in mechanical ventilation, addressing the place of noninvasive mechanical ventilation (NIV), high-flow nasal cannula (HFNC) and positive airway pressure both in acute and chronic respiratory care. Also discussed were updates from the Global Consensus Conference on acute respiratory

distress syndrome (ARDS), a summary of coronavirus disease 2019 (COVID-19) recommendations on the management of complex pleural diseases and factors linked to the quality of survival after intensive care unit (ICU) admissions for ARDS.

Acute respiratory distress syndrome: update and future treatment

L. Ware (Nashville, TN, USA) presented the new proposed global definition of ARDS, focusing on different criteria and limitations on the Berlin definition [3], adding some minor modifications. The new definition of ARDS includes patients who require high-flow nasal oxygen at >30 $L \cdot min^{-1}$ and using peripheral oxygen saturation (S_{pO_2})/inspiratory oxygen fraction (F_{IO_2}) as a noninvasive alternative to arterial oxygen tension (P_{aO_2})/F_{IO_2} for the oxygenation criteria [4, 5]. The global expert committee recommended the use of ultrasound as an alternative to radiographic imaging for diagnosing alveolar infiltrates [6].

C. Karagiannidis (Cologne, Germany) presented the new European Society of Intensive Care Medicine guidelines for ARDS and focused on nonpharmaceutical treatments of ARDS (figure 1). Future randomised trials are needed to assess whether noninvasive respiratory support techniques (*i.e.* HFNC, continuous positive airway pressure (CPAP) or NIV) reduce mortality or intubation rate [7]. NIV should be carefully applied in ARDS patients because it can lead to patient self-inflicted lung injury [8]. High-pressure lung recruitment manoeuvres are currently not recommended in ARDS patients [9–12].

D. McAuley (Belfast, UK) highlighted the importance of identifying the two main phenotypes in ARDS, *i.e.* hyper-inflammatory (high interleukin (IL)-6, IL-8 and soluble tumour necrosis factor receptor 1) or hypo-inflammatory (low bicarbonate, protein C and systolic blood pressure), in order to personalise medical treatments in critical care [13, 14]. According to a retrospective analysis, hyper-inflammatory phenotypes may benefit from simvastatin administration [15].

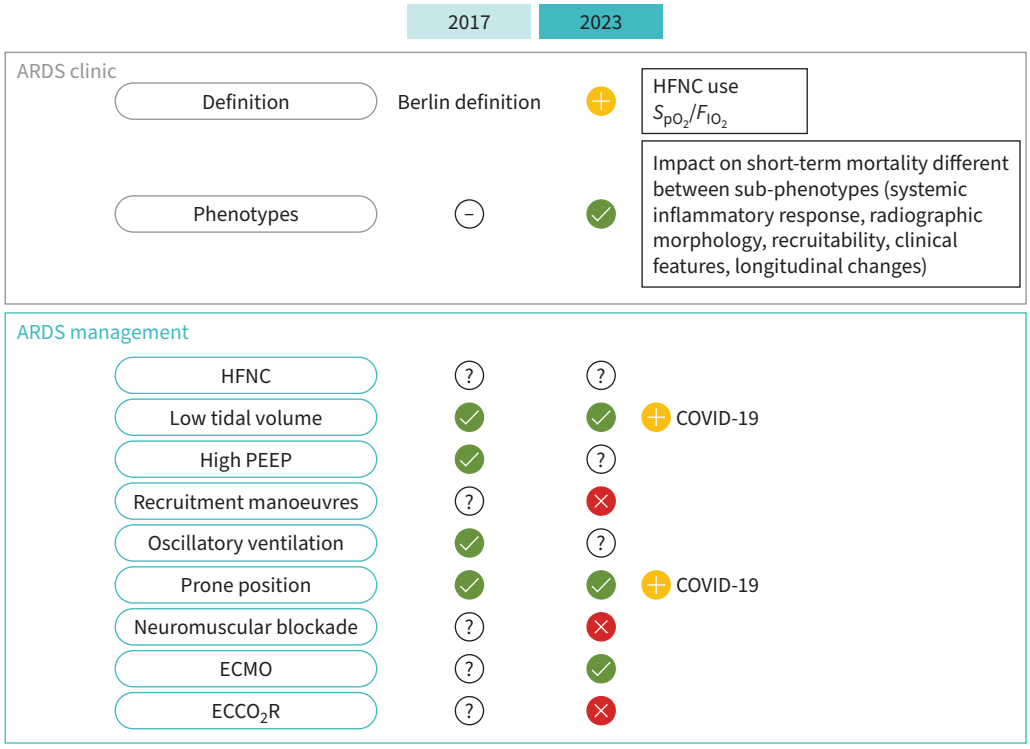

FIGURE 1 Figure summarising the changes in the European Society of Intensive Care Medicine recommendations concerning the clinical definition and therapeutic management of acute respiratory distress syndrome (ARDS). The left-hand column shows the 2017 recommendations and the right-hand column the changes established or not in 2023, with the additions concerning the management of coronavirus disease 2019 (COVID-19) patients. HFNC: high-flow nasal cannula; S_{pO_2}: peripheral oxygen saturation; F_{IO_2}: inspiratory oxygen fraction; PEEP: positive end-expiratory pressure; ECMO: extracorporeal membrane oxygenation; $ECCO_2R$: extracorporeal carbon dioxide removal.

L. Heunks (Amsterdam, the Netherlands) concluded the session by presenting the WEAN-SAFE study [16]. The 90-day mortality rate was nearly 30% in patients who received mechanical ventilation for at least 2 days. The modifiable factors for weaning success were the level of sedation and the delay in weaning initiation.

Take-home messages

- The Global Consensus Conference on ARDS recommended an update to the Berlin definition criteria by adding ultrasound, S_{pO_2}/F_{IO_2} ratio and the use of high-flow nasal oxygen in the diagnosis of ARDS patients.
- Future studies focusing on sub-phenotypes among ARDS patients are needed to develop individual-targeted treatments.
- Weaning success rates may be improved by optimising the sedation levels and avoiding weaning delay.

Noninvasive and invasive mechanical ventilation in acute respiratory diseases

M. Witzenrath (Berlin, Germany) discussed therapeutic targets for endothelial dysfunction in ventilator-induced lung injury. Adrenomedullin reduced endothelial permeability in mice models [17] and adrenomedullin-targeting antibody (Adrecizumab) has been tested in phase 2a trials [18]. New therapies targeting C5a and vilobelimab reduced endothelial dysfunction in mice models and improved outcomes in ventilated COVID-19 patients, respectively [19]. The roles of Tie-2 [20], transient receptor potential vanilloid 4 (TRPV4) [21] and basic helix-loop-helix ARNT like 1 (B-MAL) [22] in developing ventilator-induced lung injury have been explored *in vivo* and are future potential therapeutic targets.

L. Piquilloud (Lausanne, Switzerland) provided an evidence-based medicine update for ARDS. New recommendations by expert consensus suggested broadening the ARDS diagnostic criteria to include non-intubated patients, lung ultrasound findings and modified criteria for resource-variable settings [4]. The updated European Society of Intensive Care Medicine guidelines recommended the use of controlled tidal volumes (4–8 $mL \cdot kg^{-1}$) and prone positioning but recommended against routine use of neuromuscular blockers [7].

C. Karagiannidis (Cologne, Germany) specified that extracorporeal membrane oxygenation (ECMO) should be managed in experienced centres using the EOLIA (ECMO to Rescue Lung Injury in Severe ARDS) trial method and criteria [10] for an acceptable outcome [23]. Prone positioning should be applied in ECMO patients [24] whereas use of extracorporeal carbon dioxide removal is not recommended [11] and the use of corticosteroid is of uncertain usefulness and should be studied further [25].

L. Heunks (Amsterdam, the Netherlands) set out steps to optimise weaning from mechanical ventilation. First, it is necessary to quantify effort to limit the adverse effects of high or low drive using occlusion pressure [26]. When weaning eligibility criteria are achieved, a zero assist spontaneous breathing test (t-tube trial) [27] should be performed with the lowest possible level of sedation and without delay [16]. But, more importantly, the underlying cause of weaning failure must be identified and treated accordingly.

Take-home messages

- Controlled tidal volumes and prone positioning are recommended for patients with severe ARDS.
- Use of neuromuscular blockers and extracorporeal carbon dioxide removal are not recommended for patients with severe ARDS.

Hot topics: noninvasive high-flow nasal therapy or positive pressure ventilation in acute and chronic respiratory care

L. Pisani (Bologna, Italy) emphasised that HFNC therapy is widely employed in acute respiratory failure. This therapy increases expiratory airway resistance, thus extending respiratory cycles [28]. Additionally it decreases carbon dioxide re-breathing by dead-space washout and applies positive nasopharyngeal pressure [29], which collectively yield improved clinical outcomes. Physiological studies have revealed that a greater prong/nare area ratio of the cannula and maintaining mouth closure during therapy can enhance nasopharyngeal pressure [30–32].

C. Crimi (Catania, Italy) elucidated the various physiological and clinical benefits of CPAP and NIV in the treatment of acute respiratory failure [33, 34]. Emerging evidence suggests that NIV strategies, compared to standard oxygen therapy, are significantly associated with a reduced risk of death in *de novo* acute hypoxaemic respiratory failure [35]. A thorough physical examination (assessing respiratory effort) and vigilant monitoring are crucial for optimising treatment, mitigating the risk of treatment failure and patient self-inflicted lung injury, and avoiding delays in intubation [36, 37].

R. D'Cruz (London, UK) discussed flow treatment in chronic respiratory care. High-flow treatment has long been studied in patients with airways disease [38], reducing arterial carbon dioxide tension (P_{aCO_2}) in patients with chronic hypercapnia [39]. Furthermore, in patients with COPD, treatment with 8 $h \cdot day^{-1}$ HFNC demonstrated a reduction in exacerbation frequency and symptoms [40–42]. Emerging evidence suggests palliative HFNC treatment may be of use for refractory breathlessness [43] because it is well tolerated in end-of-life patients [44].

W. Windisch (Witten, Germany) summarised pressure treatment in chronic respiratory disease. Long-term high-intensity NIV confers improvements in lung function, gas exchange and symptoms, and is better tolerated than standard NIV [45, 46]. Further studies have shown that long-term NIV improves survival and quality of life in patients with COPD [47–49]. Current ERS guidance recommends long-term NIV for patients with stable hypercapnia, suggesting pressures be titrated to normalise P_{aCO_2} [50].

Take-home messages

- Flow and pressure treatment have proven beneficial in the acute and chronic setting.
- Further clinical trials are required to elucidate which modality is optimal for selected patients.

Hot topics in intensive care medicine

A. Ceccato (Barcelona, Spain) showed from a multicentre national cohort [51] using a k-prototype algorithm that ARDS patients can be clustered into two groups (cluster 1 having less organ failure and higher P_{aO_2}/F_{IO_2} ratio than cluster 2) that have differing prognoses [52].

Duarte Herrera *et al.* [53] presented the results of transcriptomic profiling of ARDS survivors in a prospective cohort. Latent class analysis identified a persistent weakness group with 22 genes differentially expressed at admission.

Soipetkasem *et al.* [54] showed in a prospective cohort of 80 patients intubated for acute respiratory failure that a predicted change in transpulmonary pressure $\leqslant$20 cmH_2O was independently associated with more ventilator-free days.

Wiest *et al.* [55] showed that pulmonary superinfections were more frequent and with more aspergillosis in patients treated with veno-venous ECMO for COVID-19 than for influenza.

E.H.T Lim (Amsterdam, the Netherlands) presented the results of a worldwide randomised controlled trial of vilobelimab showing a significant reduction of 28-day all-cause mortality in intubated ARDS COVID-19 patients [19].

Jayasimhan *et al.* [56] discussed the influence of an elevated dead-space and ventilatory ratio as independent predictors of mortality in patients with ARDS, based on a systematic review and meta-analysis of 21 studies.

González *et al.* [57] showed the evolution of pulmonary sequelae, symptoms and quality of life throughout the 2 years after a critical COVID-19 episode, highlighting a long-term negative impact of invasive mechanical ventilation.

Prével *et al.* [58] illustrated the different compositions of both bacteriobiota and lung mycobiota among patients with influenza, COVID-19 and bacteria-related ARDS by analysing endotracheal aspirates of 28 patients.

Gaffier *et al.* [59] shared the data of a monocentric retrospective study evaluating nebulised tranexamic acid in patients requiring ICU for haemoptysis without immediate arterioembolisation, showing no reduction in bleeding recurrence.

Take-home message

- Clustering, transcriptomics and bacteriobiota are promising new tools for exploring the heterogeneity of ARDS patients for future research.

Mini symposium: rise of the machines – advances in home mechanical ventilation

Windisch *et al.* [60] highlighted that the Severe Respiratory Insufficiency questionnaire is a valuable tool for assessing the quality of life in COPD patients receiving NIV. Exacerbation history, presence of

anaemia, autonomy level and participation in rehabilitation programmes affect quality-of-life scores [61, 62]. HFNC is an interesting treatment option in patients with chronic respiratory failure owing to its respiratory physiological effects, but more trials are needed to recommend it as a first-line treatment, especially in hypercapnic patients owing to the absence of a significant reduction in hypercapnia [63].

P. Murphy (London, UK) focused his presentation on the description of auto-titrating NIV and the use of these algorithms and devices in the management of patients with chronic respiratory failure. He raised the question of whether there might be more effective modes than the spontaneous-timed mode, which might not always be able to meet the respiratory demands during the different sleep cycles. He introduced auto-expiratory positive airway pressure and auto-inspiratory positive airway pressure modes, which can sense and respond to obstructive events in the upper airway and hypoventilation, respectively. Theses modes improve quality of sleep, gas exchange and compliance [40, 64–66]. NIV can be an adjunct to respiratory rehabilitation and physical activity, particularly during because it improves endurance exercise capacity and recovery after physical activity [67]. Small portable devices are a good option for this indication.

M. Duiverman (Groningen, the Netherlands) highlighted the challenges and evidence of telemonitoring in patients on home mechanical ventilation. Telemonitoring may not necessarily prevent acute COPD exacerbations but could potentially shorten their duration [68]. The challenges associated with telemonitoring are the increased time required by nursing staff in the management around telemonitoring and trying to assure its cost-effectiveness by saving hospitalisation days [69, 70]. Nevertheless, telemonitoring increases patient empowerment, enables patient- and family-centred care, and facilitates knowledge sharing between healthcare providers and across healthcare systems [71–73]. Home initiation of NIV with telemonitoring is feasible and noninferior regarding efficiency in comparison to in-hospital initiation [74].

Take-home messages

- Long-term NIV for chronic hypercapnic COPD patients is standard of care, improves long-term survival and improves quality of life.
- HFNC improves respiratory mechanics but has a small effect on P_{aCO_2} reduction; its role in chronic respiratory diseases still needs to be defined.
- Auto-NIV modes enhance physiological control of sleep disordered breathing and improve NIV tolerance and compliance.
- Home initiation of NIV with telemonitoring is feasible and noninferior regarding efficiency in comparison to in-hospital initiation.

Quality of survival

S. Eggmann (Bern, Switzerland) discussed the best strategy for rehabilitation in the ICU, presenting data from the TEAM trial. High-intensity rehabilitation did not reduce mortality nor hospital stay and had more adverse events than the usual intensity group [75]. Importantly, no rehabilitation is not an option. The optimal strategy is reviewed in figure 2 and should include close monitoring of patients, a stepwise increment in intensity using individualised, short and frequent sessions, prioritising out-of-bed and functional exercises [76].

D. Langer (Leuven, Belgium) demonstrated how inspiratory muscle training facilitates weaning from mechanical ventilation. In the only randomised trial with a sham arm, inspiratory muscle training improved weaning rates from 47% to 71% [77]. Presenting unpublished data from the IMTCO study [78], high-intensity inspiratory muscle training did not improve weaning above lower intensity. In both groups, muscle activation was similar, suggesting pre-existing low respiratory compliance can be sufficient to generate enough workload [79].

M. Vitacca (Pavia, Italy) explored the multiple dimensions of post-ICU disability [80–83], post-intensive care syndrome, which leads to long-term impairments [84], and the high level of disability in weaning centre patients. The need to evaluate patients in these centres with a variety of tools was stressed [85, 86] as well as the importance of multidimensional [65] and volitional assessments [87] (such as spirometry and muscle strength) and preventive actions [88].

C. Rochester (New Haven, CT, USA) discussed implications [89] and prevention [90] of post-intensive care syndrome. Evidence supporting improvement of outcomes with rehabilitation programmes is scarce [91] even though several programmes have been tested. To optimise rehabilitation, at-risk patients [92] and patients' rehabilitation needs [92] must be identified, in association with optimised early post-hospital care [93]. A multidisciplinary team is necessary to implement these post-ICU rehabilitation programmes [94, 95].

FIGURE 2 Recommendations for rehabilitation during post-critical care admission regarding frequency, intensity, duration and type of sessions of rehabilitation.

Take-home messages

- Post-ICU disability has multiple dimensions, which must be evaluated using several tools and assessments to improve rehabilitation outcomes.
- Rehabilitation from critical illness should be individualised to patients' needs because the workload intensity that may lead to overload without adding extra benefit varies between patients.
- Inspiratory muscle training improves weaning from mechanical ventilation, although the optimal regimen has not yet been established.

COVID-19 diagnosis and treatment summary

Respiratory-related mortality remains up to 30% higher than pre-pandemic levels in Spain, as evidenced by Soriano and co-workers [96, 97]. Vaccination strategies could be impacted by the findings of Hazan *et al.* [98], who demonstrated improved immune response and reduced infection risk with mid-morning COVID-19 vaccination in a trial of 1.5 million patients.

Novel ambulatory diagnosis of COVID-19 was proposed by S. Grassin Delyle (Montigny le Bretonneux, France) using real-time mass spectrometry breath analysis. Volatile organic compound signatures alongside clinical data accurately identified COVID-19 cases with 98% sensitivity and 74% specificity [99]. Semenova *et al.* [100] presented liquid chromatography of matched serum and bronchoalveolar liquid to create disease-specific signatures to differentiate COVID-19 from other causes of pneumonia, as well as showing unique protein profiles on the first day of intubation that were sustained for 45 days after intubation.

E. Duijvelaar (Amsterdam, the Netherlands) demonstrated disruption of protein expression in COVID-19 infection; this more accurately predicted critical illness progression than clinical data. Imatinib reversed dysregulated protein pathways in COVID-19-induced critical illness [101].

Lindö *et al.* [102] identified decreased IL-33 concentrations and elevated plasma levels of soluble ST2 receptor in lung tissue of COVID-19 fatalities *versus* controls; particularly prominent changes were found in areas of diffuse alveolar damage.

A novel prophylactic treatment of influenza infection, including a Toll-like receptor 2/6 agonist nasal spray, was presented by F. Mercuri (Melbourne, Australia). This treatment induced increased expression of antiviral immune genes and a reduced infection duration [103]. Frent *et al.* [104] showed in a small trial that vagal nerve stimulation resulted in fewer ICU admissions and low mortality in COVID-19 patients, hypothesising an anti-inflammatory response reducing critical illness.

O. Elneima (Leicester, UK) presented PHOSP-COVID trial outcomes showing more than 60% of patients hospitalised with COVID-19 have ongoing symptoms and physical impairment at 1 year [105]. This correlates with the findings presented by Cruz *et al.* [106] showing T-cell exhaustion and altered cytokine profiles in patients with persisting respiratory symptoms, and objective decline in the diffusing capacity of the lung for carbon monoxide <80%, at 1 year after infection.

Take-home messages

- Proteomics may hold the key to developments in COVID-19 diagnosis and treatment targets.
- There is objective evidence of immune dysfunction in long-COVID patients.

Mini symposium: complex pleural disease – management in the critically ill patient

M. Nardini (London, UK) discussed pneumothorax in critically ill patients. Pneumothorax in these patients is most commonly a result of a surgical or intensive care procedure [107]. Chest computed tomography is the most sensitive imaging method for pneumothorax detection [108]. Thoracic ultrasound also has a very important role in detecting pneumothorax in the critically ill, because it can be performed at the bedside [109]. Treatment options include watchful waiting, tube thoracostomy and surgery. Furthermore, the role of endobronchial valves as a treatment option for patients with persistent air leaks was highlighted [110]. Finally, the question regarding the need for dedicated guidelines for management of pneumothorax in critically ill patients was raised.

D. Sanchez (Barcelona, Spain) discussed the management of complex pleural effusion in critically ill patients. He highlighted the rising incidence of pleural infection. He further addressed the role of thoracic ultrasound, which is superior to chest radiography or computed tomography for the diagnosis of complex pleural effusion [111]. Furthermore, management strategies based on early antibiotic administration and early complex pleural effusion evacuation were discussed. Additionally, the role of intrapleural fibrinolytic therapy was highlighted, as well as surgical modalities and alternative options for those not fit for surgery.

M. Nosotti (Milan, Italy) discussed chylothorax and bronchopleural fistula. Chylothorax is a condition with a high morbidity. Traumatic chylothorax is mainly caused by surgery (90%), whereas nontraumatic causes include malignancy and nonmalignant diseases [112]. Conservative management should be the first-line treatment. Interventional management includes surgical ligation and embolisation [113, 114].

Bronchopleural fistula can occur post lobectomy/pneumonectomy and post lung transplant. Other causes include chemotherapy, radiation therapy and chest trauma. Symptoms can be acute, *e.g.* tension pneumothorax, or subacute, *e.g.* symptoms of empyema. A computed tomography scan and/or bronchoscopy is necessary for diagnosis. A chest drain is generally required for management. Other options include surgery and stenting or occluder devices, depending on patient suitability, the size and timing postoperatively [115].

Take-home message

- There are many complex pleural diseases that can be encountered in critically unwell patients and a multidisciplinary management approach is necessary to achieve the most optimal outcome.

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