Research

Preoperative prediction of pediatric patients with effusions and edema following cardiopulmonary bypass surgery by serological and routine laboratory data

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Abstract

Aim: Postoperative effusions and edema and capillary leak syndrome in children after cardiac surgery with cardiopulmonary bypass constitute considerable clinical problems. Overshooting immune response is held to be the cause. In a prospective study we investigated whether preoperative immune status differences exist in patients at risk for postsurgical effusions and edema, and to what extent these differences permit prediction of the postoperative outcome.

Methods: One-day preoperative serum levels of immunoglobulins, complement, cytokines and chemokines, soluble adhesion molecules and receptors as well as clinical chemistry parameters such as differential counts, creatinine, blood coagulation status (altogether 56 parameters) were analyzed in peripheral blood samples of 75 children (aged 3–18 years) undergoing cardiopulmonary bypass surgery (29 with postoperative effusions and edema within the first postoperative week).

Results: Preoperative elevation of the serum level of C3 and C5 complement components, tumor necrosis factor-α, percentage of leukocytes that are neutrophils, body weight and decreased percentage of lymphocytes (all $P < 0.03$) occurred in children developing postoperative effusions and edema. While single parameters did not predict individual outcome, >86% of the patients with postoperative effusions and oedema were correctly predicted using two different classification algorithms. Data mining by both methods selected nine partially overlapping parameters. The prediction quality was independent of the congenital heart defect.

Conclusion: Indicators of inflammation were selected as risk indicators by explorative data analysis. This suggests that preoperative differences in the immune system and capillary permeability status exist in patients at risk for postoperative effusions. These differences are suitable for preoperative risk assessment and may be used for the benefit of the patient and to improve cost effectiveness.

Keywords complement, discriminant analysis, interleukin, predisposition, selectin

Introduction

Patients undergoing cardiopulmonary bypass (CPB) surgery frequently develop systematic inflammatory response syndrome, ranging from mild to severe complications such as pericardial, pleural and/or abdominal effusion, liver enlargement and edema. These complications are characterized by

CLS, capillary leak syndrome; CPB, cardiopulmonary bypass; CRP, C-reactive protein; EDTA, ethylenediaminetetracetic acid; Ig, immunoglobulin; IL, interleukin; LFA-1, leukocyte function associated molecule-1; MOD, multiple organ dysfunction; POEE, postoperative effusions and edema; sE-selectin, soluble endothelial-selectin; sL-selectin, soluble leukocytic-selectin; Th1/2, T-helper type 1/2; TNF, tumor necrosis factor.

increased capillary permeability, a shift of fluid and protein from the intravascular to the interstitial space and may further progress into hypovolemia, massive generalized edema, acute respiratory distress syndrome, or even capillary leak syndrome (CLS) or multiple organ dysfunction (MOD) or failure, with a substantial morbidity and mortality [1–4]. Although the incidence of postoperative effusion in children is substantial (>25%) its etiology is yet not well understood. Nearly 97,000 (Germany 1998) [5] and 800,000 (USA 1996, American Heart Association, http://www.amheart.org) patients undergo CPB surgery annually (~10% for congenital heart disease [5]), hence postoperative complications constitute a significant clinical problem.

The extensive contact between heparin anticoagulated blood and foreign surfaces of the extracorporal circuit during CPB, in combination with anesthetics and other medication used during and after surgery stimulates the immune system [2,6–8]. Cytokines play a key role in the inflammatory cascade associated with CPB [7,9]. Tumor necrosis factor-α (TNF-α), interleukin (IL)-6 and IL-8 (proinflammatory cytokines) may contribute to myocardial dysfunction and increased apoptosis [10] and increased neutrophil activation [11], and IL-10 may contribute to immune depression [12] and increased susceptibility to infection.

There is some evidence that patients who later develop postoperative complications may be identified in the early perioperative or even in the preoperative period [13–18]. Several scoring systems use clinical and/or laboratory data acquired during or after therapy to predict cardiac patients outcome [13,14] with informative serum parameters like soluble endothelial (sE)-selectin for restenosis [16] or perioperative C-reactive protein (CRP) [15], lactate [3], IL-6 [17] or altered blood coagulation [19] after open heart surgery. Recently, prediction of postoperative complications based on preoperative parameters were published [18,20]. The prediction of patients at risk for postoperative complications is important for the individual preoperative prophylactic treatment. Preoperative prediction is based on the hypothesis that the primed immune system amplifies the immune response to cardiosurgical trauma; for example, TNF-α or fibronectin primed neutrophils respond more strongly to stimulation in vitro [21,22]. Priming in the patients may be caused by an allergic/atopic predisposition [1,6,15] but can also be a result of fresh or reactivated viral infection [1]. A recent study in this journal indicates gender as a predisposing factor for MOD in children [23].

In a recent study we showed that children who suffered from postoperative effusions and edema (POEE) are, 24 hours before surgery, already exhibiting altered antigen expression on leukocytes, by which risk assessment would be possible using discriminant analysis [18]. Based on these results we hypothesized that children at risk of POEE have an altered preoperative level of markers of immunoactivation, allergic/atopic predisposition or T-helper type 2 (Th2) phenotype, which may be used as predictors for risk assessment. In addition, we also included readily available standard laboratory parameters in order to test predictive strength. The advantage of a serological classifier over that based on antigen expression data by flow cytometry is that these data and methods are accessible for virtually all clinical facilities and are easily standardized. In the present study we show that children at risk of POEE are already predisposed to the condition and can be predicted from these data.

Methods

Study groups

This prospective non-randomized study was conducted between November 1995 and May 2001 following approval by the ethical committee of the medical faculty at the University of Leipzig, Germany. A total of 75 patients who underwent cardiac surgery with CPB were analyzed [inclusion criteria: aged 3–18 years, body weight >12 kg; exclusion criteria: missing informed consent of parents, palliative cardiac surgery (e.g. if single ventricle circulation was the aim of surgery, (Glenn, Fontan or total cavopulmonary connection [TCPC]). The surgical procedures included were: closure of atrial septal defect ($n = 39$) or ventricular septal defect ($n = 11$); replacement of pulmonary valve by an allogeneic heart valve ($n = 18$); resection of an aortic subvalvular stenosis resulting from a subaortic membrane or fibrous cap ($n = 6$); correction of tetralogy of Fallot ($n = 1$). All children received similar anesthesia, medication and intraoperative and postoperative care and CPB as detailed elsewhere [2]. After delivery to the intensive care unit postoperatively, the incidence of pericardial-, pleural- and/or abdominal-effusion was monitored by echocardiography, chest X-ray or sonography. If patients developed detectable effusions after removal of the thoracic drainage (which was usually one day after surgery) until discharge they were allocated into the POEE group ($n = 29$), or into the non-POEE group (no effusion, $n = 46$). As evaluated visually, all POEE patients had edema of the face and/or hands and/or feet. Incidence of edema was not used for POEE discrimination because quantitative measures of extravascular body fluid volume (such as scintigraphy following labelling of the extravascular fluid by radiolabelled sulphide or bromide) were ethically not feasible in children. Massive generalized edema, CLS or MOD as defined by Seghaye *et al.* [24] was not observed in any of the patients. However, 65% of the POEE patients fulfilled at least one MOD criterion as defined by Trotter *et al.* [23]. Postpericardiotomy syndrome with effusions and fever of non-infectious origin within a week, or later, of surgery [25] was not present in any of the patients.

Complement, cytokines, soluble adhesion molecules

Blood was obtained one day (median: 20 hours) before surgery in untreated tubes as well as in ethylenediaminetetracetic acid (EDTA) and heparin tubes, centrifuged at 2800 ***g*** for 10 min at 4°C and the supernatant was collected. Urine was sampled in untreated tubes. Within 1 hour after

Table 1

Clinical and surgical data of POEE and non-POEE patients (means ± SD)

Surgical parameters and patient data	Non-POEE ($n = 46$)	POEE ($n = 29$)	*P*-value
Age (years)	8.8 ± 4.4	9.8 ± 3.6	0.23*
Body weight (kg)	27.3 ± 11.9	35.0 ± 13.7	0.009+
Gender (F/M)	23/23	16/13	NS†
Aortic cross-clamping (min)	34.0 ± 27.8	47.7 ± 34.7	0.13*
CPB (min)	65.9 ± 37.1	98.4 ± 62.9	0.04+
Surgery + anesthesia (min)	177.1 ± 58.5	213.7 ± 98.6	0.10*
Reperfusion (min)	18.7 ± 18.2	25.4 ± 29.0	0.54+
Hypothermia (minimal temperature °C)	30.6 ± 3.1	30.7 ± 2.8	0.80*
Length of stay on ICU (days)	1.9 ± 0.9	2.9 ± 4.1	0.25+
Mechanical ventilation on ICU (hours)	10.1 ± 5.0	11.7 ± 6.6	0.36+
Discharge (days after surgery)	9.4 ± 5.2	10.7 ± 4.7	0.031+

†Chi-squared test, NS = not significant, * two-tailed Student's *t*-test, +Mann-Whitney U-test. CPB, cardiopulmonary bypass; ICU, intensive care unit; POEE, postoperative effusions and edema.

collection, serum, EDTA-plasma and urine samples were stored in aliquots at –80°C. The concentration of the complement components (C3, C4, C5, C1-inhibitor, C3d) and immunoglobulin (Ig)G2 was determined by radial immune diffusion (The Binding Site, Heidelberg, Germany) with serum or EDTA-plasma (C3d) and total hemolytic complement CH100 by lysis of antibody-coated sheep erythrocytes (The Binding Site). All other parameters were quantified using enzyme-linked immunosorbent assay [IgE, interleukin (IL)-1β, TNF-α, interferon-γ, RANTES, histamine: Beckman-Coulter, Krefeld, Germany; IL-4, IL-10, IL-13, soluble intracellular adhesion molecule-1 (sICAM-1), platelet endothelial cell adhesion molecule-1 (PECAM): Bender MedSystems, Vienna, Austria; IL-5, IL-6 high sensitivity, IL-10 high sensitivity, IL-12 p40/p70, soluble leukocytic (sL)-selectin, sE-selectin: R&D Systems GmbH, Wiesbaden, Germany; IL-2, IL-2-receptor, serum and urine neopterin: DPC Biermann GmbH, Bad Nauheim, Germany; IL-4 high sensitivity, IL-11: Natutec, Frankfurt, Germany; IL-12 p70, IL-13: Biozol Diagnostica Vertrieb GmbH, Eching, Germany; C5a: Behringwerke AG, Marburg, Germany]. The complement fragment ratios C3d/C3, C5a/C5 and immunoglobulin ratio IgE/IgG2, were calculated as measures for complement activation and Th2/Th1 imbalance, respectively. Additionally, routine laboratory and clinical chemistry parameters were determined (cell count, differential blood count, CRP, creatinine, electrolytes, protein, hematocrit, blood coagulation parameters). In total 56 parameters were analyzed per patient including age, gender and body weight.

Statistical analysis

Data are displayed as mean ± standard deviation (SD). Between-group comparison was undertaken by unpaired Student's *t*-test or Mann-Whitney U-test as appropriate [Statistical Program for Social Sciences Version 8.0 (SPSS), Knowledge Dynamics, Canyon Lake, TX]. Discrimination of patients into the POEE and control group was tested by data pattern analysis using two different methods as detailed [18]. Classification for individual risk assessment was performed by stepwise multivariate discriminant analysis using SPSS. This classifier was optimized by increasing the *F*-probability followed by determination of the unstandardized canonical discriminant function. Missing data were substituted by column means, if necessary. No more than one value per patient was extrapolated. In parallel, the triple matrix data pattern analyzer CLASSIF1 [18] was used as an algorithmic data mining approach. With CLASSIF1 no replacement of missing data values and no mathematical assumptions on parameter distributions are required.

Results

Clinical data are comparable in the control group and among those patients at risk for POEE. Data on patients and surgical parameters were grouped according to the clinical outcome in non-POEE and POEE groups (Table 1). Patients with POEE were of similar age and gender, while duration of surgery + anesthesia and extracorporal circulation were longer. Other parameters, including priming and infusion volume, duration of hypothermia and hemofiltration volume (i.e. volume of fluid that has been removed from the blood to accomplish normal hematocrit values at the end of surgery) were not significantly different (not shown). POEE patients had a higher body weight (Table 2) and stayed in hospital one day longer after surgery. All patients were discharged in good condition.

Patients at risk of POEE exhibited signs of inflammation. Children with POEE had preoperatively significantly higher levels

Table 2

Twenty-four hour preoperative serum parameters in postoperative non-POEE and POEE patients (means ± SD). From the 56 determined parameters, those selected by one of the classification programs or exhibiting significant differences are shown

Parameter (units)	Non-POEE (*n*)	POEE (*n*)	*P*-value	Classifier
C1-inhibitor (mg/l)	937 ± 270 (46)	888 ± 342.0 (29)	0.49*	C
C3 (mg/l)	1329 ± 200 (46)	1467 ± 325.0 (29)	0.022*	C
C5 (mg/l)	128.7 ± 54.3 (46)	177.4 ± 87.4 (28)	0.001+	C
C5a (mg/l)	0.45 ± 0.36 (46)	0.73 ± 1.08 (29)	0.09+	S
C5a/C5-ratio	0.38 ± 0.29 (46)	0.51 ± 0.72 (28)	0.39+	S
TNF-α (ng/l)	36.2 ± 118.8 (45)	63.5 ± 222.4 (29)	0.028+	
IL-10 (ng/l)	1.50 ± 4.89 (46)	3.95 ± 11.15 (29)	0.18+	S
sL-selectin (μg/l)	1299 ± 294 (44)	1434 ± 37 (24)	0.27*	S,C
% lymphocytes	41.7 ± 11.0 (46)	34.9 ± 10.1 (29)	0.010*	
% neutrophils	46.7 ± 11.3 (46)	54.9 ± 11.8 (29)	0.005*	S
Neutrophils (cells/μl)	3506 ± 1500 (45)	4219 ± 1490 (27)	0.086*	C
Monocytes (cells/μl)	579 ± 219 (45)	634 ± 242 (27)	0.23*	S
Eosinophils (cells/μl)	218 ± 195 (45)	206 ± 226 (27)	0.83+	C
Serum protein (g/l)	72.3 ± 5.0 (41)	70.9 ± 5.9 (28)	0.27*	S
Hematocrit (%)	37.3 ± 5.0 (44)	40.2 ± 10.8 (27)	0.14+	S,C
Partial thrombin time (s)	35.9 ± 3.7 (45)	35.2 ± 4.6 (28)	0.56*	C
Potassium (mmol/l)	4.2 ± 0.3 (45)	4.1 ± 0.5 (28)	0.55*	C
Body weight (kg)	27.3 ± 11.9 (46)	35.0 ± 13.7 (29)	0.008+	S

*Two-tailed Student's *t*-test, +Mann-Whitney U-test. Parameter used by S = SPSS classifier, C = CLASSIF1 classifier or S,C= both classifiers. *n* = number of patients. IL, interleukin; POEE, postoperative effusions and edema; sL-selectin, soluble leukocytic-selectin; TNF-α, tumor necrosis factor-alpha.

of several complement components, TNF-α, neutrophilic granulocyte count and percentage (Table 2). These data indicate increased immune activation/alteration of at risk patients.

At risk patients can be identified preoperatively by data classification. The use of single parameters for individual risk assessment is insufficient, as most data for the POEE patients (>75%) showed significant overlap with non-POEE patients. The highest discrimination by a single parameter was obtained with C3 (specificity: 55%; sensitivity: 67%). On multivariate analysis, however, the majority of patients from both groups were correctly classified irrespective of the classification program applied (SPSS/CLASSIF1; specificity: 80.4%/97.8%; sensitivity: 86.2%/72.4%; and negative: 90.2%/84.9%; and positive: 73.5%/91.3% predictive values) (Table 3). Only nine of the 56 parameters were required for these classifications (Table 4). Five parameters were unique to each classifier, while increased C5 and sL-selectin serum concentration, increased neutrophil percentage or count and elevated hematocrit were selected by both classification methods as discriminant factors. Misclassifications were not assigned to a certain type of cardiac defect (Chi-squared test; see also Table 3, classification of subgroups), indicating that POEE prediction is independent of the surgery performed. This interpretation is also supported by the result that atrial septal defect patients and the patients who underwent other types of surgeries were both classified with nearly identical sensitivity, specificity and negative and positive predictive values (Table 3).

Conclusion

There are two major findings of our study. First, that cardiac surgery patients with problematic postoperative disease already exhibit elevated serum concentration of complement components C3 and C5, TNF-α and neutrophils (count and percentage) one day preoperatively. Second, that preoperative risk assessment based on serological and clinical chemistry data is possible, with high levels of accuracy.

The preoperative predictive risk assessment represents a clear advantage over assays relying on data acquired during or after cardiac intervention. Preoperative differences, as selected by our explorative data analysis, indicate a preoperative activation of the immune system, for example, by a subclinical inflammatory response [1,15], an atopic/allergic predisposition or a condition resulting from the congenital

Table 3

Classification of POEE and non-POEE patients (confusion matrices) of 24 h preoperative serological parameters by the SPSS and the CLASSIF1 classifiers (see Table 4)

Clinical outcome		Patients (*n*)	Prediction (% correct) Non-POEE	POEE
SPSS				
Non-POEE	(all patients)	46	80.4	19.6
	(ASD)	(25)	(80.0)	(20.0)
	(residual)	(21)	(81.0)	(19.0)
POEE	(all patients)	29	13.8	86.2
	(ASD)	(14)	(14.3)	(85.7)
	(residual)	(15)	(13.3)	(86.7)
Negative/positive predictive values		90.2	73.5	
	(ASD)	(90.9)	(70.5)	
	(residual)	(89.4)	(76.4)	
CLASSIF1				
Non-POEE	(all patients)	46	97.8	4.3*
	(ASD)	(25)	(96.0)	(4.0)
	(residual)	(21)	(100.0)	(4.7)*
POEE	(all patients)	29	27.6	72.4
	(ASD)	(14)	(35.7)	(64.3)
	(residual)	(15)	(20.0)	(80.0)
Negative/positive predictive values		84.9	91.3	
	(ASD)	(82.7)	(90.0)	
	(others)	(87.5)	(92.3)	

Classification result shown separately for ASD patients or the residual patients applying the identical classification algorithms as for the total group of patients. *Simultaneous classification non-POEE/POEE for one patient increases line sum above 100%. ASD, atrial septal defect; POEE, postoperative effusions and edema.

heart disease [26,27]. In contrast to the recent report that MOD in children is gender related [23], gender was not a predisposing factor in our study.

Inflammatory response

Preoperative serological alteration or activation indicates specific pathobiochemical problems. The parameters selected by the two classifiers in this study indicate increased POEE risk for patients with elevated inflammatory response by increased complement and neutrophil activation and coagulation (see Table 4). In different cardiac situations, CRP [15], sE-selectin [16], sICAM-1 and neutrophil adhesion molecule expression [28,29] have been discussed as risk factors. As already suggested by others [19], preoperatively altered blood coagulation values such as partial thrombin time were found to be prognostic for postoperative blood loss. Fibrinogen and fibrin are ligands for Mac-1 [30], inducing neutrophil, monocyte or resting platelet activation. Our study indicates this activation by elevated sL-selectin level as an important discriminant parameter. CPB is associated with major qualitative and quantitative alterations of humoral pathways and changes in leukocyte subsets, generating a systemic inflammatory response [2,4,7,31] with interactions between vascular endothelium, platelets and leukocytes including signal exchanges, adhesion molecule expression and secretion of cytokines or chemokines in a multi-step process. Patients with an altered immune profile before surgery might show a more pronounced or sustained immune response after surgery. In an unstimulated immune system, CPB exposure constitutes the initial stimulus that might prime the system for postoperative complications [32]. In patients with a primed or predisposed immune profile, CPB as the second stimulus may facilitate an enhanced immune response, which, in turn, may lead to POEE, CLS or multiple organ failure.

The main discriminators of at risk patients (elevated levels of complement and activated complement components, TNF-α and IL-10) indicate the significance of complement system and monocyte activation. Activated monocytes liberate TNF-α and IL-10 as important modulators of the inflammatory response. TNF-α stimulates human vascular endothelium, thus mediating leukocyte recruitment to sites of inflammation. IL-10 release is specific to CPB surgery [7] and patients with POEE or MOD release higher quantities of IL-10 [7,23]. Increased IL-10 release as an indicator of MOD or effusions is also supported by the finding that perioperative methylprednisolone administration, that enhances IL-10 release during CPB surgery in adults [33], aggravates postoperative effusions and bleeding in children with postcardiotomy syndrome [34]. Elevated preoperative IL-10 concentration was a risk factor in our patients. An observation that contrasts with the finding that children with MOD had reduced IL-10 serum levels [23] prior to CPB. Patients from our study had no gender-related differences in any of the analyzed laboratory parameters. We have no explanation for this discrepancy, but differences in the age distribution and the congenital heart diseases of patients included in our study, as compared to Trotter et al. [23], may play a role.

Severe allergic reactions with cardiac surgery [6,34] and allergic predisposition in adults at risk for cardiovascular death have been reported [35]. The interpretation of allergic/atopic predisposition in POEE risk was indicated by our recent observation of elevated leukocyte function asscoiated molecule-1 (LFA-1) expression on leukocytes of at risk patients [18], as LFA-1 expression is increased on leukocytes of atopic children [36]. We reported earlier that patients at risk for POEE also had increased preoperative histamine and eosinophil counts, among others [7,29]. The results from the present study do not clearly support the hypothesis of risk prevalence for atopic/allergic patients because only few of the selected markers could indicate an atopic/allergic predisposition (e.g. TNF-α and IL-10). We conclude from these differences that both increased inflammatory status and allergic/atopic predisposition are predictors of increased POEE in children.

Clinical implications

Taken together, the data indicate at least three risk groups for pediatric POEE. Risk patients might have: (i) latent infection;

Table 4

Preoperative parameters and coefficients for prediction of postoperative cardiac surgery outcome by the SPSS and CLASSIF1 classifiers

SPSS classifier		CLASSIF1 classifier	
Parameter (p_i)	Coefficients (c_i)*	Parameters	POEE patients classification mask**
		C1-Inhibitor	–
		C3	+
C5	0.005105	C5	+
C5a/C5-ratio	0.788609		
IL-10	0.086488		
sL-selectin	0.001721	sL-selectin	+
% Neutrophils	0.024991		
		Neutrophil count	+
Monocyte count	0.002542		
		Eosinophil count	–
Hematocrit	0.06021	Hematocrit	+
Serum protein	–0.136055		
Body weight	0.067000		
		Partial thrombin time	–
		Potassium	–
(Constant	–0.939490)		

Formula of the discriminant function: *Constant $+\sum_{i=1}^{i=9}(p_i \times c_i)$, resulting value <0, non-POEE risk, if >0, POEE risk.

p_i = measured parameter values; c_i = classifier coefficients. **Parameter on average above (+) or below (–) the 25–75% percentile thresholds for C1-inhibitor: 300/377 mg/l (25%/75%); C3: 1181/1456 mg/l; C5: 100/131 mg/l; sL-selection: 1102/1501 µg/l, neutrophil count: 3900/5520 cells/µl; eosinophil count: 85/269 cells/µl; hematocrit: 34.0/39.8%; partial thrombin time: 33.3/37.9 s; K^+: 4.04/4.38 mmol/l. Non-POEE patients have, on average, all parameters unchanged (0) between the 25–75% percentile thresholds. *Unknown patients* are classified according to the highest number of positional coincidences, with the POEE or the non-POEE patients classification mask.

(ii) atopic/allergic predisposition; or (iii) immune alterations as a result of the congenital heart disease. These hypotheses have to be further scrutinized by future studies.

Because children with postoperative complications usually have a longer stay on the ICU, a longer period of mechanical ventilation and stay longer in hospital, preoperative risk assessment is of clear therapeutic advantage and can be cost-effective by reducing any stay in intensive care. By prospective classification, up to 86% of the patients at risk were correctly identified preoperatively. In view of the fact that such predictions were not possible at all until now, these predictive values are promising. However, the classifier will be optimized by increasing the number of patients enrolled in studies and by combining this serological classifier with additional parameters such as flow-cytometric data [18].

Individual risk assessment before cardiac surgery of this type might open new ways to develop individual treatment strategies with two possible clinical consequences: first, postponement of surgery until the normalization of clinical parameters (e.g. elimination of stress or a latent infection); and, second, application of individual prophylaxis [31] in the case of endogenous reasons for immune system alterations [28,34,35]. The hypothesis that postponement or individual prophylaxis will reduce POEE has to be scrutinized in additional studies.

Key messages

- The development of postoperative edema and effusion (POEE) in children after cardiopulmonary bypass surgery can be predicted preoperatively.
- POEE develops on the background of a pre-existing immune activation.
- The immune activation has cellular (neutrophil, eosinophil, monocyte counts, hematocrit) and humoral (C1-inhibitor, C3, C5a/C5, IL-10, sL-selectin, partial thrombin time, serum potassium) components.
- Preoperative normalization of the immune activation status has the potential of decreasing the intensive care treatment and the overall level of postoperative complications.

The proposed serological classifier should permit individual risk assessment in hospitals with lower patient numbers. It is planned to set up and optimize an on-line classifier for POEE risk assessment on the internet. One of the practical consequences of this would be that diseases could be categorized at institutions where no sufficient database can be generated in a reasonable time period. Risk assessments for patients at other institutions can be calculated for test purposes using the indicated SPSS classifier formula (Table 4). Each required parameter value is multiplied with a local data correction factor. The local data correction factor is obtained as a ratio between the parameter mean from non-POEE patients from Table 2 of this study and the mean of the respective parameter from the local non-POEE group of 20 to 40 complication-free patients. The local data correction factor for the establishment of the individual patient's triple matrix for the CLASSIF1 classification is determined in the same way.

Competing interests

None declared.

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