



Research article

High summation of preoperative and postoperative Interleukin-6 levels predicts prolonged mechanical ventilation in patients with acute DeBakey type I aortic dissection: A single center retrospective study

Qingsong Wu^{a,1}, Qinghua Lin^{a,1}, Linfeng Xie^c, Zhihuang Qiu^a, Liangwan Chen^{a,b,*}^a Department of Cardiovascular Surgery, Union Hospital, Fujian Medical University, Fuzhou, Fujian, PR China^b Key Laboratory of Cardio-Thoracic Surgery Fujian Medical University, Fujian Province University, Fuzhou, Fujian, PR China^c Fujian Medical University, Fuzhou, Fujian, PR China

ARTICLE INFO

Keywords:

Interleukin-6

Acute DeBakey type I aortic Dissection

Prolonged mechanical ventilation

ABSTRACT

Objective: This study aimed to investigate the predictive effect of preoperative and postoperative interleukin-6 (IL-6) levels on the duration of mechanical ventilation in patients with acute DeBakey Type I aortic dissection (I-AAD) after emergency surgery.

Methods: We retrospectively enrolled 381 patients with I-AAD who underwent surgery in our hospital, between June 2018 and June 2022. Patients were divided into two groups according to whether prolonged mechanical ventilation (PMV) occurred after surgery. The baseline data, biochemical indicators at admission, surgical data, biochemical indicators at postoperative 6 h, and the postoperative data of the two groups were recorded and analyzed.

Results: The PMV group comprised 199 patients, and the non-PMV group 182. The postoperative in-hospital mortality was different between the two groups (11.1% vs. 3.3%, $p = 0.004$). The length of intensive care unit and hospitalization time in the PMV group were significantly longer than those in the non-PMV group. Multiple regression analysis showed postoperative IL-6 (post-IL-6) ≥ 67.1 pg/mL and summation of preoperative and postoperative IL-6 (total IL-6) ≥ 83.4 pg/mL were associated risk factors for PMV [odds ratio (OR) 3.259, 95% confidence interval (CI) 1.922–5.524, $p < 0.001$], [(OR) 4.515, 95% CI 2.241–9.098, $p < 0.001$]. Furthermore, determined by the receiver operating characteristics(ROC) curve, the cut-off point was total IL-6 ≥ 83.4 pg/mL (area under curve(AUC) = 0.825). The sensitivity and specificity of predicting postoperative PMV of patients with I-AAD were 91.5% and 78.2%, respectively (95% CI 0.782–0.868, $p < 0.001$).

Conclusion: For predicting postoperative PMV in patients with I-AAD, post IL-6 ≥ 67.1 pg/mL is potentially valuable and summation of preoperative and postoperative IL-6 (total IL-6) ≥ 83.4 pg/mL has a more pronounced predictive value.

* Corresponding author. Department of Cardiovascular Surgery, Union Hospital, Fujian Medical University, Xinquan Road 29, Fuzhou, Fujian, 350001, PR China.

E-mail address: chenliangwan@tom.com (L. Chen).

¹ Qingsong Wu and Qinghua Lin are contributed equally to this study and share first authorship.

<https://doi.org/10.1016/j.heliyon.2023.e15465>

Received 20 September 2022; Received in revised form 6 April 2023; Accepted 10 April 2023

Available online 13 April 2023

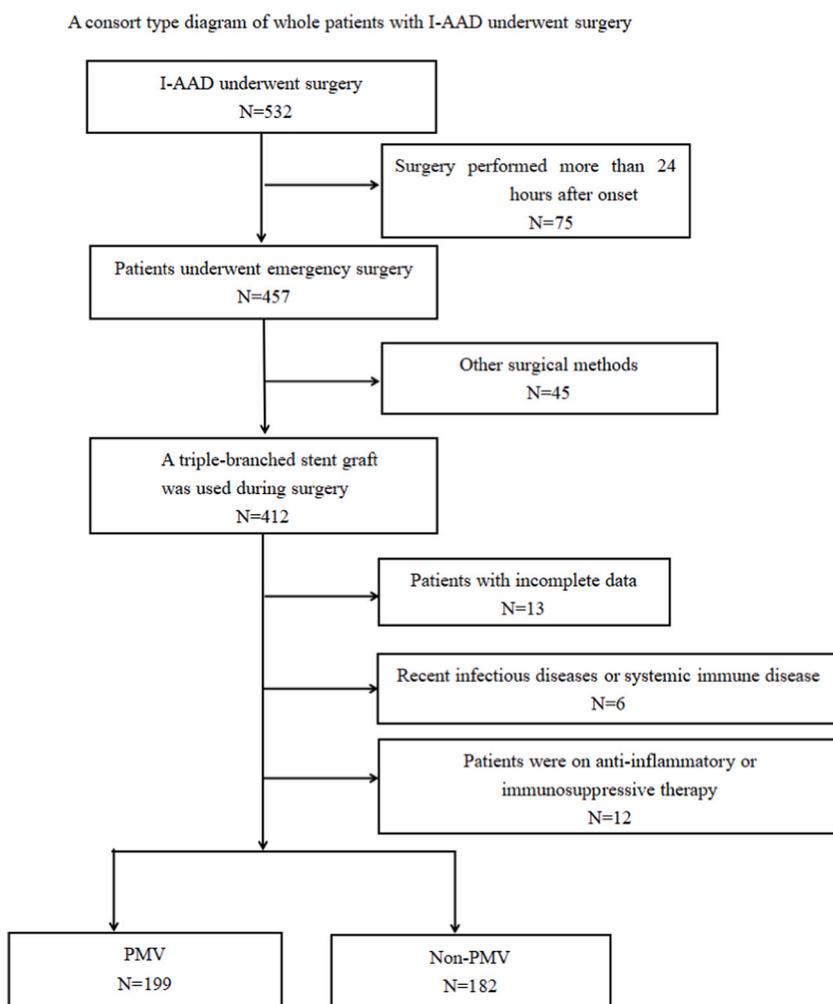
2405-8440/© 2023 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

List of abbreviations

AAD	acute aortic dissection
I-AAD	Acute DeBakey Type I Aortic Dissection
IL-6	interleukin-6
PMV	prolonged mechanical ventilation
ROC	receiver operating characteristics
OR	odds ratios
AUC	area under curve
CI	confidence interval
CPB	cardiopulmonary bypass

1. Background

Acute DeBakey type I aortic dissection (I-AAD) is a deadly cardiovascular emergency. Surgical treatment is urgent, as mortality increases by approximately 1% for every hour that surgical intervention is delayed [1,2]. The perioperative management of I-AAD is characterized by its urgent presentation, complexity of surgical management, organ dysfunction, and high in-hospital mortality.



I-AAD - Acute DeBakey Type I Aortic Dissection
 PMV - prolonged mechanical ventilation

Fig. 1. A consort type diagram of whole patients with I-AAD underwent surgery.

Although overall surgical techniques are improving and mortality rates decreasing, postoperative complications remain common [3–5]. Many considerable efforts to improve postoperative morbidity and mortality for acute type A aortic dissection have been made. Studies have shown that inflammation plays a very important role in I-AAD and is related to I-AAD severity, morbidity, and mortality closely [5–8]. The presence of an aortic dissection and surgical procedures under hypothermic cardiopulmonary bypass (CPB) stimulate the inflammatory system in the body, which then frequently releases substantial amounts of inflammatory mediators, such as interleukin-6 (IL-6) [9–11]. As a vital proinflammatory mediator, IL-6 is well-characterized during the development and progression of the inflammatory process [12,13]. The close relationship between IL-6 and trauma after acute aortic dissection surgery makes IL-6 a potentially useful parameter for predicting surgical outcome in patients with I-AAD.

Some studies have indicated that postoperative respiratory dysfunction often occurs after I-AAD, which is mainly caused by systemic inflammation and ischemia-reperfusion injury [14]. In this critical condition, a subset of patients requires PMV, which is associated with increased nosocomial infections, morbidity, and mortality after cardiac surgery [15]. Previous studies have shown that increased IL-6 levels before cardiac surgery predicts PMV [16], but there is no study on the relationship between the summation of preoperative (pre-IL-6) and postoperative IL-6 (post-IL-6) levels and PMV in patients with I-AAD. Therefore, the purpose of this study was to investigate the predictive effect of the summation of pre-IL-6 and post-IL-6 (total IL-6) levels on PMV in patients with I-AAD.

2. Patients and methods

2.1. Study population

Patients with I-AAD, confirmed by computerized tomography imaging, were enrolled. We retrospectively analyzed the medical records of 381 patients with I-AAD who underwent emergency surgery at our cardiac center from June 2018 to June 2022. The inclusion criteria were as follows: patients who underwent emergency surgery within 24 h of onset with total aortic arch replacement using a triple-branched stent graft, as previously described by Chen et al. [17]. We excluded patients with incomplete data, surgery performed more than 24 h after onset, patients with history of recent infectious diseases or systemic immune disease, and those who were on anti-inflammatory or immunosuppressive therapy (Fig. 1). Extubation was only performed when the patient was fully awake, with sufficient muscle contraction, normal body temperature, stable heart rate and blood pressure, stable hemodynamics, no active bleeding, spontaneous respiratory gas exchange, and adequate respiratory mechanics.

3. Definitions

PMV was defined as mechanical ventilation lasting more than 48 h after surgery, or when the patient was re-intubated after extubation and the cumulative duration of mechanical ventilation was more than 48 h [18]. Pre-IL-6 was defined as peripheral blood IL-6 levels measured within 24 h of symptom onset before surgery. Post-IL-6 was defined as peripheral blood IL-6 levels measured 6 h after surgery. Total IL-6 was defined as the summation of pre- and post-IL-6 levels. A surgery was defined as an emergency surgery when the doctors' assessment was that surgery was needed within a short period of time, or the patient's life was in danger. Acute renal insufficiency was defined as the serum creatine level greater than 188 $\mu\text{mol/L}$, with no previous history of renal insufficiency. Acute liver insufficiency was defined as more than three times higher than the high end of normal levels of alanine aminotransferase or aspartate aminotransferase.

3.1. Data collection

The patients' clinical data were recorded and analyzed retrospectively. Study data included baseline data, serum measurements performed within 24 h after onset and 6 h after surgery, preoperative complications (diabetes, hypertension, coronary heart disease), surgical data (operation time, cardiopulmonary bypass time, aortic clamp time, blood transfusion volume), postoperative complications, and in-hospital mortality.

3.2. Statistical analysis

Mean \pm standard deviation (SD) or median (interquartile range) were used for continuous variables according to whether they followed a normal distribution. The variables were analyzed using *t*-test for normally distributed continuous variables. Numbers and percentages (n, %) were used for categorical variables, and tested using a chi-squared test or Fisher's exact probability test. Univariate and multivariate logistic regression analyses were used to identify each potential risk factor for PMV. Those factors with $p < 0.100$ in the univariate model were entered into the multivariate model. The cut-off point was determined by the ROC curve, the AUC, and sensitivity and specificity were determined. For continuous variables, the corresponding value of the highest Youden index was taken as the dichotomous segmentation point through the ROC curve. All data were completed using the SPSS 19.0 statistical software package (IBM Corp., Armonk, NY, USA). P values < 0.05 were statistically significant.

4. Results

PMV occurred in 199 patients (PMV group), while 182 patients did not require PMV (non-PMV group). There were significant differences between the PMV and non-PMV groups in age [55.0 (48.5, 61.0) vs. 52.5 (43.0, 61.0) years, $p = 0.039$], smoking [126

(63.3%) vs. 81 (44.5%), $p = 0.002$], pre IL-6 level [65.8 (42.8, 83.5) vs. 39.4 (25.6, 48.9) pg/mL, $p < 0.001$] (Fig. 2), preoperative D-dimer [7.55 (3.60, 14.80) vs. 4.95 (2.98, 9.25) mmol/L, $p < 0.001$], lactic acid [1.73 ± 0.99 vs. 1.45 ± 0.95 mmol/L, $p = 0.005$], and intraoperative blood transfusion volume [2.7 ± 1.1 vs. 2.4 ± 1.0 units, $p = 0.012$]. The factors that did not show significant differences between the two groups are summarized in Table 1.

There were significant differences between the PMV and non-PMV groups in post-IL-6 level [103.5 (53.7, 147.0) vs. 52.1 (34.6, 67.9) pg/mL, $p < 0.001$] (Fig. 3), total IL-6 [162.8 (110.9, 208.6) vs. 86.2 (70.1, 117.2) pg/mL, $p < 0.001$] (Fig. 4), seroma volume of drainage in 24 h after surgery [372.1 ± 256.6 vs. 315.0 ± 215.9 mL, $p = 0.020$], length of intensive care unit stay [6.0 (4.0, 7.5) vs. 3.0 (2.0, 4.0) days, $p < 0.001$], hospitalization time [20.0 (15.0, 25.0) vs. 16.0 (13.0, 19.0), $p < 0.001$], and in-hospital mortality [22 (11.1%) vs. 6 (3.3%), $p = 0.004$]. The factors that did not show significant differences between the two groups are summarized in Table 2.

The cut-off point was determined by the ROC curve. Multiple regression analysis showed that smoking, preoperative D-Dimer ≥ 7.62 $\mu\text{g/mL}$, post-IL-6 ≥ 67.1 pg/mL, and total IL-6 ≥ 83.4 pg/mL were associated risk factors for PMV. OR of smoking, preoperative D-Dimer ≥ 7.62 $\mu\text{g/mL}$, post-IL-6 ≥ 67.1 pg/mL, and total IL-6 ≥ 83.4 pg/mL were [1.681, 95% confidence interval (CI) 1.010–2.797, $P = 0.046$], [2.687, 95% CI 1.599–4.514, $p < 0.001$], [3.259, 95% CI 1.922–5.524, $p < 0.001$], and [4.515, 95% CI 2.241–9.098, $p < 0.001$], respectively (Table 3).

Furthermore, the AUC was 0.594 for smoking, 0.651 for preoperative D-dimer ≥ 7.62 $\mu\text{g/mL}$, 0.775 for post-IL-6 ≥ 67.1 pg/mL, and 0.825 for total IL-6 ≥ 83.4 pg/mL. The sensitivity and specificity of smoking for predicting postoperative PMV in patients with I-AAD were 63.3% and 55.5%, respectively (95% CI 0.537–0.651, $P < 0.001$); preoperative D-dimer ≥ 7.62 $\mu\text{g/mL}$ were 58.8% and 64.5%, respectively (95% CI 0.596–0.706, $P < 0.001$); post-IL-6 ≥ 67.1 pg/mL were 75.9% and 62.1%, respectively (95% CI 0.727–0.823, $P = 0.002$); and total IL-6 ≥ 83.4 pg/mL were 91.5% and 78.2%, respectively (95% CI 0.782–0.868, $P < 0.001$) (Table 4 and Fig. 5).

5. Discussion

Numerous studies have explored the postoperative prognosis of patients with AAD [19–21], and the prediction of morbidity and mortality after I-AAD surgery is important, especially during postoperative mechanical ventilation in the intensive care unit. During this phase, the patient’s vital signs are usually unstable, their body is damaged by the I-AAD and CPB procedure, and a large number of inflammatory mediators are produced. Prediction of these inflammatory mediators are critical for intensive care unit managers and clinicians to effectively treat the patient, as well as for patient outcomes. These inflammatory mediators could also be used as medical treatment quality control tools. Among existing literature, no reports were found relating to the association between total IL-6 and PMV in patients with I-AAD. In this study, we retrospectively recruited 381 patients with I-AAD who underwent emergency surgery at a cardiac center, and found that pre-IL-6, post-IL-6, and total IL-6 levels were higher in the PMV than the non-PMV group. We concluded that higher IL-6 could be an independent predictor for PMV in patients with I-AAD. In addition, the predictive performance of total IL-6 was superior to that of post-IL-6 levels alone. Hence, the study suggested that total IL-6 is a good predictor for identifying

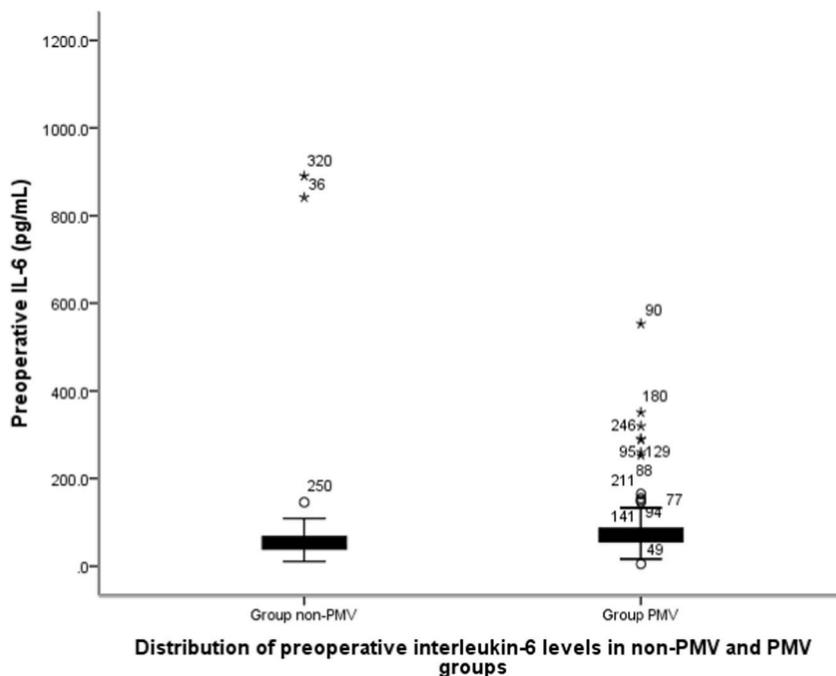


Fig. 2. Distribution of preoperative interleukin-6 levels in non-PMV and PMV groups.

Table 1
Preoperative and intraoperative data on PMV and non-PMV patient groups.

Variables	Group PMV (n = 199)	Group non-PMV (n = 187)	P value
Preoperative data			
Male , n (%)	157 (78.9)	132 (72.5)	0.147
Age, n (year)	55.0 (48.5, 61.0)	52.5 (43.0, 61.0)	0.039
Body mass index (kg/M ²)	26.0 ± 4.0	25.7 ± 4.1	0.586
Smoking , n (%)	126 (63.3)	81 (44.5)	0.002
Drinking , n (%)	77 (38.7)	57 (31.3)	0.132
Hypertension , n (%)	144 (72.4)	139 (76.4)	0.371
Diabetes , n (%)	12 (6.0)	9 (4.9)	0.643
Coronary heart disease , n (%)	19 (9.5)	13 (7.1)	0.398
Acute renal insufficiency , n (%)	7 (3.5)	6 (3.3)	0.906
Acute liver insufficiency , n (%)	2 (1.0)	2 (1.1)	0.679
Pre IL-6 (pg/mL)	65.8 (42.8, 83.5)	39.4 (25.6, 48.9)	< 0.001
D-Dimer (ug/mL)	7.55 (3.60, 14.80)	4.95 (2.98, 9.25)	0.015
Albumin (g/L)	37.2(34.8, 40.2)	38.0 (35.4, 40.7)	0.264
Creatinine (umol/L)	75.0 (64.0, 103.0)	78.0 (68.0, 108.0)	0.237
Leukocyte (10 ⁹ /L)	12.1 (9.5, 14.3)	12.3 (9.3, 14.3)	0.961
Neutrophil granulocyte (10 ⁹ /L)	10.2 (7.6, 12.5)	10.5 (7.7, 12.7)	0.299
Heamoglobin (g/L)	131.0 (119.0, 146.0)	132.0 (118.0, 144.0)	0.500
Platelet counts (10 ⁹ /L)	188.0 (152.0, 227.0)	182.0 (155.0, 235.0)	0.383
Prothrombin time (sec)	13.7 (13.1, 14.4)	13.8 (13.3, 14.8)	0.232
N-terminal pro brain natriuretic peptide (pg/mL)	973.1 ± 2974.4	1463.8 ± 5003.2	0.296
Lactic acid (mmol/L)	1.73 ± 0.99	1.45 ± 0.95	0.005
Alanine aminotransferase (IU/L)	35.0 (25.0, 44.0)	32.0 (23.0, 42.0)	0.111
Aspartate aminotransferase (IU/L)	33.0 (21.0, 46.0)	29.0 (20.0, 46.0)	0.138
Ejection fraction (%)	63.4 ± 6.9	63.3 ± 7.3	0.901
History of cardiac surgery , n (%)	13 (6.5)	10 (5.5)	0.671
Surgical data			
Operation time (min)	302.9 ± 55.0	300.2 ± 52.5	0.632
Cardiopulmonary bypass time (min)	140.9 ± 24.4	140.6 ± 26.6	0.884
Aortic clamp time (min)	49.5 ± 15.0	48.9 ± 16.1	0.711
Blood transfusion volume (unit)	2.7 ± 1.1	2.4 ± 1.0	0.012

Continuous normally distributed variables were expressed as mean(±standard deviation) and not-normally distributed variables as medians(interquartile range). Counts are expressed as percentages. χ^2 test for categorical variables and wilcoxon rank sum test for continuous variables.

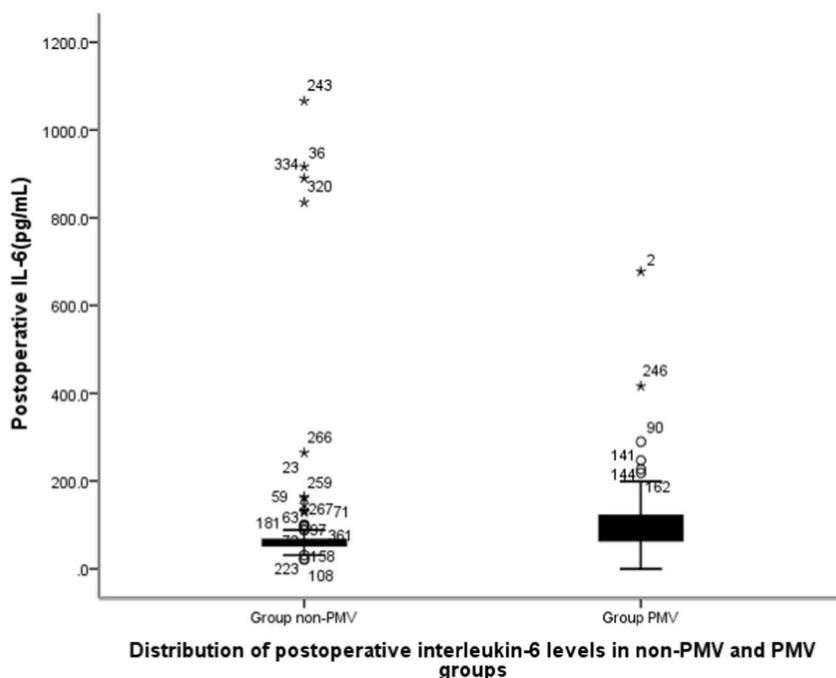


Fig. 3. Distribution of postoperative interleukin-6 levels in non-PMV and PMV groups.

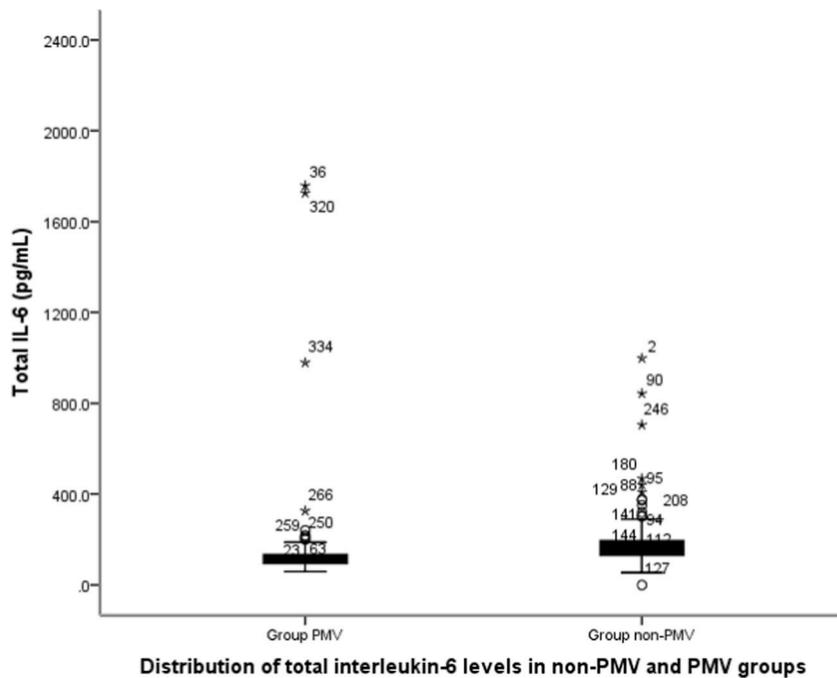


Fig. 4. Distribution of total interleukin-6 levels in non-PMV and PMV groups.

Table 2

Postoperative data on PMV and non-PMV patient groups.

Valuables	Group PMV (n = 199)	Group non-PMV (n = 182)	P value
Mechanical ventilation (h)	72.0 (59.5, 105.5)	29.0 (22.0, 37.0)	< 0.001
Seroma volume of drainage in 24 h after surgery (mL)	372.1 ± 256.6	315.0 ± 215.9	0.020
Length of intensive care unit (d)	6.0 (4.0, 7.5)	3.0 (2.0, 4.0)	< 0.001
Hospitalization time (d)	20.0 (15.0, 25.0)	16.0 (13.0, 19.0)	< 0.001
In-hospital mortality, n (%)	22 (11.1)	6 (3.3)	0.004
Serum parameters at 6 h after operation			
Post IL-6 (pg/mL)	103.5 (53.7, 147.0)	52.1 (34.6, 67.9)	< 0.001
Total IL-6 (pg/mL)	162.8 (110.9, 208.6)	86.2 (70.1, 117.2)	< 0.001
Postoperative D-Dimer (ug/mL)	7.98 (3.62, 13.51)	6.58 (3.60, 11.39)	0.330
Postoperative lactic acid (mmol/L)	2.83 ± 2.21	2.67 ± 1.89	0.299

Continuous normally distributed variables were expressed as mean(±standard deviation) and not-normally distributed variables as medians(interquartile range).

patients with I-AAD at high risk of PMV. This will be of great help in our future clinical practice to evaluate the occurrence of postoperative PMV in patients with I-AAD and provides a good basis for our next randomized controlled trials.

As an inflammatory cytokine, IL-6 is closely related to cardiovascular diseases [22,23]. The main reason is that IL-6 plays a vital role in both immune and inflammation response, is an important inflammatory marker of cardiovascular diseases, and will increase in the early stages of AAD. Some studies have shown that increased IL-6 has a high predictive value for early poor prognosis after AAD [24]. When body tissue injury occurs, monocytes and macrophages rapidly produce IL-6. IL-6 helps restore damaged tissue by activating immune and acute phase responses, and is released in the bloodstream by the vascular endothelium and stimulates the liver to produce acute-phase proteins, such as C-reactive protein and fibrinogen. Therefore, in AAD when inflammation plays a dominant role, IL-6 is elevated, which corroborates our findings of significantly increased pre-IL-6 in the PMV group. This result is consistent with some existing studies [16,25].

CPB is also known to activate a severe inflammatory response [26], which leads to the release of inflammatory cytokines and neutrophil activation. Studies have shown that CPB demonstrates the entire inflammatory response through induced leukocytosis and elevated plasma IL-6 levels, and that systemic inflammation is mainly induced in the process of reperfusion [27]. The procedure previously described by Chen et al. were used in the total arch replacement of the aorta for all patients included in this study. Even though this surgical method has shown sufficiently excellent performance [3,28,29], ischemia-reperfusion injury cannot be avoided in total arch replacement of the aorta [8]. Ischemia-reperfusion injury results in the degranulation of leukocytes and the release of inflammatory mediators, such as interleukins. IL-6 plays an important role in understanding the pathogenesis and development of inflammation in the body, mainly derived from the involvement of lymphocytes, macrophages, fibroblasts and endothelial cells [23,

Table 3
Univariate and multivariate analyses for patients with prolonged mechanical ventilation.

Variable	Univariate Model			Multivariate Model		
	OR	95% CI	P value	OR	95% CI	P value
Age ≥56 (years)	3.561	1.941–6.535	< 0.001	1.261	0.748–2.126	0.384
Male	0.891	0.476–1.652	0.202	–	–	–
Smoking, presence	2.152	1.427–3.245	< 0.001	1.681	1.010–2.797	0.046
Drinking, presence	1.384	0.906–2.114	0.133	–	–	–
Body mass index ≥27.5 (kg/m ²)	0.986	0.643–1.513	0.950	–	–	–
Pre IL-6 ≥ 44.3 (pg/mL)	3.397	2.220–5.198	< 0.001	1.520	0.862–2.682	0.148
Preoperative D-Dimer ≥7.62 (ug/mL)	2.568	1.697–3.886	< 0.001	2.687	1.599–4.514	< 0.001
Leukocyte ≥12.1 (10 ⁹ /L)	1.177	0.836–1.412	0.158	–	–	–
Neutrophil granulocyte ≥8.9 (10 ⁹ /L)	1.111	0.936–1.267	0.112	–	–	–
Heamoglobin ≥128.4 (g/L)	0.918	0.610–1.382	0.683	–	–	–
Platelet counts ≥186.5 (10 ⁹ /L)	1.220	0.816–1.824	0.333	–	–	–
Albumin < 33.6 (g/L)	1.312	0.675–2.549	0.424	–	–	–
Prothrombin time ≥15.2 (sec)	1.112	0.717–2.021	0.395	–	–	–
N-terminal pro brain natriuretic peptide ≥165.5 (pg/mL)	1.551	0.799–2.870	0.489	–	–	–
Lactic acid ≥1.85 (mmol/L)	1.833	1.171–2.868	0.008	1.681	0.929–2.855	0.089
Alanine aminotransferase ≥40.0 (IU/L)	1.276	0.704–2.314	0.422	–	–	–
Aspartate aminotransferase ≥46.0 (IU/L)	1.170	0.629–2.176	0.619	–	–	–
Creatinine ≥98.5 (umol/L)	1.412	0.795–2.293	0.113	–	–	–
Left ventricular ejection fraction ≥62.3 (%)	0.545	0.241–1.235	0.146	–	–	–
Marfan's syndrome, presence	1.212	0.618–1.873	0.331	–	–	–
Hypertension, presence	1.266	0.616–2.602	0.520	–	–	–
Diabetes, presence	0.692	0.215–2.099	0.316	–	–	–
Coronary heart disease, presence	1.772	0.526–1.920	0.352	–	–	–
History of cardiac surgery, presence	1.403	0.310–6.350	0.660	–	–	–
Acute renal insufficiency, presence	1.485	0.509–3.012	0.221	–	–	–
Acute liver insufficiency, presence	1.824	0.663–2.128	0.239	–	–	–
Operative time ≥299.5 (min)	2.180	1.444–3.292	< 0.001	1.608	0.920–2.812	0.095
CPB time ≥164.0 (min)	3.171	1.750–5.745	< 0.001	1.889	0.844–4.229	0.122
Aortic clamp time ≥48.5 (min)	1.618	1.071–2.443	0.022	1.284	0.732–2.252	0.383
Blood transfusion volume ≥3.0 (unit)	1.605	0.938–2.746	0.084	1.495	0.750–2.979	0.253
Seroma volume of drainage in 24 h after surgery ≥335.0 (mL)	1.763	1.147–2.710	0.010	1.401	0.831–2.362	0.206
Post IL-6 ≥ 67.1 (pg/mL)	5.326	3.438–8.252	< 0.001	3.259	1.922–5.524	< 0.001
Total IL-6 ≥ 83.4 (pg/mL)	8.950	5.185–15.448	< 0.001	4.515	2.241–9.098	< 0.001
Postoperative D-Dimer ≥7.79 (ug/mL)	1.172	0.812–1.794	0.190	–	–	–
Postoperative lactic acid ≥2.55 (mmol/L)	1.655	0.736–2.798	0.231	–	–	–

Confidence interval (CI), odds ratios (OR).

Table 4
The prognostic performances of parameters in predicting prolonged mechanical ventilation in patients with I-AAD.

	Post IL-6	Total IL-6	Smoking	Preoperative D-dimer
AUC	0.775	0.825	0.594	0.651
95% CI	0.727–0.823	0.782–0.868	0.537–0.651	0.596–0.706
p value	0.002	< 0.001	< 0.001	< 0.001
Cut-off value	≥67.1 (pg/mL)	≥83.4 (pg/mL)	Yes/no	≥7.62 (ug/mL)
Sensitivity, %	75.9	91.5	63.3	58.8
Specificity, %	62.1	78.2	55.5	64.3

Postoperative in-hospital mortality (POIM), acute type A aortic dissection (ATAAD), blood urea nitrogen (BUN), serum albumin (SA), blood urea nitrogen to serum albumin ratio (BA-R), area under curve (AUC), confidence interval (CI).

30,31]. In general, plasma IL-6 significantly increases 1 h after CPB and peaks at 6 h [32,33]. Therefore, our focus shifted to the postoperative increase in IL-6 from the baseline or preoperative level.

Whether the CPB procedure itself directly contributes to overall postoperative pulmonary dysfunction, remains controversial. Improvements in CPB technology, such as the use of Drew-Anderson technique, heparin-coated circuits, or ultrafiltration may help to reduce the activation of systemic inflammatory response syndromes, or to remove various proinflammatory cytokines [34–36]. Indirect factors associated with lung dysfunction include ischemia and reperfusion of the cardiomyocytes, which are associated with increased secretion of some proinflammatory factors. Cardioplegic perfusion and myocardial cooling have been shown to mitigate the negative cardiac effects of ischemia after aortic clipping by reducing the metabolic demands of the myocardium [37,38]. It has also been shown that reperfusion during CPB can cause inflammatory reactions, impair hemostatic function, enhance inflammatory reactions, and impair pulmonary function after surgery [39–41]. Hauser et al. found that after CPB the IL-6 levels in lung alveolar lavage fluid and serum significantly increased, and was closely related to postoperative morbidity [42]. Therefore, perioperative detection of IL-6 levels is of great significance for clinical treatment. Our current findings suggest that post-IL-6 ≥67.1 pg/mL and total IL-6 ≥83.4

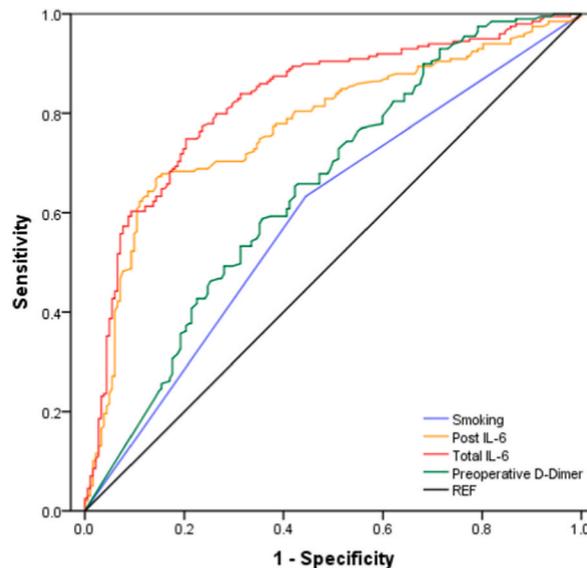


Fig. 5. Comparison of the receiver operating characteristic curves of post-IL-6 level, total IL-6 level, preoperative D-dimer level, and smoking.

pg/mL were associated risk factors for postoperative PMV. The sensitivity and specificity of post-IL-6 ≥ 67.1 pg/mL for predicting postoperative PMV in patients with I-AAD were 75.9% and 62.1%, respectively, while those of total IL-6 ≥ 83.4 pg/mL were even higher, at 91.5% and 78.2%, respectively.

We also found significant statistical differences in smoking and age between the two groups and multivariate analysis showed that smoking was a potential risk factor for PMV. Therefore, in order to achieve early extubation while reducing the incidence of re-intubation, physicians should carefully consider the extubation time, and take appropriate additional measures for older patients and patients with a smoking history.

In conclusion, we combined the different levels of IL-6, including pre-, post- and total IL-6, in patients with I-AAD to predict the risk of postoperative PMV. Using combinations of these levels provides more comprehensive results than studying preoperative IL-6 alone. By doing this we also considered the influence of surgical and CPB factors on IL-6. Total IL-6 is thus better in predicting postoperative PMV in patients with I-AAD; this provides a good foundation for subsequent research and an improved basis for clinical treatment.

5.1. Limitations

The study had unavoidable limitations related to retrospective studies. A multicenter, prospective study is the next step for further validation. In this study, IL-6 level comparisons were limited to 24 h before and 6 h after surgery; we need to further study the changes of IL-6 in individuals over time.

6. Conclusion

Post-IL-6 ≥ 67.1 pg/mL is potentially valuable for predicting postoperative PMV in patients with I-AAD and total IL-6 ≥ 83.4 pg/mL has a more pronounced predictive value.

Declarations

Ethics approval and consent to participate

The study's retrospective was approved by the Ethics Committee of Union Hospital of Fujian Medical University, and conformed to the Declaration of Helsinki. The requirement for informed consent was waived by the ethics committee Union Hospital of Fujian Medical University based on the study's retrospective analysis of patient data.

Consent for publication

Not applicable.

Funding

This work was funded by the National Natural Science Foundation of China (U2005202), Startup Fund for Scientific Research at Fujian Medical University (2020QH1076) and Key Laboratory of Cardio-Thoracic Surgery Fujian Medical University, Fujian Province University Construction Project (No. 2019-67)

Author contribution statement

- 1 - Conceived and designed the experiments : Liangwan Chen.
- 2 - Performed the experiments: Zhihuang Qiu;
- 3 - Analyzed and interpreted the data: Zhihuang Qiu;
- 4 - Contributed reagents, materials, analysis tools or data: Linfeng Xie;
- 5 - Wrote the paper: Qingsong Wu and Qinghua Lin, and Qingsong Wu and Qinghua Lin are contributed equally to this study and share first authorship.

Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no conflict of interest.

Acknowledgements

We would like to thank Editage (www.editage.cn) for English language editing.

References

- [1] W. Maisat, S. Siriratwarangkul, A. Charoensri, et al., Perioperative risk factors for delayed extubation after acute type A aortic dissection surgery, *J. Thorac. Dis.* 12 (9) (2020 Sep) 4796–4804.
- [2] L.A. Pape, M. Awais, E.M. Woznicki, et al., Presentation, diagnosis, and outcomes of acute aortic dissection: 17-year trends from the International Registry of Acute Aortic Dissection, *J. Am. Coll. Cardiol.* 66 (2015) 350–358.
- [3] Q. Wu, J. Xiao, Z. Qiu, et al., Long-term outcomes of treatment with different stent grafts in acute DeBakey type I aortic dissection, *J. Card. Surg.* 35 (11) (2020 Nov) 3078–3087.
- [4] C.A. Nienaber, R.E. Clough, Management of acute aortic syndrome, *Lancet* 385 (2015) 800–811.
- [5] V. Rampold, S. Trimarchi, K.A. Eagle, C.A. Nienaber, et al., Simple risk models to predict surgical mortality in acute type A aortic dissection: the International Registry of Acute Aortic Dissection score, *Ann. Thorac. Surg.* 83 (2007) 55–61.
- [6] M. Wen, Y. Han, J. Ye, et al., Peri-operative risk factors for in-hospital mortality in acute type A aortic dissection, *J. Thorac. Dis.* 11 (9) (2019 Sep) 3887–3895.
- [7] R.H. Mehta, T. Suzuki, P.G. Hagan, et al., Predicting death in patients with acute type a aortic dissection, *Circulation* 105 (2002) 200–206.
- [8] M. Ghoreishi, E.S. Wise, L. Croal-Aprahams, et al., A novel risk score predicts operative mortality after acute type a aortic dissection repair, *Ann. Thorac. Surg.* 106 (2018) 1759–1766.
- [9] A. Brocca, G.M. Virzi, M. de Cal, et al., Elevated levels of procalcitonin and interleukin-6 are linked with postoperative complications in cardiac surgery, *Scand. J. Surg.* 106 (2017) 318–324.
- [10] M. Wen, Y. Han, J. Ye, et al., Peri-operative risk factors for in-hospital mortality in acute type A aortic dissection, *J. Thorac. Dis.* 11 (2001) 3887–3895.
- [11] P. Nagareddy, S.S. Smyth, Inflammation and thrombosis in cardiovascular disease, *Curr. Opin. Hematol.* 20 (2013) 457–463.
- [12] E. Squicciarro, C. Labriola, P.G. Malvindi, et al., Prevalence and clinical impact of systemic inflammatory reaction after cardiac surgery, *J. Cardiothorac. Vasc. Anesth.* 33 (6) (2019 Jun) 1682–1690.
- [13] J.R. Day, K.M. Taylor, The systemic inflammatory response syndrome and cardiopulmonary bypass, *Int. J. Surg.* 3 (2005) 129–140.
- [14] F. Sanfilippo, G.J. Palumbo, E. Bignami, et al., Acute respiratory distress syndrome in the perioperative period of cardiac surgery: predictors, diagnosis, prognosis, management options, and future directions, *J. Cardiothorac. Vasc. Anesth.* 36 (4) (2022 Apr) 1169–1179.
- [15] A. Suarez-Pierre, C.D. Fraser, X. Zhou, et al., Predictors of operative mortality among cardiac surgery patients with prolonged ventilation, *J. Card. Surg.* 34 (2019) 759–766.
- [16] A. Bauer, I. Korten, G. Juchem, et al., EuroScore and IL-6 predict the course in ICU after cardiac surgery, *Eur. J. Med. Res.* 26 (1) (2021 Mar 26) 29.
- [17] L.W. Chen, X.F. Dai, X.J. Wu, et al., Ascending aorta and hemiarch replacement combined with modified triple-branched stent graft implantation for repair of acute DeBakey type I aortic dissection, *Ann. Thorac. Surg.* 103 (2017) 595–601.
- [18] C.N. Li, L. Chen, Y.P. Ge, et al., Risk factors for prolonged mechanical ventilation after total aortic arch replacement for acute DeBakey type I aortic dissection, *Heart Lung Circ.* 23 (9) (2014 Sep) 869–874.
- [19] M. Luehr, J. Merkle-Storms, S. Gerfer, et al., Evaluation of the GERAADA score for prediction of 30-day mortality in patients with acute type A aortic dissection, *Eur. J. Cardio. Thorac. Surg.* 59 (5) (2021) 1109–1114.
- [20] Y. Lin, Q. Chen, Y. Peng, et al., Prognostic nutritional index predicts in-hospital mortality in patients with acute type A aortic dissection, *Heart Lung* 50 (1) (2021 Jan-Feb) 159–164.
- [21] M. Yamasaki, H. Yoshino, T. Kunihara, et al., Risk analysis for early mortality in emergency acute type A aortic dissection surgery: experience of Tokyo Acute Aortic Super-network, *Eur. J. Cardio-Thor. Surg.* 60 (4) (2021) 957–964. Oct 22.
- [22] A. Forrer, F. Schoenrath, M. Torzewski, et al., Novel blood biomarkers for a diagnostic workup of acute aortic dissection, *Diagnostics* 11 (4) (2021 Mar 30) 615.
- [23] P.M. Ridker, M. Rane, Interleukin-6 signaling and anti-interleukin-6 therapeutics in cardiovascular disease, *Circ. Res.* 128 (11) (2021 May 28) 1728–1746.
- [24] Q. Wu, J. Li, L. Chen, et al., Efficacy of interleukin-6 in combination with D-dimer in predicting early poor postoperative prognosis after acute stanford type a aortic dissection, *J. Cardiothorac. Surg.* 15 (1) (2020 Jul 16) 172.
- [25] X. Chen, J. Zhou, M. Fang, et al., Procalcitonin, interleukin-6 and C-reactive protein levels predict renal adverse outcomes and mortality in patients with acute type A aortic dissection, *Front. Surg.* 9 (2022 Apr 28), 902108.

- [26] F. Yildirim, D. Amanvermez Senarslan, et al., Systemic inflammatory response during cardiopulmonary bypass: axial flow versus radial flow oxygenators, *Int. J. Artif. Organs* 45 (3) (2022 Mar) 278–283.
- [27] M. Engels, E. Bilgic, A. Pinto, et al., A cardiopulmonary bypass with deep hypothermic circulatory arrest rat model for the investigation of the systemic inflammation response and induced organ damage, *J. Inflamm.* 11 (2014) 26.
- [28] L.W. Chen, X.J. Wu, X.F. Dai, et al., A self-adaptive triple-branched stent graft for arch repair during open type A dissection surgery, *J. Thorac. Cardiovasc. Surg.* 149 (5) (2015 May) 1278, 12783.e1.
- [29] Z.H. Qiu, L.W. Chen, L.M. Liao, et al., Efficiency of modified triple-branched stent graft in type I aortic dissection: two-year follow-up, *Ann. Thorac. Surg.* 110 (3) (2020 Sep) 925–932.
- [30] P. Libby, Targeting inflammatory pathways in cardiovascular disease: the inflammasome, interleukin-1, interleukin-6 and beyond, *Cells* 10 (4) (2021 Apr 20) 951.
- [31] S.M. Yuan, Interleukin-6 and cardiac operations, *Eur. Cytokine Netw.* 29 (1) (2018 Mar 1) 1–15.
- [32] A. Jenke, M. Yazdanyar, S. Miyahara, et al., AdipoRon attenuates inflammation and impairment of cardiac function associated with cardiopulmonary bypass-induced systemic inflammatory response syndrome, *J. Am. Heart Assoc.* 10 (6) (2021 Mar 16), e018097.
- [33] A. Sablotzki, M. Dehne, T. Menges, et al., Alterations of the cytokine network in patients undergoing cardiopulmonary bypass, *Perfusion* 12 (1997) 393–403.
- [34] E. Squicciarro, A. Stasi, R. Lorusso, et al., Narrative review of the systemic inflammatory reaction to cardiac surgery and cardiopulmonary bypass, *Artif. Organs* 46 (4) (2022 Apr) 568–577.
- [35] J.A. Richter, H. Meisner, P. Tassani, et al., Drew-Anderson technique attenuates systemic inflammatory response syndrome and improves respiratory function after coronary artery bypass grafting, *Ann. Thorac. Surg.* 69 (2000) 77–83.
- [36] P.G. Jansen, V.H. te, R.A. Huybregts, et al., Reduced complement activation and improved postoperative performance after cardiopulmonary bypass with heparin-coated circuits, *J. Thorac. Cardiovasc. Surg.* 110 (1995) 829–834.
- [37] A. Margraf, N. Ludwig, A. Zarbock, et al., Systemic inflammatory response syndrome after surgery: mechanisms and protection, *Anesth. Analg.* 131 (6) (2020 Dec) 1693–1707.
- [38] A. Al-Fares, T. Pettenuzzo, L. Del Sorbo, Extracorporeal life support and systemic inflammation, *Intens. Care Med.* 7 (Suppl 1) (2019 Jul 25) 46.
- [39] H. Budde, J. Riggert, S. Vormfelde, T. Tirilomis, M.G. Friedrich, The effect of a novel turbulence-controlled suction system in the prevention of hemolysis and platelet dysfunction in autologous surgery blood, *Perfusion* 34 (1) (2019 Jan) 58–66.
- [40] J. Gäbel, C.S. Hakimi, M. Westerberg, et al., Retransfusion of cardiomyotomy suction blood impairs haemostasis: ex vivo and in vivo studies, *Scand. Cardiovasc. J.* 47 (6) (2013 Dec) 368–376.
- [41] M. Westerberg, A. Bengtsson, A. Jeppsson, Coronary surgery without cardiomyotomy suction and autotransfusion reduces the postoperative systemic inflammatory response, *Ann. Thorac. Surg.* 78 (1) (2004 Jul) 54–59.
- [42] G.J. Hauser, J. Ben-Ari, M.P. Colvin, et al., Interleukin-6 levels in serum and lung lavage fluid of children undergoing open heart surgery correlate with postoperative morbidity, *Intensive Care Med.* 24 (1998) 481–486.