

Received: 2015.11.05
Accepted: 2016.03.02
Published: 2016.04.02

Effects of MIAVS on Early Postoperative ELWI and Respiratory Mechanics

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

B **Wei Li***
C **Qian Xue***
B **Kai Liu***
B **Jiang Hong**
E **Jibin Xu**
E **Lihui Wu**
F **Guangyu Ji**
G **Zhinong Wang**
AG **Yufeng Zhang**

Department of Cardiothoracic Surgery, Changzheng Hospital, Second Military Medical University, Shanghai, P.R. China

* Wei Li, Qian Xue and Kai Liu contributed equally to this work

Corresponding Authors: Yufeng Zhang and Zhinong Wang, e-mail: zyf19810824@163.com

Source of support: This work was supported by the National Natural Science Foundation of China (No. 81300120)

Background: The effects of minimally invasive aortic valve surgery (MIAVS) on the early postoperative extravascular lung water index (ELWI) and respiratory mechanics have rarely been studied.

Material/Methods: A total of 90 patients were divided into 3 groups: a conventional full sternotomy (CS) group (n=30), an upper ministernotomy (US) group (n=30), and a right anterior thoracotomy (RT) group (n=30). Hemodynamic and respiratory mechanics parameters were recorded at perioperative time points, including before skin incision (T(-1)); at sternum closing (T0); and 4 h (T4), 8 h (T8), 12 h (T12), and 24 h (T24) after the operation. The ventilator support time, ICU length of stay, and postoperative hospitalization time, as well as the thoracic drainage volume and blood transfusion volume, were recorded.

Results: The ELWI and pulmonary vascular permeability index (PVPI) increased at T4, and the values were significantly lower in the US group than in the RT group and CS group (P<0.05). At T8, the ELWI and PVPI in the US group and RT group were significantly lower than in the CS group. At T12, there were no significant differences among the 3 groups. In addition, at T4 static lung compliance decreased, plateau airway pressure increased, and airway resistance changed non-significantly. There were no significant differences between the US group and the RT group, but both groups showed better results than the CS group did.

Conclusions: The ELWI and PVPI may transiently increase after aortic valve surgery with cardiopulmonary bypass. Compared with the 12 h required to recover from a conventional sternotomy operation, it may only take 8 h to recover from MIAVS.

MeSH Keywords: **Hemodynamics • Respiratory Mechanics • Surgical Procedures, Minimally Invasive • Vascular Resistance**

Full-text PDF: <http://www.medscimonit.com/abstract/index/idArt/896558>

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Background

Minimally invasive aortic valve surgery (MIAVS) is used at many cardiac centers because it generates less trauma, allows for quicker recovery, and increases patient satisfaction [1–3]. Currently, right anterior thoracotomy (RT) and upper ministernotomy (US) are the most common approaches in MIAVS [2]. Although many studies have shown that MIAVS can reduce bleeding and shorten the postoperative ventilation support time, ICU length of stay, and postoperative hospitalization time [4–7], few studies have focused on the effects of MIAVS on variation in the extravascular lung water index (ELWI) and pulmonary vascular permeability index (PVPI), and, particularly, the effects of MIAVS on respiratory mechanics after cardiac surgery with cardiopulmonary bypass (CPB).

Postoperative respiratory dysfunction is a major complication of CPB and is primarily caused by gas exchange impairment due to pulmonary intestinal edema after CPB [8]. Compared with physical examination and chest radiography, ELWI is a more reliable index for evaluation of pulmonary interstitial edema [9]. Studies have reported that ELWI and PVPI are predictors of acute respiratory distress syndrome (ARDS) in the early postoperative period and are independent predictive factors of 28-day mortality in patients with ARDS [10,11]. Therefore, the present study explored the effects of MIAVS on ELWI, PVPI, and respiratory mechanics postoperatively and the correlations of these parameters with early lung function recovery after MIAVS.

Material and Methods

Subjects and study design

A total of 146 patients who underwent aortic valve surgery for the first time between April 2011 and April 2014 at Changzheng Hospital, affiliated with Second Military Medical University, were selected. All patients signed an informed consent form before inclusion in this study.

The inclusion criteria were: 18–70 years of age, isolated aortic valve disease and ineligible for conservative treatment, clear indication for surgery, both minimally invasive operation and conventional median sternotomy incision operation were alternative treatment options, signed informed consent, and left ventricle ejection fraction (LVEF) $\geq 45\%$.

The exclusion criteria were: presence of preoperative acute pulmonary edema, severe pulmonary hypertension, chronic obstructive pulmonary disease (COPD), infective endocarditis, femoral artery stenosis or severe peripheral vascular disease; discontinuation of antiplatelet drugs less than 7 days

prior to surgery or a history of unexplained hemorrhagic disease; coronary artery disease or congenital heart disease that required treatment at the time of the isolated aortic valve disease; a history of right empyema, right chest trauma, infection or right thoracic operation; a history of chronic inflammation of the right pleura or chest area; poor general health (such as cachexia); liver or renal dysfunction; pregnancy and other special cases; a body mass index (BMI) < 18 or > 35 (normal 18.5–24.9) kg/m^2 ; severe aortic valve stenosis; and calcification that might require annulus reconstruction.

Ninety patients were enrolled in this study, including 37 cases of aortic stenosis, 34 cases of aortic insufficiency, and 19 cases of aortic stenosis and regurgitation. The clinical data of these patients are presented in Table 1. The patients were divided into 3 groups: a conventional sternotomy group (CS group, $n=30$), an upper ministernotomy group (US group, $n=30$), and a right anterior thoracotomy group with a small incision (RT group, $n=30$). This study was approved by the Second Military Medical University Ethics Committee.

Anesthesia and operation

All operations were performed under general anesthesia with mild hypothermic CPB and were performed by the same physicians, perfusionists, and anesthesiologists.

Anesthesia was induced with 0.1 mg/kg midazolam, 1–2 g/kg sufentanil, and 0.2 mg/kg vecuronium. Tracheal intubation was completed through the mouth (a double-lumen tube was used in the RT group). Ventilation was performed in IPPV mode with the following initial parameters: tidal volume (TV), 8 ml/kg; respiratory frequency (RF), 16 times/min; fraction of inspired oxygen (FiO_2), 0.5; and positive end expiratory pressure (PEEP), 5 cmH_2O . The FiO_2 and minute ventilation volume were adjusted regularly according to the arterial blood gas results to maintain the PaO_2 above 90 mmHg and the PaCO_2 between 35 and 40 mmHg. Anesthesia was maintained with propofol, sufentanil, and vecuronium. After successful anesthesia, a 7.5F Swan-Ganz CCombo V (Edwards Lifesciences LLC, USA) catheter was inserted via the right internal jugular vein, and a 4F PiCCO (PULSION Medical Systems, Germany) catheter was inserted via the right femoral artery.

Postoperative treatment

Goal-directed therapy was administered to all patients, including vasoactive drugs, crystal (GUM) fluids, and blood products, to maintain hemodynamic stability if necessary. The goal-directed therapy aimed to maintain the following hemodynamic parameters within the indicated ranges: intrathoracic blood volume index (ITBVI)=850–1000 ml/m^2 , mean arterial pressure (MAP)=60–100 mmHg, HR $< 90/\text{min}$, cardiac index (CI)

Table 1. General clinical characteristics of the patients.

	CS group (n=30)	US group (n=30)	RT group (n=30)	P-value
Age [Y]	57.3±9.6	52.5±11.6	54.4±11.7	0.243
Male gender [n (%)]	19 (63)	16 (53)	14 (47)	0.427
BMI [kg/m ²]	24.9±4.6	25.2±4.2	25.8±3.5	0.647
Aortic valve pathophysiology				0.749
AS [n (%)]	10 (33)	13 (43)	14 (47)	
AR [n (%)]	14 (47)	11 (37)	9 (30)	
AS and AR [n (%)]	6 (20)	6 (20)	7 (23)	
Heart function (NYHA)				0.581
Class II [n (%)]	13 (43)	15 (50)	11 (37)	
Class III [n (%)]	17 (57)	15 (50)	19 (63)	
Atrial fibrillation [n (%)]	0	0	0	–
Hypertension [n (%)]	4 (13)	7 (23)	6 (20)	0.602
Diabetes [n (%)]	7 (23)	6 (20)	5 (17)	0.812

BMI – body mass index; AS – aortic valve stenosis; AR – aortic valve regurgitation; NYHA – New York Heart Association. The clinical data of the patients were comparable among the 3 groups.

>2 L/min/m², Hct >8%, ScvO₂ >60%, and average urine volume >1 ml/kg/h. Insulin was used to control hyperglycemia. The SIMV mode was used for the mechanical ventilation (initial settings: TV, 8 ml/kg; RF, 16 times/min; FiO₂, 0.5; and PEEP, 5 cmH₂O). The PEEP was kept at 5 cmH₂O in all 3 groups, and the FiO₂ and minute ventilation volume were adjusted regularly according to the arterial blood gas results to maintain the PaO₂ above 90 mmHg and the PaCO₂ between 35 and 40 mmHg. Dexmedetomidine and sufentanil were used for sedation and analgesia.

Evaluation of circulatory and respiratory function

Hemodynamic parameters (HR, MAP, CVP, mean pulmonary artery pressure, and pulmonary capillary wedge pressure) were continuously monitored with PiCCO2 (PULSION Medical Systems, Germany) and Vigilance II (Edwards Lifesciences, USA). CI, global end-diastolic volume index (GEDVI), ELWI and PVPI measurements were obtained by triplicate central venous injections of 20 ml of iced (<8°C) 0.9% NaCl (saline) and recorded as the mean of the 3 measurements. These parameters were monitored with thermodilution at the following time points: before skin incision (T(-1)); at sternum closing (T0); and 4 h (T4), 8 h (T8), 12 h (T12), and 24 h (T24) after the operation. Respiratory mechanics parameters, including static lung compliance (Cst), plateau airway pressure (Pplat), and airway resistance (Raw), were recorded using Engstrom Carestation software (GE Healthcare, USA) at T(-1), T0, T4, and T8. Arterial

gas was monitored with GEM Premier 3000 (Instrumentation Laboratory, USA), and PaO₂/FiO₂ was calculated. The CPB time, aortic clamping time, ventilation support time, ICU length of stay, postoperative hospitalization time, thoracic drainage volume, and blood transfusion volume were also recorded.

Statistical methods

For data collection and analysis, we used IBM SPSS 21.0 (SPSS, Inc., Armonk, NY). All continuous variables are presented as the mean ± standard deviation. Repeated-measures ANOVA and post hoc Bonferroni tests were used to compare the hemodynamic parameters, ELWI, PVPI, parameters of air exchange, and parameters of respiratory mechanics. One-way ANOVA and a post hoc Tukey's significant difference test were used to establish differences in the independent variables. Discrete data are expressed as the patient number or percentage and were analyzed using a 2-sided chi-square test. For all tests, a P-value of less than 0.05 was considered as significant.

Results

Clinical data and complications of patients

The clinical data of the patients were comparable among all 3 groups (Table 1). No conversions of sternotomy occurred in any of the 90 patients. Additionally, no re-thoracotomies were

Table 2. Intra- and post-operative clinical characteristics.

	CS group (n=30)	US group (n=30)	RT group (n=30)	P-value
CPB time (min)	88.4±10.4	92.2±9.7	93.3±10.9	0.156
Cross-clamp time (min)	37.0±4.4	39.1±3.4	38.4±3.6	0.097
Intraoperative colloid requirement (ml/kg)	10.6±1.7	10.4±1.5	10.2±1.1	0.599
Intraoperative crystalloid requirement (ml/kg)	51.2±8.3	49.8±13.6	50.8±13.8	0.897
Postoperative colloid requirement within 24h (ml/kg)	3.4±0.8	3.1±0.6	3.1±0.5	0.237
Postoperative crystalloid requirement within 24h (ml/kg)	36.0±4.2	36.0±4.2	37.1±3.9	0.459
Blood transfusion volume (ml)	983.3±100.3	563.3±122.4	526.7±135.7	<0.001* 0.468#
Drainage volume (ml)	534.9±70.8	278.9±59.6	288.3±61.0	<0.001* 0.835#
Duration of mechanical ventilation (h)	14.5±1.2	6.9±1.2	7.4±1.5	<0.001* 0.319#
Duration of ICU stay (h)	38.0±4.5	28.9±3.1	28.5±3.9	<0.001* 0.923#
Duration of hospitalization (d)	11.5±2.3	7.5±1.7	7.4±1.9	<0.001* 0.943#
30-d mortality [n (%)]	0	0	0	–
Stroke [n (%)]	0	0	0	–
Perioperative myocardial infarction [n (%)]	0	0	0	–
Postoperative IABP [n (%)]	0	0	0	–
Renal failure requiring dialysis [n (%)]	0	0	0	–
Atrial fibrillation or flutter [n (%)]	14 (47)	11 (37)	12 (40)	0.725
Re-exploration for bleeding [n (%)]	0	0	0	–
Deep venous thrombosis [n (%)]	0	0	0	–
Inguinal lymphatic leakage [n (%)]	–	2 (7)	3 (10)	1.000
Deep sternal wound infection [n (%)]	0	0	–	–

* Comparing to CS group; # Comparing US group with RT group.

performed due to hemorrhage or respiratory failure requiring re-intubation in any of the 3 groups.

There were no significant differences in the CPB time, aortic clamping time, or perioperative volume expansion among the 3 groups. There were also no significant differences in the complication rate and 30-day mortality among the 3 groups. The ventilation support time, ICU length of stay, hospitalization time, blood transfusion volume, and drainage volume were all lower in the US and RT groups than in the CS group, and none of these variables significantly differed between the US and the RT groups (Table 2).

Circulatory function of patients

There were no significant differences in the hemodynamics parameters at any time point among the 3 groups (Figure 1).

At T(-1) there were no significant differences in ELWI or PVPI among the 3 groups (P=0.307 and P=0.620). At T4, ELWI and PVPI were increased compared to T(-1). Furthermore, and ELWI and PVPI were significantly higher in the CS group than in the RT group (P<0.05) and were significantly higher in the RT group than in the US group (P<0.05). From T8 to T12, ELWI and PVPI were significantly higher in the CS group than in the RT and US groups (P<0.05), and there were no significant

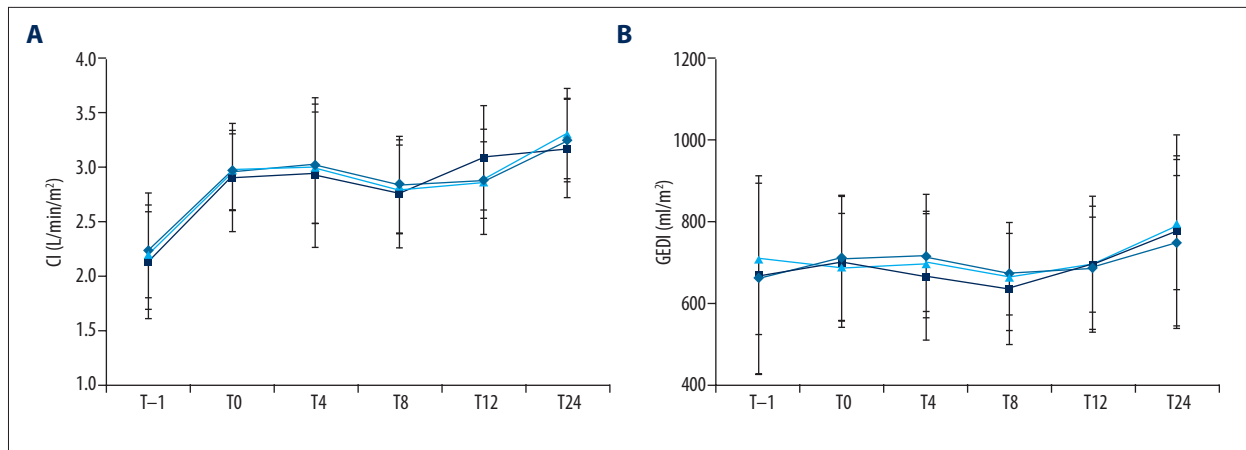


Figure 1. (■) CS group, (▲) US group, (◆) RT group. CI – cardiac index; GEDVI – global end-diastolic volume index. **(A)** Variation trends of the CI in the 3 groups at different time points. **(B)** Variation trends of the GEDVI in the 3 groups at different time points. There were no significant differences in the hemodynamic parameters at any time point among the 3 groups.

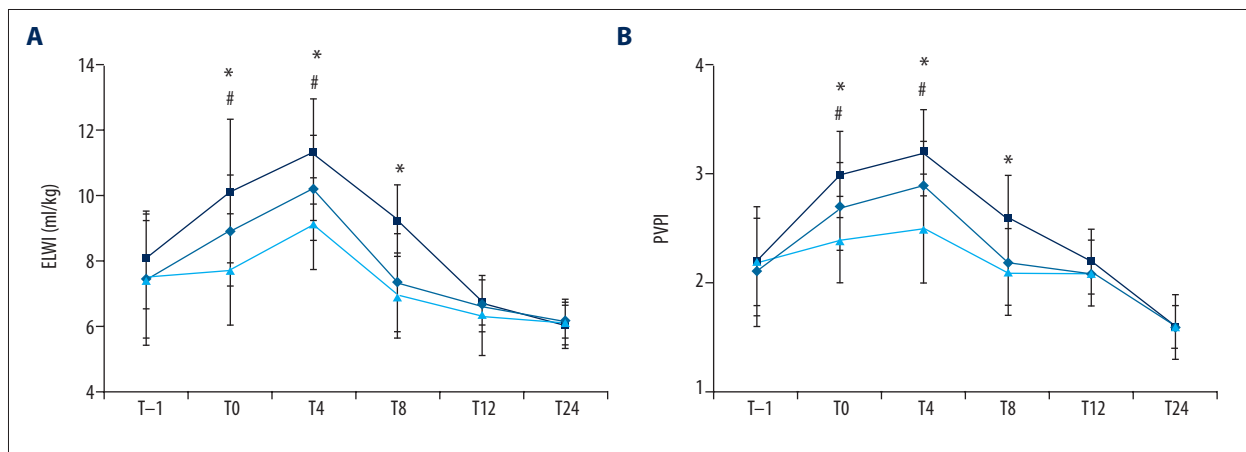


Figure 2. (■) CS group, (▲) US group, (◆) RT group. * Compared with the CS group ($P < 0.05$); # Comparing the US group with the RT group. ELWI – extravascular lung water index; PVPI – pulmonary vascular permeability index. **(A)** Variation trends of the ELWI in the 3 groups at different time points. **(B)** Variation trends of the PVPI in the 3 groups at different time points.

differences between the RT and US groups. At T12, ELWI and PVPI stabilized and were not significantly different among the 3 groups (Figure 2).

Respiratory function of patients

There were no significant differences in $\text{PaO}_2/\text{FiO}_2$ or the alveolar-arterial oxygen gradient (PA-aO_2) at T(-1) among the 3 groups ($P=0.315$ and $P=0.174$). $\text{PaO}_2/\text{FiO}_2$ decreased after the operation compared with the baseline level in the CS group, and increased in the US and RT groups ($P < 0.05$). PA-aO_2 increased significantly within 12 h after the operation compared with the baseline level, and the increase was significantly greater in the CS group than in the RT group ($P < 0.05$) and was also significantly greater in the RT group than in the US group within 4 h after the operation ($P < 0.05$). After T12,

PA-aO_2 stabilized, and there were no significant differences in PA-aO_2 among the 3 groups after T24 (Figure 3).

There were no significant differences in Cst or Pplat at T(-1) among the 3 groups ($P=0.243$ and $P=0.126$). Cst decreased within 4 h after the operation and returned to the normal range within 8 h. At that time point, Cst was significantly higher in the US and RT groups than in the CS group ($P < 0.05$) and was not significantly different between the US and the RT groups ($P < 0.05$). Pplat increased significantly within 4 h after the operation and returned to the normal range within 8 h. At that time point, Pplat was significantly lower in the US and RT groups than in the CS group ($P < 0.05$) and was not significantly different between the US and the RT groups ($P < 0.05$). Additionally, there were no significant differences in Raw among the 3 groups at any time point (Figure 4).

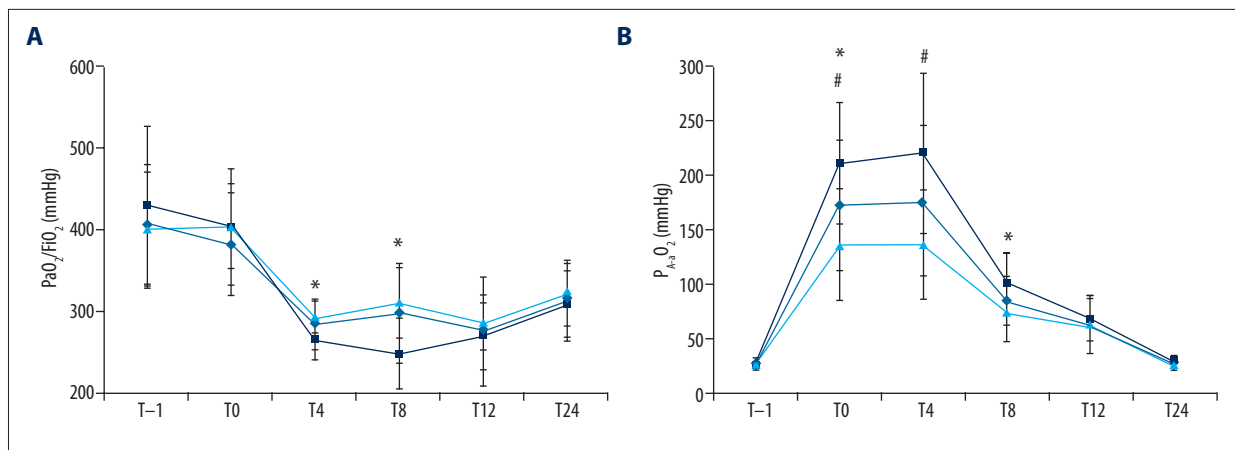


Figure 3. (■) CS group, (▲) US group, (◆) RT group. * Compared with the CS group (P<0.05); # Comparing the US group with the RT group (P<0.05). (A) Variation trends of PaO₂/FiO₂ in the 3 groups at different time points. (B) Variation trends of PA-aO₂ in the 3 groups at different time points.

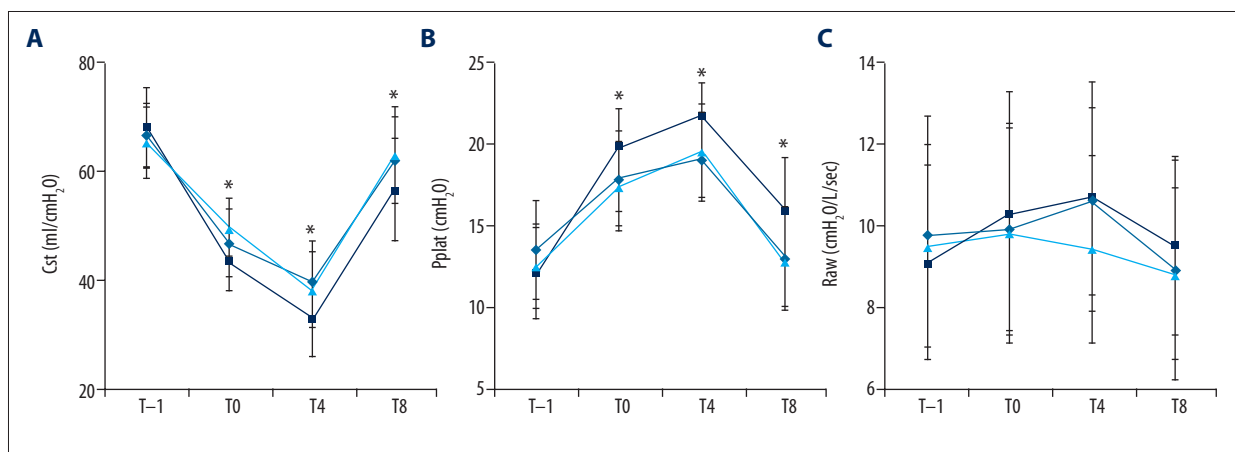


Figure 4. (■) CS group, (▲) US group, (◆) RT group. * Compared with the CS group (P<0.05). Cst – static lung compliance; Pplat – plateau airway pressure; Raw – airway resistance. (A) Variation trends of Cst in the 3 groups at different time points. (B) Variation trends of Pplat in the 3 groups at different time points. (C) Variation trends of Raw in the 3 groups at different time points.

Correlation between changes of respiratory parameters and ELWI

There was a negative correlation between ELWI and Cst (r=-0.466, P<0.001), and ELWI was also negative correlated with PaO₂/FiO₂ (r=-0.138, P=0.023); however, ELWI was positively correlated with Pplat (r=0.375, P<0.001), as shown in Figure 5.

Discussion

Aortic valve surgery with CPB is an important method for the treatment of aortic valve disease [12]. Theoretically, this operation reduces the afterload of the heart and eliminates tension in the ventricular wall, which in turn optimizes hemodynamics and improves heart function. Therefore, pulmonary interstitial

edema and the ELWI should be attenuated after the operation relative to preoperative values. However, an inflammatory reaction induced by CPB causes pulmonary vasoconstriction and increases the permeability of the lung vessels, which increases the ELWI [13]. In addition, ischemia reperfusion injury of the lung and micro-embolisms created during CPB can damage pulmonary capillary endothelial cells, which can increase the permeability of the pulmonary vasculature [13], thereby further increasing the ELWI. The present study examined the variation in the ELWI after cardiac surgery with CPB. Within 4 h after the operation, the ELWI increased significantly, and it subsequently returned to the normal range at 8 h postoperatively. As mentioned previously, considering the relationship between the ELWI and the inflammatory reaction after CPB, we hypothesized that variation in the ELWI may to a certain extent reflect changes in the inflammatory reaction.

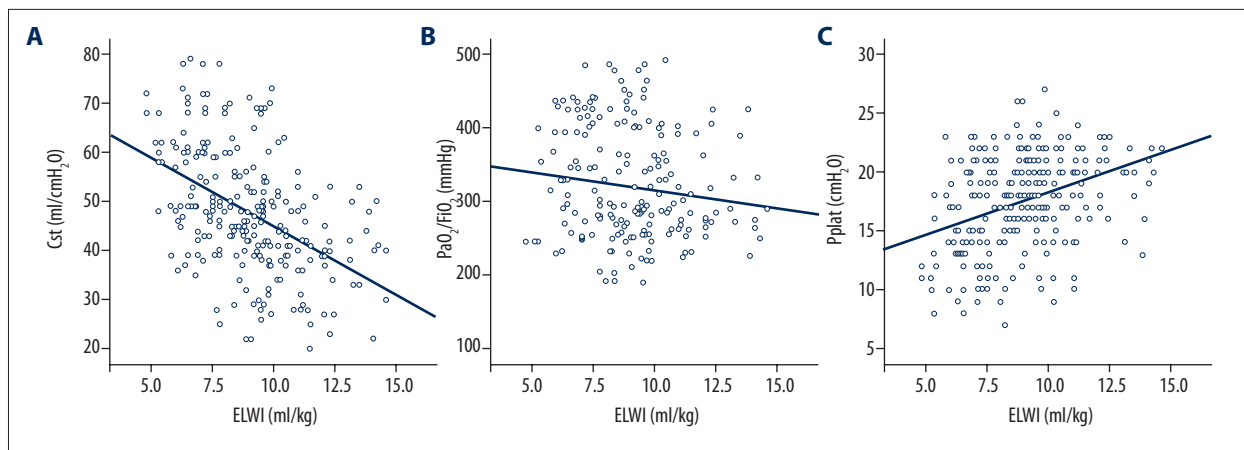


Figure 5. (A–C) ELWI – extravascular lung water index; Cst – static lung compliance; Pplat – plateau airway pressure; Raw – airway resistance.

Previous studies have demonstrated that the inflammatory response reaches its peak within 4–6 h after cardiac surgery with CPB [14], which is consistent with the variation in lung water observed in the present study. The fact that the ELWI reached its peak within 4–6 h and began to decline 8 h after the operation suggests that anti-inflammatory and appropriate fluid transfusion therapies are important within 4–6 h after the operation to maintain patient stability and protect patients during the inflammatory reaction peak. According to the experience of our heart center, although “fast tracking” has become increasingly popular, extubation within 4–6 h should be considered with caution, especially for patients who underwent CPB long ago, those who have experienced severe operative trauma, and those who are likely to have a strong inflammatory reaction. Before extubation, the risk of the inflammatory response peak should be fully understood, and a comprehensive evaluation should be performed, including measurement of the ELWI, arterial gas, and respiratory mechanics. For extubation performed within 4 h after the operation, intensivists should particularly focus on the patient’s heart and lung functions, especially with respect to changes in ELWI and arterial blood gas, to address the corresponding problems in a timely manner.

This study demonstrated that the ELWI and PVPI were significantly increased within 4 h after aortic valve surgery. Moreover, ELWI and PVPI were significantly lower in the US group than in the RT group and were also significantly lower in the RT group than in the CS group. Beyond 8 h after the operation, ELWI and PVPI did not significantly differ between the RT and the US groups and remained significantly lower in those groups than in the CS group. At 12 h after the operation, ELWI and PVPI did not significantly differ among the 3 groups. Similarly, Cst decreased and Pplat increased within 4 h after the operation and gradually returned to normal levels 8 h after the operation. During this time period, Cst and Pplat were significantly

better in the MIAVS group than in the CS group. These results suggest that the effects of the operation on the ELWI and respiratory mechanics in the MIAVS group were superior to those in the CS group, especially within 8 h after the operation. In our opinion, this finding may be in part due to protection of the integrity of the thorax during the MIAVS operation, allowing lung function to recover quickly. In contrast, the integrity of the thorax is broken during the CS operation, so lung function may take at least 12 h to recover. In addition, blood transfusion volume in the CS group was significantly higher. Considering the association between ELWI and fluid balance, the higher ELWI in the CS group might partly be attributed to higher blood transfusion volume.

In this study, ELWI and PVPI were significantly higher in the RT group than in the US group within 4 h after the operation. This effect was likely due to transient one-lung ventilation increasing the risk of hypoxic injury, crush injury of the right lung, and barotrauma of the left lung during the operation. In fact, hypoxic injury and crush injury are considered to be the main causes of increased pulmonary vascular permeability and extravascular lung water.

This study also found that MIAVS was not superior to the traditional median sternotomy approach with respect to CPB and the aortic blocking time, but the postoperative ventilation support time, length of ICU stay, postoperative hospitalization time, blood transfusion volume, and drainage volume were superior for MIAVS relative to traditional median sternotomy, which was consistent with the results of similar studies conducted previously [1].

In addition, goal-directed therapy was applied in this study, with the aim of optimizing circulatory function and avoiding the effect of liquid capacity on extravascular lung water. The ELWI stabilized within 12 h after the operation, with stabilization

occurring more quickly in the MIAVS group than in the CS group. This effect may have been occurred because the integrity of the chest was destroyed during the median sternotomy operation, or because of a higher blood transfusion volume in the CS group due to a higher drainage volume [15]. Regardless of the cause of the anti-inflammatory reaction, the alleviation of lung injury and the reduction of the blood transfusion volume with the MIAVS operation were beneficial for the recovery of lung function.

There were certain limitations in this study. First, patients with severe aortic valve stenosis and calcification were excluded. However, these patients are likely to require reconstruction of a valve annulus and to have a relatively longer duration of CPB, so postoperative inflammation may be more severe in these patients and could have caused inconsistencies in the baseline values of the different groups. Second, to ensure the comparability of the 3 groups, the patients enrolled in the study had a relatively short history of valvular disease, less severe lesions, and LVEF >45%; therefore, no perioperative deaths occurred. As a result, for patients with severe pathological changes, a long history of valvular disease, or poor preoperative cardiac function, the variation trends of the ELWI and respiratory mechanics require further clinical study. Third, in this study, due to the short CPB time, ELWI returned to baseline within 24 h, and most patients were extubated within 8 h after the

operation; therefore, extravascular lung water was recorded through 24 h after the operation, and respiratory mechanics were recorded through 8 h after the operation. For patients with a long CPB time or preoperative lung dysfunction, the variation trend of extravascular lung water and its effect on postoperative fluid therapy require further verification by multi-center clinical studies. Finally, because there were no complete data on specific proinflammatory cytokine levels, we could not confirm the inflammatory hypothesis, which is another limitation of this study.

Conclusions

ELWI and PVPI increased transiently after the cardiac surgery. Right anterior thoracotomy incision may have less of an effect on ELWI, PVPI, and lung function than upper sternum incision does, but both are clearly superior to traditional median sternotomy incision. Compared with traditional aortic valve surgery through median sternotomy, patients who underwent MIAVS recovered sooner.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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