“Obesity Paradox” in Acute Respiratory Distress Syndrome Among Patients Undergoing Cardiac Surgery: A Retrospective Study

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Background: The “obesity paradox” exists in many diseases. It is unclear whether it also exists in acute respiratory distress syndrome (ARDS). The purpose of our study was to clarify the relationship between obesity and the development of and hospital mortality from ARDS among patients who underwent cardiac surgery.

Material/Methods: This retrospective case-control study included 202 patients with ARDS and 808 matching patients without ARDS. We clarified the relationship between obesity and the development of ARDS after adjusting for confounding factors by multiple logistic regression analysis. A total of 202 ARDS patients were divided into survival and mortality groups. After all confounding factors were adjusted by multiple logistic regression analysis, we demonstrated the relationship between obesity and mortality from ARDS.

Results: We found a significant association between body mass index (BMI) and the development of ARDS; the cutoff point of BMI was 24.78 kg/m² by adjusting for confounding factors for the development of ARDS. When the BMI was lower than 24.78 kg/m², the higher BMI was a protective factor (odds ratio [OR] 0.68, \( P=0.000 \), 95% confidence interval [CI] 0.55-0.84). When the BMI was higher than 24.78 kg/m², the higher BMI was a risk factor (OR 1.07, \( P=0.050 \), 95% CI 1.00-1.14). However, obesity was found to be associated with decreased ARDS mortality by adjusting for confounding factors (OR 0.91, \( P=0.039 \), 95% CI 0.83-1.00).

Conclusions: An “obesity paradox” may exist in ARDS among patients with obesity who undergo cardiac surgery.

Keywords: Hospital Mortality • Obesity • Respiratory Distress Syndrome, Adult • Thoracic Surgery

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Background

The obesity epidemic continues as obesity’s increased prevalence has been reported throughout the world. Recent data have shown that more than two-thirds of citizens in the United States have either obesity or overweight. Similarly, China has the largest number of affected people worldwide, with approximately 46% of adults having obesity or overweight [1,2]. Given its rising prevalence and association with many diseases, it is not surprising that the percentage of critically ill patients with obesity is also increasing. In those patients, including those with acute respiratory distress syndrome (ARDS), the relationship between obesity and morbidity and mortality seems to be complex and at times counterintuitive, which is known as the “obesity paradox”. There are conflicting results in the literature on whether obesity is a risk factor or protective factor for morbidity and mortality in ARDS and acute lung injury [3-9].

Considering the contradictory findings, we carried out a retrospective case-control and cohort study with data gathered from an observational database to clarify the effect of body mass index (BMI) at hospital admission on the development of and mortality from ARDS. Cardiac surgery is one of the most important causes of ARDS. To minimize possible selection bias due to differences in ARDS induction, we limited the study sample to a population that underwent cardiac surgery. It is important to understand the relationship between obesity and the development of and mortality from ARDS. Furthermore, this relationship, once elucidated, can be used to develop guidelines for patients to maintain their weight at an appropriate level before cardiac surgery.

Material and Methods

Study Population

Our study included 202 patients with ARDS from our hospital who underwent cardiac surgery from January 2005 to December 2015. The 202 patients with ARDS were classified as the ARDS group. We selected patients of the same sex and age who underwent cardiac surgery in the same year to match each of the patients in the ARDS group. We randomly selected 4 patients among all candidates using a random number table. As a result, 808 patients were classified as the contrast group.

Research coordinators screened all patients for ARDS using a result, 808 patients were classified as the contrast group. Emergency surgery was defined as a surgery that was needed within a short time because of the urgency of treating a disease after a doctor’s assessment. There were 5 types of surgery: isolated valvular surgery, isolated coronary artery bypass grafting (CABG) surgery, valvular combined with overload or cardiac failure; (4) PaO2/FiO2 less than 300 mm Hg with positive end-expiratory pressure or continuous positive airway pressure was more than 5 cm H2O. Two physicians reviewed chest radiographs. A third physician was responsible for the arbitration if there was a disagreement. A consensus training session was conducted for all physicians on the radiologic criteria for ARDS. The clinical status of patients was absent for all physicians.

Exclusion criteria for ARDS were as follows: (1) patients younger than 18 years old; (2) patients diagnosed as having a malignant tumor before surgery; (3) patients with major risk factors for lung injury or respiratory failure, such as trauma, sepsis, aspiration, shock, and acute congestive heart failure; (4) requirement of therapies such as mechanical ventilation, continuous renal replacement therapy, and intra-aortic balloon pump or extracorporeal membrane oxygenation (ECMO) therapy before surgery; (5) idiopathic interstitial pneumonia with diffuse bilateral infiltrates on chest radiography and pneumonia or respiratory failure at any point before surgery and during hospitalization (Figure 1).

Variables

We calculated the BMI from the height and weight recorded at hospital admission with the formula BMI=weight (kg)/height (m²). Patients with missing height or weight measurements were excluded. BMI was categorized as overweight (BMI ≥25 to <30 kg/m²), obese (BMI ≥30 kg/m²), normal weight (BMI ≥18.5 to <25 kg/m²), and underweight (BMI <18.5 kg/m²), according to the National Institutes of Health’s definition of obesity. The smoking index was defined as the number of cigarettes-years, calculated as the number of years of smoking multiplied by the number of cigarettes smoked per day. Ejection fraction values were determined by M-mode echocardiography, which all patients should have undergone at least twice (once before surgery and once within 24 h after surgery). The hemoglobin levels of all patients were determined using the sodium lauryl sulfate-hemoglobin method. Albumin levels were determined using the chemical colorimetric method before surgery. We calculated Acute Physiology and Chronic Health Evaluation II (APACHE II) scores on the first day after surgery. Comorbidities such as hypertension, diabetes mellitus, acute myocardial infarction, and previous cardiac surgery were considered present if a physician documented the diagnosis in the electronic medical record before the surgical procedure. The information on each surgery, such as duration, patient blood loss, and number of transfusions, was recorded using surgery recorders. Emergency surgery was defined as a surgery that was needed within a short time because of the urgency of treating a disease after a doctor’s assessment. There were 5 types of surgery: isolated valvular surgery, isolated coronary artery bypass grafting (CABG) surgery, valvular combined with
CABG surgery, aortic surgery, and others (such as ventricular/atrial septal defect and atrial myxoma surgeries).

Follow-Up

Patients with ARDS were followed-up for all-cause mortality before discharge or death.

Statistical Analysis

Data were demonstrated as the mean±standard deviation or median (interquartile) for continuous variables. Frequency or percentage was used for categorical variables. We used Mann-Whitney and chi-squared tests to determine statistical differences between the means and proportions of the 2 groups. We used multiple logistic regression models to evaluate the relationship between BMI and the development of and mortality from ARDS. We used Kaplan-Meier curves (log-rank tests) to evaluate the effects of BMI on survival. All analyses were performed with the statistical software package R (http://www.R-project.org; The R Foundation) and EmpowerStats (http://www.empowerstats.com; X&Y Solutions, Inc., Boston, MA, USA). We used a 2-sided significance level of 0.05 to evaluate statistical significance.

Results

BMI and Development of ARDS

Between January 2005 and December 2015, 1010 patients were enrolled in our study. Of these patients, 35% of patients had overweight and 6% of patients had obesity. There was more hypertension among patients with obesity and more acute myocardial infarction and diabetes among patients with overweight. Patients with overweight tended to undergo isolated valvular or isolated CABG surgeries, and patients with obesity tended to undergo aortic surgeries (Supplementary Table 1).

Between January 2005 and December 2015, a total of 202 patients developed ARDS, and 808 patients were classified as the contrast group. After univariate analysis for the development of ARDS, albumin level before surgery (OR 0.9, P<0.001, 95% CI 0.9-0.9) was identified as a protective factor. Risk factors included APACHE II value (OR 1.2, P<0.001, 95% CI 1.2-1.3), duration of surgery (OR 1.6, P<0.001, 95% CI 1.4-1.7), history of cardiac surgery (OR 4.8, P<0.001, 95% CI 2.4-9.7), history of hypertension (OR 1.4, P<0.001, 95% CI 1.1-1.9), emergency surgery (OR 8.6, P<0.001, 95% CI 4.7-15.6), and type of surgery (OR 6.6, 95% CI 3.7-11.6; OR 9.3, 95% CI 5.4-16.0; and OR 2.2, 95% CI 1.4-3.4 for valvular combined with CABG surgery, aortic surgery, and others, respectively, P<0.001) (Supplementary Table 2).

We investigated the relationship between BMI and the development of ARDS using 3 approaches. BMI was included as a continuous variable, a categorical variable, and a trend in 3 logistic regression models after assuming that the logic was linear (Table 1). There was no linear relationship between BMI and the development of ARDS. However, we found a threshold nonlinear association in a generalized additive model (Figure 2).

When the BMI was lower than 24.78 kg/m^2, there was a decreased likelihood of ARDS with an increasing BMI (OR 0.68, P=0.000, 95% CI 0.55-0.84). When the BMI was higher than
24.78 kg/m², there was an increased likelihood of ARDS with an increasing BMI (OR 1.07, \( P = 0.050, 95\%\ CI 1.00-1.14\)) (Table 2).

**BMI and Mortality from ARDS**

There were 202 patients diagnosed with ARDS, of whom, more than 30% of patients had overweight, and almost 9% of patients had obesity. There was a higher hemoglobin level before surgery in patients with overweight and obesity. Patients with a higher proportion of body fat showed a higher ejection fraction value after surgery. Patients with obesity may have experienced a longer period of intubation. On the other hand, leaner patients had a higher chance of a second intubation after surgery. More patients with overweight had undergone isolated valvular or isolated CABG surgeries, and more patients with obesity had undergone aortic surgeries (Supplementary Table 3).

During hospitalization, 134 patients died, and the rate of mortality from ARDS among patients who had undergone cardiac surgery was 66.34%. After univariate analysis for mortality from ARDS, the protective factors included BMI (OR 0.89, \( P = 0.003, 95\%\ CI 0.82-0.96\)), age (OR 0.98, \( P = 0.038, 95\%\ CI 0.95-1.00\)), hemoglobin level before surgery (OR 0.99, \( P = 0.049, 95\%\ CI 0.97-1.00\)), and history of diabetes (OR 0.46, \( P = 0.022, 95\%\ CI 0.23-0.89\)). The only risk factor was second intubation after surgery (OR 2.56, \( P = 0.002, 95\%\ CI 1.41-4.66\)) (Supplementary Table 4).

We used multiple logistic regression models to evaluate the relationship between BMI and mortality from ARDS. We observed a stable linear relationship between BMI and mortality from ARDS. In the adjusted model II, after adjusting for sex, age, albumin level before surgery, APACHE II value, duration of surgery, history of cardiac surgery, history of hypertension, emergency surgery and type of surgery, BMI was still a protective factor (OR 0.91, \( P = 0.039, 95\%\ CI 0.83-1.00\)) (Table 3).

After in-hospital follow-up, we found a significant difference among the 4 groups (\( P = 0.013 \)) based on the Kaplan-Meier curve (Figure 3). On the 60th day, the mortality of patients with underweight and normal weight was higher than that of patients with overweight and obesity, and on the 90th day, patients with overweight and obesity were still at higher risk of mortality compared to patients with normal weight.
the difference became more significant, demonstrating that patients with ARDS with a higher proportion of body fat had a better prognosis.

Discussion

A review of the literature on the relationship between obesity and the development of ARDS revealed that most studies consistently demonstrated that obesity was associated with an increased possibility of ARDS [3,7,8,11,12]. In a cohort study including 1795 patients with risk factors for ARDS at admission, the results showed that patients with obesity were more likely to develop ARDS based on multivariate analysis (OR 1.24, 95% CI 1.11-1.39) [3]. A similar result was observed for an obstructive sleep apnea group [5] and critically injured patients with blunt trauma [6]. A meta-analysis conducted by Zhi et al [13] demonstrated that there was higher ARDS morbidity among patients with obesity in the intensive care unit (ICU) population.

Why do patients with obesity tend to develop ARDS? The mechanism is unclear thus far; nevertheless, we propose some potential mechanisms. First, compared with the control patients with normal weight, the patients with obesity experience several changes in their physiology. One key parameter in patients with obesity is trans-pulmonary pressure, which becomes less positive with an increased pleural pressure resulting from obesity. Therefore, patients with obesity have considerable atelectasis, which results in impaired gas exchange and decreased lung compliance [14]. Second, patients with obesity show chronic changes in circulating inflammatory mediators derived from adipose tissue. They have increased circulating levels of cytokines, increased chemokine production, and altered levels of adipocyte-produced hormones such as leptin and adiponectin [15,16]. Finally, because of body habitus, patients with obesity can be more likely to fulfill the Berlin Definition for ARDS, which can contribute to the difficulty of interpreting chest radiographs. However, our study minimized this possibility by having at most 3 physicians interpret the imaging results.

Interestingly, in our study, there was a cutoff point for BMI in the development of ARDS. When the patient’s BMI was higher than 24.78 kg/m², the higher BMI was associated with increased ARDS development (OR 1.07, P=0.050, 95% CI 1.00-1.14), which was consistent with most previous studies. Additionally, our results showed that when the patient’s BMI was lower than 24.78 kg/m², the higher BMI was associated with decreased ARDS development (OR 0.68, P=0.000, 95% CI 0.55 to 0.84, P=0.000).

| Inflection point of BMI | Effect size (OR) | 95% CI | P value |
|-------------------------|------------------|--------|---------|
| <24.78                  | 0.68             | 0.55 to 0.84 | 0.000   |
| ≥24.78                  | 1.07             | 1.00 to 1.14 | 0.050   |

Table 2. The result of 2-piecewise linear regression model.

Table 3. Relationship between body mass index and mortality of acute respiratory distress syndrome in multiple logistic regression model.

| Variable | Crude model | Adjust I | Adjust II |
|----------|-------------|----------|-----------|
|          | β (95% CI)  | P value  | β (95% CI) | P value |
| BMI      | 0.89 (0.82, 0.96) | 0.003 | 0.87 (0.80, 0.95) | 0.002 | 0.91 (0.83, 1.00) | 0.039 |

Crude model adjust for none. Adjust I model adjust for gender and age. Adjust II model adjust for gender, age, hemoglobin level before surgery, diabetes and second intubation after surgery.
0.55-0.84). We can conclude from the above that the higher the BMI is, the more likely the patient with obesity is to develop ARDS. But for patients with normal weight, the leaner patients had a higher possibility to develop ARDS, with a cut-off point of 24.78, which corresponds to a normal weight and cannot represent patients with obesity; nevertheless, it was close to obesity standards. Patients with underweight have a bad nutritional state, and their ability to resist surgery shock is weak, which may explain why the patients in the present study with the lower BMI had a higher possibility of developing ARDS than did the patients with normal weight; however, this still needs further study [17].

Conflicting results in the relationship between obesity and mortality from ARDS can be found in the previous literature. A recent study [18] in Canada demonstrated no difference in hospital mortality across BMI strata in patients with moderate to severe ARDS. Similar results were obtained for mechanically ventilated patients with ARDS [9] and critically injured patients with blunt trauma and ARDS [6]. However, another study demonstrated that BMI can be associated with decreased mortality (OR 0.81, 95% CI 0.71-0.93) after adjusting for mortality predictors [8]. Similar results were obtained for patients with ARDS on ECMO [19]. These results were confirmed in a recent meta-analysis, in which Ni et al [20] analyzed the relationship between BMI and clinical prognosis in patients with ARDS in 5 studies [3,8,11,12,21]. The authors concluded that obesity and ARDS are associated with a better prognosis. Another recent meta-analysis that included 4 additional studies [13] reported similar results. Our study also demonstrated the association of obesity with decreased ARDS mortality (OR 0.91, P=0.039, 95% CI 0.83-1.00).

Why are ARDS outcomes improved in the obesity population? The “obesity paradox” of patients with ARDS is still unclear. A review [22] conducted by Umbrello et al proposed some possible mechanisms. First, patients with obesity with lung injury have lower levels of several cytokines [21]. Second, lipids and lipoproteins, such as cholesterol, can bind to endotoxins and reduce their inflammatory actions [17]. Third, healthy patients with obesity accumulate macrophages that switch during critical illnesses. Patients with obesity can be protected by extensive M2 macrophage activation [23,24]. Fourth, obesity can induce a state of low-grade inflammation that can precondition and protect the lungs from further damage [25]. Fifth, adiposity can confer protection against ventilator-induced lung injury via altered chest wall dynamics, which can reduce the effect of airway pressure. Moreover, clinicians tend to consider patients with obesity as having a higher risk for worse outcomes, which can result in earlier admission to the ICU for monitoring purposes, the increased use of prophylactic measures, and more attention paid to mechanical ventilation parameters [26].

There are some limitations in our study. Patients with severe obesity (BMI ≥40 kg/m²) were not included. The highest BMI in our study was 37.0 kg/m², which could not account for the association between severe obesity and ARDS. Furthermore, we used BMI as a measurement of obesity; however, compared with other measurements, such as waist circumference, it may not accurately reflect obesity syndromes [27,28]. BMI measurements can be altered by intravenous fluid administration for patients in the ICU before weight measurements are obtained and by the erroneous assessment of height for supine critically ill patients. Large-scale multicenter trials are necessary to elucidate the relationship between obesity and ARDS.

**Conclusions**

Our study is the first to clarify the relationship between obesity and ARDS among patients undergoing cardiac surgery, including the development of and mortality for ARDS. Among patients with obesity undergoing cardiac surgery, the patients with a higher BMI were more likely to develop ARDS, while for all patients undergoing cardiac surgery, obesity was a protective factor against ARDS mortality. Therefore, the “obesity paradox” may exist in ARDS among patients with obesity undergoing cardiac surgery.

**Conflicts of Interest**

None.
## Supplementary Table 1. Baseline characteristics of patients (n=1010).

| BMI    | <18.5 | ≥18.5, <25 | ≥25, <30 | ≥30 | P value |
|--------|-------|------------|----------|-----|---------|
| N (%)  | 41 (4.06%) | 548 (54.26%) | 357 (35.34%) | 64 (6.33%) | –       |
| Age, years | 42.63±17.90 | 58.85±13.47 | 60.55±11.79 | 56.00±12.62 | 0.001   |
| Smoking index | 250.0 (125.0-675.0) | 450.0 (210.0-800.0) | 500.0 (300.0-800.0) | 400.0 (210.0-800.0) | 0.517   |
| EF value before surgery, % | 61.24±8.80 | 60.29±10.19 | 60.06±8.74 | 62.22±9.81 | 0.934   |
| Hemoglobin level before surgery, g/l | 129.10±22.37 | 132.68±18.84 | 134.44±17.98 | 133.72±20.77 | 0.267   |
| Albumin level before surgery, g/l | 43.25±3.47 | 40.49±5.34 | 40.45±5.14 | 40.51±5.16 | 0.011   |
| APACHE II value | 15.54±3.56 | 16.64±3.68 | 16.81±3.67 | 17.12±4.88 | 0.167   |
| Duration of surgery, hours | 4.81±1.91 | 4.72±1.90 | 4.73±1.85 | 5.06±2.30 | 0.579   |
| Blood loss, ml | 600.00 (400.00-1000.00) | 600.00 (400.00-1000.00) | 700.00 (500.00-1000.00) | 600.00 (350.00-1000.00) | 0.383   |
| Transfusion of red blood cells, ml | 400.00 (200.00-600.00) | 400.00 (233.50-800.00) | 400.00 (239.00-770.00) | 400.00 (200.00-625.00) | 0.665   |
| Transfusion of plasma cells, ml | 0.00 (0.00-400.00) | 0.00 (0.00-400.00) | 0.00 (0.00-200.00) | 0.00 (0.00-0.00) | 0.048   |
| EF value after surgery, % | 50.50±18.33 | 48.52±22.70 | 46.16±23.33 | 49.91±21.14 | 0.458   |
| ARDS, % | – | – | – | – | 0.004   |
| No | 26 (63.41%) | 445 (81.20%) | 293 (82.07%) | 44 (68.75%) | –       |
| Yes | 15 (36.59%) | 103 (18.80%) | 64 (17.93%) | 20 (31.25%) | <0.001  |
| Gender, % | – | – | – | – | 0.030   |
| Male | 24 (58.54%) | 351 (64.05%) | 272 (76.19%) | 43 (67.19%) | –       |
| Female | 17 (41.46%) | 197 (35.95%) | 85 (23.81%) | 21 (32.81%) | –       |
| History of cardiac surgery, % | – | – | – | – | 0.001   |
| No | 38 (92.68%) | 334 (60.95%) | 160 (44.82%) | 25 (39.06%) | –       |
| Yes | 4 (9.76%) | 26 (4.74%) | 3 (0.84%) | 1 (1.56%) | –       |
| History of hypertension, % | – | – | – | – | <0.001  |
| No | 37 (90.24%) | 522 (95.26%) | 354 (99.16%) | 63 (98.44%) | –       |
| Yes | 4 (9.76%) | 36 (6.74%) | 4 (1.04%) | 1 (1.56%) | –       |
| History of diabetes, % | – | – | – | – | 0.030   |
| No | 38 (92.68%) | 464 (84.67%) | 281 (78.71%) | 57 (89.06%) | –       |
| Yes | 4 (9.76%) | 84 (15.33%) | 76 (21.29%) | 7 (10.94%) | –       |
| History of AMI, % | – | – | – | – | 0.004   |
| No | 38 (92.68%) | 446 (81.39%) | 262 (73.39%) | 49 (76.56%) | –       |
| Yes | 3 (7.32%) | 102 (18.61%) | 95 (26.61%) | 15 (23.44%) | –       |
| Emergency surgery, % | – | – | – | – | 0.068   |
| No | 41 (100.00%) | 523 (95.44%) | 338 (94.68%) | 57 (89.06%) | –       |
| Yes | 0 (0.00%) | 25 (4.56%) | 19 (5.32%) | 7 (10.94%) | –       |
### Supplementary Table 1 continued. Baseline characteristics of patients (n=1010).

| BMI       | <18.5 | ≥18.5, <25 | ≥25, <30 | ≥30 | P value |
|-----------|-------|------------|----------|-----|---------|
| Type of surgery, % |       |            |          |     | <0.001  |
| isolated valvular surgery or isolated CABG surgery | 22 (53.66%) | 421 (76.68%) | 281 (78.71%) | 42 (66.67%) |          |
| Valvular combined with CABG surgery | 4 (9.76%) | 31 (5.65%) | 15 (4.20%) | 5 (7.94%) |          |
| Aortic surgery | 1 (2.44%) | 28 (5.10%) | 24 (6.72%) | 11 (17.46%) |          |
| Others | 14 (34.15%) | 69 (12.57%) | 37 (10.36%) | 5 (7.94%) |          |

EF – ejection fraction; COPD – chronic obstructive pulmonary disease; AMI – acute myocardial infarction; CABG – coronary artery bypass grafting; APACHE – acute physiology and chronic health evaluation; ARDS – acute respiratory distress syndrome.

### Supplementary Table 2. Univariate analysis for development of acute respiratory distress syndrome.

| Covariate                          | Statistics       | OR (95% CI) | P value |
|------------------------------------|------------------|-------------|---------|
| Age, years                         | 58.6±13.5        | 1.0 (1.0, 1.0) | 0.684   |
| Smoking index                      | 450.0 (210.0-800.0) | 1.0 (1.0, 1.0) | 0.081   |
| EF value before surgery, %         | 60.2±9.6         | 1.0 (1.0, 1.0) | 0.400   |
| Hemoglobin level before surgery, g/l | 133.2±18.8    | 1.0 (1.0, 1.0) | <0.001  |
| Albumin level before surgery, g/l  | 40.6±5.2         | 0.9 (0.9, 0.9) | <0.001  |
| APACHE II value                    | 16.7±3.8         | 1.2 (1.2, 1.3) | <0.001  |
| Duration of surgery, hours         | 4.7±1.9          | 1.6 (1.4, 1.7) | <0.001  |
| Blood loss, ml                     | 600.00 (400.00-1000.00) | 1.0 (1.0, 1.0) | <0.001  |
| Transfusion of red blood cells, ml | 400.00 (200.00-800.00) | 1.0 (1.0, 1.0) | <0.001  |
| Transfusion of plasma, ml          | 0.00 (0.00-200.00) | 1.0 (1.0, 1.0) | <0.001  |
| EF value after surgery, %          | 47.9±22.7        | 1.0 (1.0, 1.0) | 0.008   |
| Gender, %                          |                  |             |         |
| Male                               | 690 (68.3%)      | 1.0         |         |
| Female                             | 320 (31.7%)      | 1.1 (0.8, 1.5) | 0.735   |
| History of cardiac surgery, %      |                  |             |         |
| No                                 | 976 (96.8%)      | 1.0         |         |
| Yes                                | 34 (3.4%)        | 4.8 (2.4, 9.7) | <0.001  |
| History of hypertension, %         |                  |             |         |
| No                                 | 557 (55.1%)      | 1.0         |         |
| Yes                                | 453 (44.9%)      | 1.4 (1.1, 1.9) | 0.023   |
| History of diabetes, %             |                  |             |         |
| No                                 | 839 (83.1%)      | 1.0         |         |
| Yes                                | 171 (16.9%)      | 1.3 (0.9, 2.0) | 0.155   |
| History of AMI, %                  |                  |             |         |
| No                                 | 795 (78.7%)      | 1.0         |         |
| Yes                                | 215 (21.3%)      | 1.2 (0.9, 1.8) | 0.249   |
### Supplementary Table 2 continued. Univariate analysis for development of acute respiratory distress syndrome.

| Covariate                                | Statistics | OR (95% CI) | P value |
|------------------------------------------|------------|-------------|---------|
| **Emergency surgery, %**                 |            |             |         |
| No                                       | 959 (95.0%)| 1.0         |         |
| Yes                                      | 51 (5.0%)  | 8.6 (4.7, 15.6) | <0.001 |
| **Type of surgery, %**                    |            |             |         |
| Isolated valvular surgery or isolated GABG surgery | 766 (75.8%) | 1.0         |         |
| Valvular combined with CABG surgery       | 55 (5.4%)  | 6.6 (3.7, 11.6) | <0.001 |
| Aortic surgery                           | 64 (6.3%)  | 9.3 (5.4, 16.0) | <0.001 |
| Others                                   | 125 (12.4%)| 2.2 (1.4, 3.4) | <0.001 |

EF – ejection fraction; COPD – chronic obstructive pulmonary disease; AMI – acute myocardial infarction; CABG – coronary artery bypass grafting; APACHE – acute physiology and chronic health evaluation; ARDS – acute respiratory distress syndrome; OR – odds ratio.

### Supplementary Table 3. Baseline characteristics of patients with acute respiratory distress syndrome (n=202).

| BMI                  | <18.5 | ≥18.5, <25 | ≥25, <30 | ≥30 | P value |
|----------------------|-------|------------|----------|-----|---------|
| N (%)                | 14 (6.93%) | 108 (53.47%) | 62 (30.69%) | 18 (8.91%) | 0.019 |
| Age, years           | 51.79±16.16 | 57.07±14.19 | 62.39±10.98 | 56.83±13.90 | 0.019 |
| Smoking index        | 300.00 (200.00-550.00) | 500.00 (400.00-800.00) | 550.00 (300.00-800.00) | 800.00 (600.00-1050.00) | 0.354 |
| EF value before surgery, % | 39.21±31.03 | 52.0±23.49 | 48.3±26.01 | 52.06±25.20 | 0.296 |
| Hemoglobin level before surgery, g/l   | 111.21±16.68 | 120.3±23.74 | 131.6±21.79 | 129.0±23.64 | 0.002 |
| Albumin level before surgery, g/l       | 41.0±3.57 | 37.8±9.43 | 36.97±7.30 | 36.0±10.23 | 0.365 |
| APACHE II value       | 17.79±4.98 | 19.4±5.28 | 20.5±6.23 | 20.0±7.10 | 0.378 |
| Duration of surgery, hours            | 5.48±1.68 | 6.53±2.77 | 6.25±2.90 | 6.26±2.89 | 0.586 |
| Blood loss, ml         | 700.00 (400.00-800.00) | 1000.00 (700.00-1300.00) | 1000.00 (725.00-1500.00) | 750.00 (500.00-1425.00) | 0.285 |
| Transfusion of red blood cells, ml     | 400.00 (300.00-575.00) | 800.00 (400.00-1000.00) | 800.00 (400.00-1181.50) | 700.00 (400.00-900.00) | 0.310 |
| Transfusion of plasma cells, ml        | 400.00 (0.00-475.00) | 400.00 (0.00-400.00) | 200.00 (0.00-400.00) | 0.00 (0.00-150.00) | 0.186 |
| EF value after surgery, %              | 30.50±23.98 | 49.31±17.24 | 50.32±16.42 | 54.78±22.05 | <0.001 |
| Duration of incubation time, hours     | 41.00 (0.00-144.00) | 115.50 (45.50-263.85) | 115.10 (48.67-394.73) | 360.00 (192.00-483.25) | 0.001 |
| Gender, %                            |         |             |          |      | 0.010 |
| Male                                  | 12 (85.71%) | 78 (72.22%) | 34 (54.84%) | 8 (44.44%) |         |
| Female                                | 2 (14.29%) | 30 (27.78%) | 28 (45.16%) | 10 (55.56%) |         |
| History of cardiac surgery, %         |         |             |          |      | 0.003 |
| No                                    | 14 (100.00%) | 88 (81.48%) | 61 (98.39%) | 17 (94.44%) |         |
| Yes                                   | 0 (0.00%) | 20 (18.52%) | 1 (1.61%) | 1 (5.56%) |         |
**Supplementary Table 3 continued.** Baseline characteristics of patients with acute respiratory distress syndrome (n=202).

| BMI          | <18.5 | 18.5, <25 | 25, <30 | ≥30 | P value |
|--------------|-------|-----------|---------|-----|---------|
| History of hypertension, % | | | | | <0.001 |
| No           | 13 (92.86%) | 60 (55.56%) | 22 (35.48%) | 0 (0.00%) |
| Yes          | 1 (7.14%)   | 48 (44.44%) | 40 (64.52%) | 18 (100.00%) |
| History of diabetes, % | | | | | 0.315 |
| No           | 13 (92.86%) | 85 (78.70%) | 46 (74.19%) | 12 (66.67%) |
| Yes          | 1 (7.14%)   | 23 (21.30%) | 16 (25.81%) | 6 (33.33%) |
| History of AMI, % | | | | | 0.013 |
| No           | 12 (85.71%) | 87 (80.56%) | 38 (61.29%) | 16 (88.89%) |
| Yes          | 2 (14.29%)  | 21 (19.44%) | 24 (38.71%) | 2 (11.11%) |
| Emergency surgery, % | | | | | 0.090 |
| No           | 14 (100.00%) | 95 (87.96%) | 50 (80.65%) | 13 (72.22%) |
| Yes          | 0 (0.00%)   | 13 (12.04%) | 12 (19.35%) | 5 (27.78%) |
| Type of surgery, % | | | | | 0.019 |
| Isolated valvular surgery or isolated CABG surgery | | | | | |
| No           | 8 (57.14%) | 50 (46.30%) | 37 (59.68%) | 9 (50.00%) |
| Valvular combined with CABG surgery | | | | | |
| No           | 3 (21.43%) | 20 (18.52%) | 4 (6.45%) | 2 (11.11%) |
| Aortic surgery | 0 (0.00%) | 15 (13.89%) | 16 (25.81%) | 6 (33.33%) |
| Others       | 3 (21.43%) | 23 (21.30%) | 5 (8.06%) | 1 (5.56%) |
| Infection after surgery | | | | | 0.745 |
| No           | 9 (64.29%) | 67 (62.04%) | 36 (58.06%) | 13 (72.22%) |
| Yes          | 5 (35.71%) | 41 (37.96%) | 26 (41.94%) | 5 (27.78%) |
| IABP after surgery | | | | | 0.676 |
| No           | 11 (78.57%) | 81 (75.00%) | 51 (82.26%) | 15 (83.33%) |
| Yes          | 3 (21.43%) | 27 (25.00%) | 11 (17.74%) | 3 (16.67%) |
| ECMO after surgery | | | | | 0.352 |
| No           | 12 (85.71%) | 95 (87.96%) | 54 (87.10%) | 13 (72.22%) |
| Yes          | 2 (14.29%) | 13 (12.04%) | 8 (12.90%) | 5 (27.78%) |
| CRRT after surgery | | | | | 0.920 |
| No           | 9 (64.29%) | 71 (65.74%) | 43 (69.35%) | 13 (72.22%) |
| Yes          | 5 (35.71%) | 37 (34.26%) | 19 (30.65%) | 5 (27.78%) |
| Tracheotomy after surgery | | | | | 0.498 |
| No           | 12 (85.71%) | 73 (67.59%) | 40 (64.52%) | 12 (66.67%) |
| Yes          | 2 (14.29%) | 35 (32.41%) | 22 (35.48%) | 6 (33.33%) |
| Second intubation after surgery | | | | | 0.009 |
| No           | 2 (14.29%) | 41 (37.96%) | 35 (56.45%) | 10 (55.56%) |
| Yes          | 12 (85.71%) | 67 (62.04%) | 27 (43.55%) | 8 (44.44%) |
**Supplementary Table 3 continued.** Baseline characteristics of patients with acute respiratory distress syndrome (n=202).

| Covariate | Statistics | HR (95% CI) | P value |
|-----------|------------|-------------|---------|
| BMI       | 24.31±3.99 | 0.89 (0.82, 0.96) | 0.003   |
| Age, years| 58.32±13.64 | 0.98 (0.95, 1.00) | 0.038   |
| Smoking index | 500.00 (400.00-800.00) | 1.00 (1.00, 1.00) | 0.320   |
| EF value before surgery, % | 50.01±25.03 | 0.99 (0.98, 1.00) | 0.129   |
| Hemoglobin level before surgery, g/l | 123.94±23.41 | 0.99 (0.97, 1.00) | 0.049   |
| Albumin level before surgery, g/l | 37.61±8.63 | 1.02 (0.99, 1.06) | 0.177   |
| APACHE II value | 19.70±5.74 | 1.00 (0.95, 1.05) | 0.949   |
| Duration of surgery, hours | 6.34±2.76 | 1.10 (0.98, 1.24) | 0.093   |
| Blood loss, ml | 1000.00 (600.00-1500.00) | 1.00 (1.00, 1.00) | 0.374   |
| Transfusion of red blood cells, ml | 750.00 (400.00-1200.00) | 1.00 (1.00, 1.00) | 0.651   |
| Transfusion of plasma cells, ml | 200.00 (0.00-400.00) | 1.00 (1.00, 1.00) | 0.089   |
| EF value after surgery, % | 50.01±25.03 | 0.99 (0.98, 1.00) | 0.129   |
| Duration of incubation time, hours | 209.43±233.70 | 1.00 (1.00, 1.00) | 0.470   |
| Gender, % | | | 0.266   |
| Male      | 132 (65.35%) | 1.0 | |
| Female    | 70 (34.65%) | 1.43 (0.76, 2.68) | |
| History of cardiac surgery, % | | | 0.846   |
| No        | 180 (89.11%) | 1.0 | |
| Yes       | 22 (10.89%) | 1.10 (0.43, 2.84) | |
| History of hypertension, % | | | 0.555   |
| No        | 95 (47.03%) | 1.0 | |
| Yes       | 107 (52.97%) | 0.84 (0.47, 1.51) | |
| History of diabetes, % | | | 0.022   |
| No        | 156 (77.23%) | 1.0 | |
| Yes       | 46 (22.77%) | 0.46 (0.23, 0.89) | |

**Supplementary Table 4.** Univariate analysis for mortality of acute respiratory distress syndrome.

EF – ejection fraction; COPD – chronic obstructive pulmonary disease; IBW – ideal body weight; AMI – acute myocardial infarction; CABG – coronary artery bypass grafting; APACHE – acute physiology and chronic health evaluation; ARDS – acute respiratory distress syndrome; IABP – intra-aortic balloon pump; ECMO – extracorporeal membrane oxygenation therapy; CRRT – continuous renal replacement therapy

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**Supplementary Table 4 continued.** Univariate analysis for mortality of acute respiratory distress syndrome.

| Covariate                                                                 | Statistics | HR (95% CI)       | P value |
|----------------------------------------------------------------------------|------------|-------------------|---------|
| History of AMI, %                                                          |            |                   |         |
| No                                                                        | 153        | (75.74%)          | 1.0     |
| Yes                                                                       | 49         | (24.26%)          | 0.74 (0.38, 1.45) | 0.382   |
| Emergency surgery, %                                                       |            |                   |         |
| No                                                                        | 172        | (85.15%)          | 1.0     |
| Yes                                                                       | 30         | (14.85%)          | 1.47 (0.62, 3.51) |         |
| Type of surgery, %                                                         |            |                   |         |
| Isolated valvular surgery or isolated CABG surgery                         | 104        | (51.49%)          | 1.0     |
| Valvular combined with CABG surgery                                        | 29         | (14.36%)          | 0.98 (0.42, 2.29) | 0.966   |
| Aortic surgery                                                            | 37         | (18.32%)          | 1.62 (0.71, 3.70) | 0.253   |
| Others                                                                    | 32         | (15.84%)          | 1.80 (0.74, 4.40) | 0.197   |
| Infection after surgery                                                    |            |                   | 0.741   |
| No                                                                        | 125        | (61.88%)          | 1.0     |
| Yes                                                                       | 77         | (38.12%)          | 0.90 (0.50, 1.64) |         |
| IABP after surgery                                                        |            |                   | 0.514   |
| No                                                                        | 158        | (78.22%)          | 1.0     |
| Yes                                                                       | 44         | (21.78%)          | 1.27 (0.62, 2.63) |         |
| ECMO after surgery                                                        |            |                   | 0.146   |
| No                                                                        | 174        | (86.14%)          | 1.0     |
| Yes                                                                       | 28         | (13.86%)          | 2.03 (0.78, 5.27) |         |
| CRRT after surgery                                                        |            |                   | 0.308   |
| No                                                                        | 136        | (67.33%)          | 1.0     |
| Yes                                                                       | 66         | (32.67%)          | 1.39 (0.74, 2.64) |         |
| Tracheotomy after surgery                                                  |            |                   | 0.779   |
| No                                                                        | 137        | (67.82%)          | 1.0     |
| Yes                                                                       | 65         | (32.18%)          | 1.09 (0.58, 2.05) |         |
| Second intubation after surgery                                           |            |                   | 0.002   |
| No                                                                        | 88         | (43.56%)          | 1.0     |
| Yes                                                                       | 114        | (56.44%)          | 2.56 (1.41, 4.66) |         |

EF – ejection fraction; COPD – chronic obstructive pulmonary disease; AMI - acute myocardial infarction; CABG – coronary artery bypass grafting; APACHE – acute physiology and chronic health evaluation; ARDS – acute respiratory distress syndrome; IABP – intra-aortic balloon pump; ECMO – extracorporeal membrane oxygenation therapy; CRRT – continuous renal replacement therapy.
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