Original Article

Analysis of risk factors for and the prognosis of postoperative acute respiratory distress syndrome in patients with Stanford type A aortic dissection

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Background: To explore the risk factors for and the prognosis of postoperative acute respiratory distress syndrome (ARDS) in patients with Stanford type A aortic dissection (AD).

Methods: This retrospective nested case-control study included 527 Stanford type A AD patients who were divided into ARDS groups and non-ARDS groups. The clinical features of the groups were examined.

Results: The fifty-nine patients in the ARDS group exhibited extended durations of cardiopulmonary bypass (CPB) (P=0.004), deep hypothermic circulatory arrest (DHCA) (P=0.000), ventilator support (P=0.013) and intensive care unit (ICU) stay (P=0.045), higher hospital costs (P=0.000), larger perioperative transfusions volumes [red blood cells (RBC): P=0.002, platelets (PLT): P=0.040, fresh frozen plasma (FFP): P=0.001], more frequent pulmonary infection (P=0.018) and multiple organ dysfunction syndrome (MODS) (P=0.040) and a higher rate of in-hospital mortality (P=0.020). The ARDS group exhibited worse statuses in terms of oxygenation index (OI) values (P=0.000) and Apache II scores (P=0.000). DHCA [P=0.000, odds ratio (OR) =2.589] and perioperative transfusion (RBC: P=0.000, OR =2.573; PLT: P=0.027, OR =1.571; FFP: P=0.002, OR =1.929) were independent risk factors for postoperative ARDS. The survival rates and median survival times after discharge were similar between the two groups (P=0.843).

Conclusions: DHCA duration and perioperative transfusion volume were independent risk factors for postoperative ARDS which warrants greater attention by the cardiac surgeons.

Keywords: Respiratory distress syndrome; adult; aortic aneurysm; cardiopulmonary bypass; circulatory arrest; deep hypothermia induced

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Introduction

Acute respiratory distress syndrome (ARDS) can occur in cases of severe infection, shock, trauma, burns and other diseases following the damage to pulmonary capillary endothelial cells and alveolar epithelial cells (1,2). Currently, most investigators believe that ischemia-reperfusion injury (IRI) and the release of massive amounts of inflammatory mediators during cardiopulmonary bypass (CPB) and circulatory arrest are responsible for ARDS after cardiac surgery (3-6).

Most cases of Stanford type A aortic dissection (AD) require emergency surgery. Due to the complicated surgical procedures involved in the reconstruction of the aorta and its branches, CPB in addition to deep hypothermic circulatory arrest (DHCA) are essential for maintaining a relatively bloodless operating field. The difficulties and

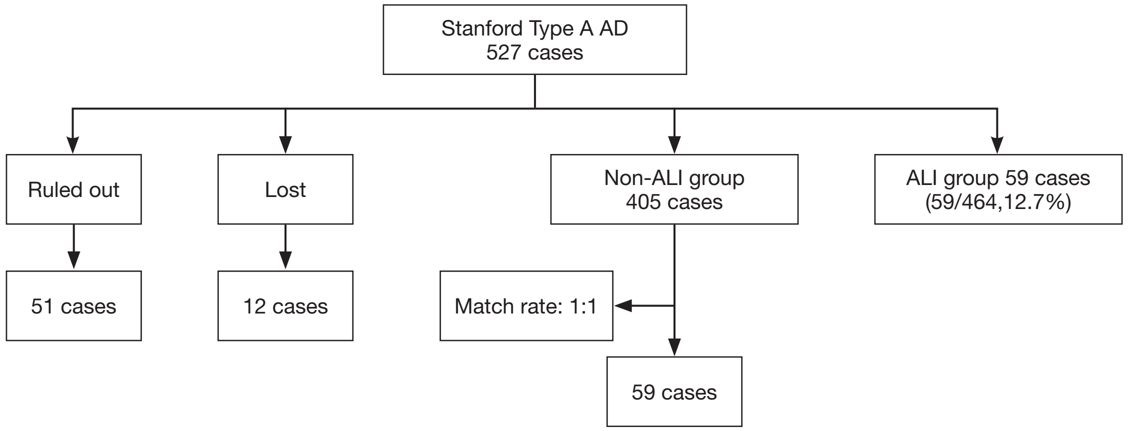

Figure 1 The patients were divided into two groups: a non-ARDS group (n=405) and an ARDS group (n=59). Fifty-nine patients from the non-ARDS group were randomly selected as matched cases. Sixty–three cases were excluded from this study according to exclusion criteria described in detail below. ARDS, acute respiratory distress syndrome.

risks associated with these surgical procedures are therefore much greater than those of other types of AD (7).

However, few reports have elaborated on relationship between the ARDS and the surgery for Stanford type A AD. The goal of this study was to perform a retrospective analysis evaluating the risk factors and adverse consequences of postoperative ARDS in patients with Stanford type A AD who underwent thoracotomy surgeries in our department.

Methods

Clinical data

This retrospective nested case-control study included 527 patients who underwent surgeries for Stanford type A AD in the Department of Cardiovascular Surgery, Union Hospital, Fujian Medical University, between January 2013 and January 2016. These patients were divided into two groups: the ARDS group (n=59) and the non-ARDS group (n=405), Additionally, 59 patients in the non-ARDS group were randomly selected to serve as the matched controls. Sixty-three patients were excluded from the study according to the exclusion criteria, which are described in detail in *Figure 1*. The general demographic characteristics, underlying diseases, etiologies, intraoperative and postoperative conditions, recent and short-term complications, and hospitalization costs were accounted for in the analysis.

Diagnostic criteria for ARDS

Postoperative ARDS is defined as an oxygenation index (OI; PaO_2/FiO_2 <300) that occurs within 7 days after surgery and that is unrelated to other documented causes of acute lung injury (e.g., cardiogenic pulmonary edema, pneumonia, pulmonary embolism and hemato- or pneumothorax). ARDS patients routinely undergo chest radiography, pleural ultrasonography, bronchoscopy with bronchoalveolar lavage (BAL) and chest computed tomography to exclude other causes of postoperative respiratory failure. Perioperative heart failure occurring before the diagnosis of postoperative ARDS was ruled out as a possible cause of pulmonary dysfunction via the performance of transesophageal echocardiography assessing left ventricular systolic and diastolic function, and a pulmonary artery catheter was used to assess the pulmonary capillary wedge pressure (<18 mmHg) when necessary (8).

Exclusion criteria

(I) Patients with severe heart failure (NYHA classification level ≥ III grade) that was recognized before the AD surgery or the diagnosis of ARDS, including acute myocardial infarction, cardiac tamponade, severe primary aortic regurgitation, congenital heart disease, or valvular heart disease;
(II) Patients with other serious lung disease that was recognized before the AD surgery or the diagnosis of ARDS, including silicosis, pneumoconiosis, chronic obstructive pulmonary disease (COPD), lung cancer, and interstitial pneumonia;
(III) Patients and/or their relatives who did not agree to participate in this clinical experimental study.

Treatment

Once the diagnosis of ARDS had been confirmed, a protective strategy employing low tidal volume ventilation (6–8 mL/kg) was initiated. Moreover, large doses of ambroxol hydrochloride (90 mg iv bid), methylprednisolone (1 mg/kg iv bid) and ulinastatin (5,000 units/kg iv bid) were injected to eliminate the effects of inflammatory mediators. Continuous renal replacement therapy (CRRT) was implemented in patients with renal insufficiency (9). Cardiac and diuretic treatments, regular anti-infection strategies, an intra-aortic balloon pump (IABP) and/or an extracorporeal membrane oxygenator (ECMO) were employed in cases of heart failure or serious pulmonary dysfunction.

Evaluation of the functions of the lung and other organs

Pulmonary function was evaluated based on the OI according to perioperative arterial blood gas analysis, and the checkpoints were defined as the perioperative time point (T_0) and 12, 24, 48, and 72 hours after DHCA (T_1, T_2, T_3, and T_4, respectively).

The health statuses of the patients were evaluated according to the criteria of the acute physiology and chronic health evaluation II (APACHE II), which includes age, rectal temperature, mean arterial pressure, heart rate, respiratory rate, pH of the arterial blood pH, venous blood bicarbonate, sodium and potassium levels in the venous blood, serum creatinine level, hematocrit, peripheral leukocyte density, Glasgow score, and chronic underlying disease. The checkpoints were identical to those applied for assessment of the OI.

Postoperative follow-up

The doctors maintained telephone contact with the patients after discharge. Periodic reviews were performed every three to six months to assess the clinical signs and symptoms, vital signs, echocardiograms, and CTAs of the thoracic and abdominal aorta. The follow-up reviews were conducted each year beginning 12 months after discharged. In cases of death after discharge, the cause was ascertained with the relatives' permission.

Ethics

The Ethics Committees of Fujian Medical University Union Hospital approved this retrospective study.

Statistical analysis

SPSS 16.0 software was used for the statistical analyses. Descriptive statistical analyses, repeated-measures ANOVAs and Wilcoxon rank sum tests were used to analyze measurement data. The chi-square test, Fisher's exact test and multivariate logistic regression analysis were used to analyze the count data. The Kaplan-Meier method was used to plot the survival curves. Statistical significance was defined as P<0.05.

Results

General clinical data

In total, 464 patients with Stanford type A AD who were treated with thoracotomy were included in our retrospective study after excluding 51 patients and 12 lost patients. Fifty-nine of the included patients (59/464, 12.7%) experienced postoperative ARDS and were matched with 59 patients from the non-ARDS group. The majority of the ARDS patients were diagnosed within 72 hours after AD surgery. The primary analyses revealed that there were no significant differences between the patients in terms of age, gender, emergency surgery, smoking, alcoholism, underlying disease, preoperative complications, or etiology (*Table 1*).

Surgical and perioperative treatments

All of the patients were divided into two groups according to the treatment of the aortic arch [i.e., open placement of a triple-branched stent graft (10) or replacement of the entire aortic arch (11)]. A Fisher's exact test revealed that the type of surgical correction had no effect on the incidence of postoperative ARDS. However, a Pearson's chi-square test revealed that the patients who underwent open placement of a triple-branched stent graft exhibited a lower incidence of postoperative ARDS (6.8% *vs.* 20.3%, P=0.031) (*Table 2*). We also discovered that the patients in the postoperative ARDS group experienced significantly longer durations of CBP (165.8±67.1 *vs.* 137.0±47.8 min, P=0.004) and DHCA (14.8±14.0 *vs.* 8.4±7.4 min, P=0.000) and received much larger perioperative transfusion volumes of RBCs (7.4±2.7 *vs.* 5.9±2.1 u, P=0.001), PLTs (1.3±0.5 *vs.* 1.1±0.3 u, P=0.040) and FFPs (389.8±155.3 *vs.* 284.8±156.3 mL, P=0.001) than the patients in the non-ARDS group. However, no significant difference in the aortic clamping time was observed between the two groups (*Table 2*).

Moreover, a chi-square test indicated that the durations

Table 1 Clinical data

Category of clinical data	ARDS (n=59)	Non-ARDS (n=59)	P
Age	51.0±12.1	51.0±12.0	0.955
Sex			0.816
Male	47 (79.7%)	48 (81.4%)	
Female	12 (20.3%)	11 (18.6%)	
Emergency surgery	29 (49.2%)	31 (52.5%)	0.713
Smoking	17 (28.8%)	14 (23.7%)	0.530
Alcoholism	4 (6.8%)	8 (13.6%)	0.223
Underlying diseases			
Diabetes	11 (18.6%)	14 (23.7%)	0.499
CHD	7 (11.9%)	10 (16.9%)	0.432
Cardiac reoperation	3 (5.1%)	3 (5.1%)	1.000
Etiologies			0.966
Hypertension	37 (62.7%)	43 (72.9%)	
Marfan syndrome	5 (8.5%)	3 (5.1%)	
Syphilis	2 (3.4%)	2 (3.4%)	
Takayasu arteritis	2 (3.4%)	2 (3.4%)	
SLE	2 (3.4%)	1 (1.7%)	
Trauma	1 (1.7%)	1 (1.7%)	
Endovascular treatment	2 (3.4%)	1 (1.7%)	
Unknown reasons	8 (13.6%)	6 (10.2%)	
Preoperative complications			
Pericardial effusion#	19 (32.2%)	18 (30.5%)	0.843
Aortic regurgitation☆	14 (23.7%)	9 (15.3%)	0.245
Renal insufficiency△	11 (18.6%)	9 (15.3%)	0.624
AMI§	3 (5.1%)	4 (6.8%)	0.696
Cerebral dysfunction@	3 (5.1%)	4 (6.8%)	1.000
Mesenteric artery Infarction◎	0 (0%)	3 (5.1%)	0.079

The primary analyses revealed that there were no significant differences between the patients in the general demographic characteristics. #, serious pericardial effusion; ☆, serious aortic regurgitation; △, acute or chronic renal insufficiency; §, clinical manifestations; @, cerebral or spinal cord infarctions and other non-organic abnormal mental statuses confirmed by tomography; ◎, confirmed by superior mesenteric artery angiography. ECG, and contents of creatine kinase and troponin in the serum that were consistent with the diagnostic criteria for acute myocardial infarction; CHD, coronary heart disease; SLE, systemic lupus erythematosus; AMI, acute myocardial infarction.

of CBP (282.4±57.1 *vs.* 130.8±22.5 min, P=0.000) and DHCA (39.6±6.9 *vs.* 7.1±2.3 min, P=0.000) were significantly longer for the group of patient receiving total aortic arch replacement than for the group of patients receiving triple-branched stent engraftment, and a significant difference in the perioperative transfusion volume was found between these two groups (*Table 3*).

Postoperative outcomes

The postoperative oxygenation index (OI) values was lower in the patients in the ARDS group than in the patients in the non-ARDS group (F=21.280, P=0.000). Moreover, the postoperative Apache II scores of the patients in the ARDS group were higher than those of the patients in the non-ARDS group (F=25.918, P=0.000) (*Figures 2,3*). These findings revealed that ARDS had seriously adverse effects on postoperative oxygenation and physiological function.

The observed postoperative complications included reoperation (debridement or thoracotomy for hemostasis), heart dysfunction that occurred after the diagnosis of ARDS, central nervous system (CNS) complications, renal insufficiency, pulmonary infection that occurred after the diagnosis of ARDS, wound infection, liver dysfunction, and multiple organ dysfunction syndrome (MODS). A total of 8 in-hospital deaths among the 118 patients (6.8%) occurred due to MODS. The remaining patients survived and were successfully discharged with a normal OI. However, the incidences of MODS (16.9% *vs.* 5.1%, P=0.040, OR=4.278; 95% CI: 1.127–16.232), lung infection (22.0% *vs.* 6.8%, P=0.018, OR=3.886; 95% CI: 1.186–12.736) and in-hospital mortality (11.9% *vs.* 1.7%, P=0.028, OR=7.808, 95% CI: 0.929–65.600) were significantly higher among the patients in the ARDS group than among the patients in the non-ARDS group (*Table 4*), and the ARDS group exhibited significantly longer durations of ventilation and ICU stay. Furthermore, the hospital costs incurred by the patients in the ARDS group were substantially higher than those incurred by the non-ARDS patients (164,727.9±14,904.1 *vs.* 126,827.6±11,635.0 RMB, P=0.000), and this difference was primarily due to the postoperative complications associated with ARDS (*Table 4*).

The non-survivors with ARDS were found to experience extended durations of CPB (233.9±60.9 *vs.* 156.6±62.9 min, P=0.003), aortic cross-clamping (113.6±63.5 *vs.* 54.8±33.1 min, P=0.012) and DHCA (35.7±17.6 *vs.* 12.0±10.9 min, P=0.000) and receive much larger perioperative transfusion volumes of FFPs (514.3±149.2 *vs.* 367.1±149.7 mL,

Table 2 Surgical and perioperative treatments

Category of perioperative treatments	ARDS (n=59)	Non-ARDS (n=59)	P
Treatment of the aortic arch			
Triple-branched stent graft placement	4 (6.8%)	55 (93.2%)	0.031
Aortic arch replacement	12 (20.3%)	47 (79.7%)	
Type of surgical correction			
Aortic sinus angioplasty	42 (71.2%)	43 (72.9%)	0.837
Bentall	18 (30.5%)	17 (28.8%)	0.840
Ascending aorta replacement	59 (100%)	59 (100%)	–
Descending aortic stent implantation	59 (100%)	59 (100%)	–
CABG	4 (6.8%)	9 (15.3%)	0.142
Intraoperative conditions			
CPB (min)	165.8±67.1	137.0±47.8	0.004
Aortic cross-clamping (min)	61.8±41.9	57.1±31.8	0.332
DHCA (min)	14.8±14.0	8.4±7.4	0.000
Perioperative transfusion			
RBC (u)	7.4±2.7	5.9±2.1	0.002
PLT (u)	1.3±0.5	1.1±0.3	0.040
FFP (mL)	389.8±155.3	284.8±156.3	0.001

Patients from the ARDS group were found to have experienced longer durations of CPB and DHCA and have received greater perioperative transfusion volumes compared with the patients in the non-ARDS group. ARDS, acute respiratory distress syndrome; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; RBC, red blood cell; PLT, platelet; FFP, fresh frozen plasma.

Table 3 Comparison of the two types of the aortic arch treatment

Category	Triple-branched stent (graft placement)	Aortic arch (replacement)	P
CPB (min)	130.8±22.5	282.4±57.1	0.000
DHCA (min)	7.2±2.4	39.6±6.9	0.000
RBC (u)	6.4±2.5	8.2±2.6	0.012
PLT (u)	1.1±0.4	1.6±0.3	0.000
FFP (mL)	320.1±150.6	446.8±204.5	0.003

The aortic arch replacement group experienced extended durations of CPB and DHCA and received perioperative transfusions of greater volumes than the triple-branched stent graft placement group. CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; RBC, red blood cell; PLT, platelet; FFP, fresh frozen plasma.

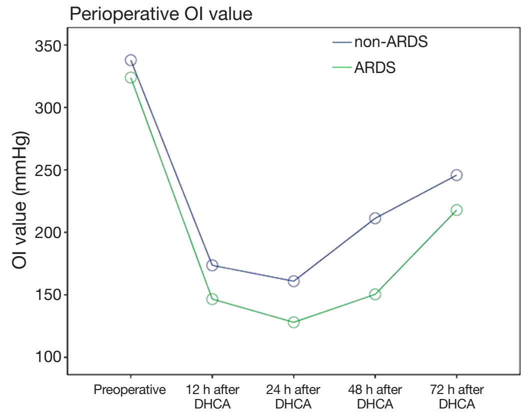

Figure 2 Repeated measures analysis revealed that the postoperative oxygenation index (OI) values was lower in the patients in the ARDS group than in the patients in the non-ARDS group (F=21.280, P=0.000). ARDS, acute respiratory distress syndrome.

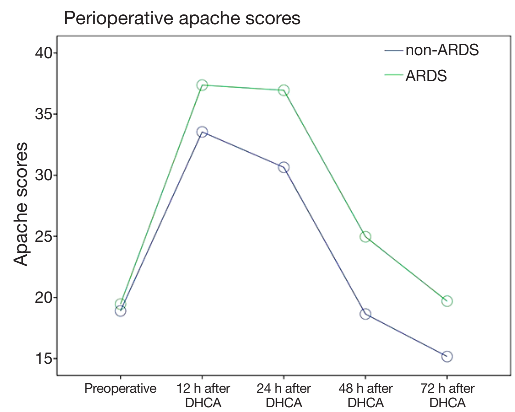

Figure 3 Repeated measures analysis revealed that the postoperative Apache II scores of the patients in the ARDS group were higher than those of the patients in the non-ARDS group (F=25.918, P=0.000). ARDS, acute respiratory distress syndrome.

P=0.009) than the survivors with ARDS (*Table 5*).

Follow-up

Twelve patients were lost within the 36-month follow-up period and were not included in this study. Four incidents of death after discharge were observed and were attributed to car accident, stroke, recrudescence of the AD and unknown cause (*Table 6*). Short-term complications included recrudescence of the AD (1 patient died and 2 patients survived with no significant sequelae after emergency

Table 4 Postoperative complications and hospital costs

Category	ARDS (n=59)	Non-ARDS (n=59)	P	OR	95%CI	
					Lower	Upper
Reoperation	5 (8.5%)	3 (5.1%)	0.462	–	–	
Heart dysfunction[#]	8 (13.6%)	4 (6.8%)	0.223	–	–	
CNS complications[&]	11 (18.6%)	10 (16.9%)	0.810	–	–	
Renal insufficiency[△]	8 (13.6%)	5 (8.5%)	0.378	–	–	
Pulmonary infection	13 (22.0%)	4 (6.8%)	0.018	3.886	1.186	12.736
Wound infection	4 (6.8%)	4 (6.8%)	1.000	–	–	
Liver dysfunction	4 (6.8%)	5 (8.5%)	0.728	–	–	
MODS	10 (16.9%)	3 (5.1%)	0.040	4.278	1.127	16.232
Ventilation time (h)	65.5±85.5	43.1±35.7	0.013	–	–	
ICU stay time (d)	17.1±15.7	11.1±9.3	0.045	–	–	
Hospital deaths	7 (11.9%)	1 (1.7%)	0.020	7.808	0.929	65.600
Hospital costs (RMB)	164,727.9±14,904.1	126,827.7±11,635.0	0.000	–	–	

The ARDS group exhibited significantly higher rates of postoperative pulmonary infection and MODS. The ARDS group exhibited significantly higher mortality and greater hospital costs than the non-ARDS group. [#], severe heart failure reached NYHA grade III-IV following the ARDS diagnosis; [&], including stroke, paraplegia and non-organic abnormal mental status; [△], consistent with the indications for renal replacement therapy. ARDS, acute respiratory distress syndrome; CNS, central nervous system; MODS, multiple organ dysfunction syndrome; RMB, Renminbi.

Table 5 Differences of surgical and perioperative treatments between survivors with ARDS and non-survivors with ARDS

Surgical and perioperative treatments	Survivors with ARDS (n=52)	Non-survivors with ARDS (n=7)	P
Treatment of the aortic arch			0.002
Triple-branched stent graft placement	45 (95.7%)	2 (4.3%)	
Aortic arch replacement	7 (58.3%)	5 (41.7%)	
Type of surgical correction			
Aortic sinus angioplasty	36 (85.7%)	6 (14.3%)	0.366
Bentall	17 (89.5%)	2 (10.5%)	0.827
Ascending aorta replacement	52 (88.1%)	7 (11.9%)	–
Descending aortic stent implantation	52 (88.1%)	7 (11.9%)	–
CABG	4 (100%)	0 (0.0%)	1.000
Intraoperative conditions			
CPB (min)	156.6±62.9	233.9±60.9	0.003
Aortic cross-clamping (min)	54.8±33.1	113.6±63.5	0.012
DHCA (min)	12.0±10.9	35.7±17.6	0.000
Perioperative transfusion			
RBC (U)	7.4±2.8	8.7±1.8	0.241
PLT (u)	1.2±0.5	1.5±0.3	0.218
FFP (mL)	367.1±149.7	514.3±149.2	0.009

The non-survivors with ARDS experienced extended durations of CPB, aortic cross-clamping and DHCA, and receive much larger perioperative transfusion volumes than the survivors with ARDS. ARDS, acute respiratory distress syndrome; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; RBC, red blood cell; PLT, platelet; FFP, fresh frozen plasma.

Table 6 Short-term follow-up

Outcomes	Event	ARDS (n=59) (%)	Non-ARDS (n=59) (%)	P
Death after discharge	car accidents	0 (0.0)	1 (1.0)	1.000
	Stroke	1 (1.7)	0 (0.0)	
	Recrudescence of aortic dissection	1 (1.7)	0 (0.0)	
	Unknown	0 (0.0)	1 (1.0)	
	Total	2 (3.4)	2 (3.4)	
Complications after discharge	Recrudescence	1 (1.7)	2 (3.4)	–1.000
	Endoleaks	5 (8.5)	3 (5.1)	–0.714
	Paraplegia	2 (3.4)	2 (3.4)	–1.000
	Infection	1 (1.7)	2 (3.4)	–1.000

No significant differences were found between the two groups in terms of mortality or complications after discharge after discharge.

Table 7 The interquartile ranges of the measurement data

Percentiles	CPB (min)	DHCA (min)	RBC (u)	PLT (u)	FFP (mL)
25	120.00	6.00	4.20	0.80	200.00
50	130.00	7.00	6.85	1.20	350.00
75	155.00	9.25	8.70	1.45	462.50

The measurement data were divided into four groups according the boundaries of the interquartile ranges. CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; RBC, red blood cell; PLT, platelet; FFP, fresh frozen plasma.

reoperation), endoleaks (3 cases that resolved in 1 to 3 months, 4 cases that were treated with endovascular stent grafts, and 1 case that was treated with a triple-branched stent graft; all 8 patients ultimately recovered), paraplegia and infection (the body temperatures and hemograms returned to normal after 12 to 21 days of anti-infection treatment). Additional chi-square tests indicated that there were no significant differences between the two groups in terms of mortality or complications after discharge (*Table 6*).

Multivariate logistic regression analysis

A total of 6 variables were analyzed in the stepwise logistic regression model to identify the independent risk factors for postoperative ARDS. DHCA and perioperative transfusion were ultimately identified as significant risk factors (*Tables 7,8*).

Survival curves

Survival curve analyses based on 36 months of observation revealed that no significant difference in the survival rate or the median survival time between the patients in the ARDS group and the patients in the non-ARDS group (*Figure 4*).

Discussion

A temporary block of the systemic circulation is required to create a relatively bloodless surgical field during treatment of Stanford type A AD treatment. Despite the application of improved surgical procedures and protective techniques such as selective cerebral perfusion and DHCA, the risk of postoperative organ dysfunction or organ failure persists. It has been reported that the frequency of ARDS following Stanford type A AD surgery is between 12.7% and 13.0% (12-15), which is similar to the 12.7% (59/464) incidence observed in our department.

In the absence of effective treatment, the mortality rate of ARDS patients over the past two decades has fluctuated between 25% and 67%. In the present study, we observed that a total of 7 of the 8 (87.5%) in-hospital deaths were associated

Table 8 Multivariate logistic regression analysis#

Category	B	S.E.	Wald	df	Sig.	Exp (B)
Surgery type	−0.562	0.919	0.374	1	0.541	0.570
CPB (min)	0.219	0.247	0.788	1	0.375	1.245
DHCA (min)	0.951	0.262	13.138	1	0.000	2.589
RBC (u)	0.945	0.239	15.672	1	0.000	2.573
PLT (u)	0.451	0.204	4.915	1	0.027	1.571
FFP (mL)	0.657	0.209	9.859	1	0.002	1.929

DHCA and perioperative transfusion were ultimately identified as significant risk factors. #, the measurement data were divided into four groups defined the boundaries of the interquartile ranges (see in *Table 7*). CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; RBC, red blood cell; PLT, platelet; FFP, fresh frozen plasma. B, regression coefficients; S.E., standard error; df, degree of freedom; Sig., significance; Exp, odds ratio.

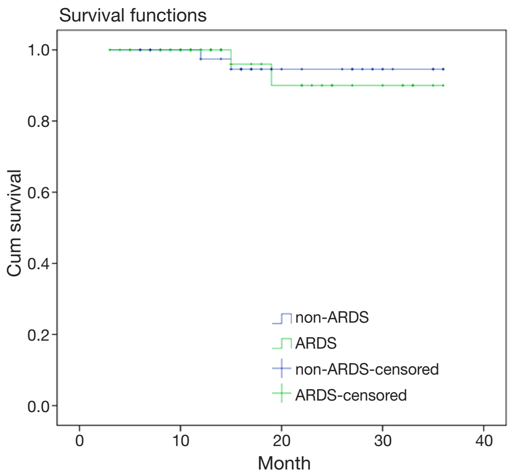

Figure 4 Kaplan-Meier plots revealing that no significant difference in the survival rate or the median survival time between the patients in the ARDS group and the patients in the non-ARDS group (log-rank result: χ^2=0.039, P=0.843), (36 *vs.* 36 months). ARDS, acute respiratory distress syndrome.

with ARDS. Moreover, a total of 7 of the 59 (11.9%) patients with postoperative ARDS died in the hospital despite receiving adequate treatment.

In addition to impairing pulmonary oxygenation and causing refractory hypoxemia, ARDS has serious irreversible effects on other vital organs and can lead to MODS. The mortality rate of MODS has been reported to be as high as 53.3% (16). Additionally, significantly lower OI and higher Apache II scores were observed in the patients in the ARDS group than in the patients in the non-ARDS group. These statistics explain why the proportion of patients with postoperative MODS was significantly higher in the ARDS group than in the non-ARDS group. This phenomenon indicated that the high mortality rate of postoperative MODS has a serious influence on the prognoses of patients with postoperative ARDS. Additionally, once postoperative ARDS occurred, the durations of ventilation and ICU stay lengthened significantly, which increased the incidences of ventilator-associated pneumonia (VAP), nosocomial infections and other complications in addition to increasing the economic burdens on the patients. Furthermore, the survival rate of the patients in the ARDS group after 36 months of follow-up was lower than that of the non-ARDS group. Preventing postoperative ARDS is therefore particularly important for patients with Stanford type A AD.

The most common causes of postoperative ARDS are pulmonary injury due to IRI resulting from DHCA during surgical treatment of Stanford type A AD treatment, cytokine-mediated inflammation during CPB, and leukocyte infiltration into the pulmonary tissue. ARDS can also result in systemic inflammatory response syndrome (SIRS) and IRI of other organs, such as the intestines (17,18), skeletal muscle (19), and liver (20). These factors account for the significantly longer DHCA and CPB times of the ARDS group compared with those of the non-ARDS group, Further, the results of a subsequent multivariate logistic regression analysis indicated that DHCA was an independent risk factor for postoperative ARDS. Thus, these results demonstrated that recipients of treatment for Stanford type A AD would benefit from reductions in the CPB and DHCA times and the mitigation of the IRI resulting from improved surgical techniques.

Transfusion-related acute lung injury (TRALI) also plays an important role in postoperative ARDS following Stanford type A AD and has been attributed to alveolar epithelial cell and endothelial cell damage by active neutrophils. The molecular mechanism underlying this phenomenon is unclear but is thought to involve the S100A12 protein (21,22) or antigen-antibody reactions. The surgical treatment of Stanford type A AD is often complicated and may involve vascular anastomosis, which requires the transfusion of a greater amount of blood products than conventional thoracotomy. This theory is consistent with our findings that the amounts of perioperative transfusions (regardless of the type of blood product) were significantly greater in the ARDS group than in the non-ARDS group. Further logistic regression prompted us to conclude that perioperative transfusion was an independent risk factor for postoperative ARDS. Thus, surgical treatment of Stanford type A AD was directly associated with TRALI. Therefore, reducing the use of blood products by improving operative techniques is critical for the prevention of postoperative ARDS and reducing the incidence of in-hospital death with ARDS in patients with Stanford type A AD patients.

Interestingly, the present study demonstrated that 20.3% of the patients with ARDS had receive replacement of the entire aortic arch (Sun's procedure), and the corresponding percentage in the non-ARDS group was only 6.8%. This difference can be explained by the longer durations of DHCA and CPB and the much greater perioperative blood transfusions associated with Sun's procedure. Because we had demonstrated that the duration of DHCA and the amount of perioperative blood transfusion were independent risk factors for postoperative ARDS, we speculate that open placement of a triple-branched stent graft is more suitable for Stanford A type AD and that implementing this procedure could effectively reduce the incidence of postoperative ARDS.

However, although the perioperative blood transfusion volumes required by the recipients of triple-branched stent engraftment were significantly less than the volumes required by the recipients of aortic arch replacement, and although the latter patients required a much longer duration of DHCA, the type of aortic arch treatment was not an independent risk factor for postoperative ARDS. Possible explanations for this observation include the following: (I) the mechanism of postoperative ARDS in patients with Stanford type A AD involves a variety of pathophysiological process; and (II) the direct pulmonary injury caused by Stanford type A AD could play an important role in ARDS.

Conclusions

ARDS results from multiple factors and has a serious influence on the prognoses of patients following surgical treatment of Stanford type A AD, and postoperative ARDS warrants greater attention by cardiac surgeons. Controlling the volume of perioperative RBC transfusions required may reduce the incidence of postoperative ARDS, and reducing the duration of CPB and DHCA times will benefits the recipients of thoracic surgeries. Open placement of a triple-branched stent graft is a more suitable treatment for Stanford A type AD and effectively reduced the incidence of postoperative ARDS.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The Ethics Committees of Fujian Medical University Union Hospital approved this retrospective study and written informed consent was obtained from all patients.

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