

# Cardiopulmonary bypass duration is an independent predictor of adverse outcome in surgical repair for acute type A aortic dissection

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## Abstract

**Objective:** This study aimed to investigate the relationship between the duration of cardiopulmonary bypass (CPB) and stroke or early death in patients with acute type A aortic dissection (ATAAD) receiving total aortic arch replacement with the frozen elephant trunk procedure (TAR with FET).

**Methods:** A retrospective cohort study of 258 consecutive patients was conducted at Beijing Anzhen Hospital from December 2014 to June 2016. Patients who received TAR with FET for ATAAD were included. An adverse outcome (AO) was defined as 30-day mortality or stroke. Additionally, an AO was compared using propensity score matching.

**Results:** The incidence of AO was 13.6% ( $n = 35$ ). The 30-day mortality rate was 10.8% and the stroke rate was 9.3%. Patients were aged  $47.9 \pm 10.6$  years old. The duration of CPB was an independent predictor of occurrence of AO after adjusting for confounding factors by multivariable logistic regression analysis (odds ratio 1.101, 95% confidence interval 1.003–1.208). In matched analysis, CPB duration remained a risk factor of AO.

**Conclusions:** The duration of CPB is an independent predictor of AO in surgical repair for ATAAD. The underlying mechanisms of this association are important for developing improved prevention strategies.

## Keywords

Cardiopulmonary bypass, aortic dissection, risk factor, stroke, mortality, adverse outcome

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## Introduction

Acute type A aortic dissection (ATAAD) is one of the most lethal diseases that requires surgical correction. Despite dramatic improvements in cerebral protection strategies over recent decades, postoperative stroke and mortality remain major complications.<sup>1,2</sup> The occurrence of stroke after ATAAD leads to a higher mortality rate, increased length of hospital stay, and reduced long-term survival. An adverse outcome (AO) is defined as either early death or stroke because a successful operation should result not only in survival, but also in good quality of life. Identifying risk factors and preventing an AO following complex aortic arch procedures are necessary to improve outcomes.

Cardiopulmonary bypass (CPB) is an indispensable procedure for surgical treatment of ATAAD. However, CPB can induce oxidative stress reactions and systemic inflammation, leading to multiorgan failure.<sup>3,4</sup> Little is known about the effect of the duration of CPB on AO in patients with ATAAD. Therefore, this study used multivariable logistic regression models and the propensity score (PS) matching method to examine the correlation between an AO and the duration of CPB in patients with ATAAD who underwent total aortic arch replacement with the frozen elephant trunk procedure (TAR with FET). We hypothesized that the risk of an AO increases as the duration of CPB increases.

## Methods

### *Patient cohort*

This retrospective study was performed at Beijing Anzhen Hospital between December 2014 and June 2016 and was approved by Beijing Anzhen Hospital Ethics Committee (No. 2019030X). The Ethics Committee waived the need for

individual informed consent. All protocols conformed to the 1975 Declaration of Helsinki. The study was registered in the Chinese Clinical Trials Registry ([www.chictr.org.cn](http://www.chictr.org.cn), ChiCTR1900022289). All patients with ATAAD who underwent TAR with FET were enrolled. Data for baseline variables, perioperative factors, and postoperative outcomes were collected by trained staff from patients who were recruited at our medical centre.

### *Definitions*

The primary endpoint of our study was the appearance of an AO. An AO was defined as either 30-day mortality or postoperative stroke. Stroke was defined as the presence of a focal neurological deficit, regardless of a transient or permanent nature, and was confirmed as a new deficit by a computed tomography (CT) examination. We defined haemodynamic instability as  $\geq 30$  minutes of hypoperfusion (systolic blood pressure  $\leq 90$  mmHg requiring catecholamine administration). A preoperative neurological defect included disturbed consciousness, transient ischaemic attack, and syncope from onset to the operation.

### *Surgical techniques*

All operations were performed through median sternotomy. Briefly, this procedure was performed using right axillary artery cannulation for CPB and selective cerebral perfusion (5–10 mL/kg•minute) under moderate hypothermic circulatory arrest. Associated operations, such as mitral valve and aortic root replacement, were performed during cooling. The surgical technique of TAR with FET (i.e., the Sun operation) has been previously described.<sup>5,6</sup> This procedure involved implantation of an FET (MicroPort Medical Company Limited, Shanghai, China) in the descending aorta, followed by total arch replacement

with a four-branched prosthetic graft (Maquet Cardiovascular, Wayne, NJ, USA). Distal reperfusion was initiated upon completion of descending aortic anastomosis. The left carotid artery was initially reconstructed to achieve bilateral perfusion, the ascending aorta was then treated to prevent coronary ischaemia, and the innominate and subclavian arteries were finally treated.

### Statistical analysis

Categorical variables are presented as frequency (percentage). Continuous variables are presented as the mean  $\pm$  standard deviation or the median (interquartile range), as appropriate. To determine the causes of AO, univariable logistic regression analysis was used. Multivariable logistic regression was used to assess the relationship between the duration of CPB and an AO. Four models were constructed as follows: (I) not adjusted; (II) adjusted for sex and age; (III) adjusted for sex/age/body mass index (BMI)/diabetes mellitus/emergency surgery/prior cerebrovascular accident (CVA)/coronary artery disease/haemopericardium/preoperative neurological defect/preoperative haemodynamic instability/preoperative platelet count; and (IV) adjusted for sex/age/BMI/diabetes mellitus/emergency surgery/prior CVA/coronary artery disease/haemopericardium/preoperative neurological defect/preoperative haemodynamic instability/preoperative platelet count/concomitant coronary artery bypass grafting (CABG)/aortic cross-clamp duration/duration of circulatory arrest/lowest nasopharyngeal temperature ( $^{\circ}$ C)/intraoperative transfusion of packed red blood cells (PRBCs)/intraoperative transfusion of fresh-frozen plasma (FFP)/intraoperative transfusion of platelets. All protocols conformed to the Strengthening the Reporting of Observational Studies in Epidemiology statement.<sup>7</sup> The four models were analysed

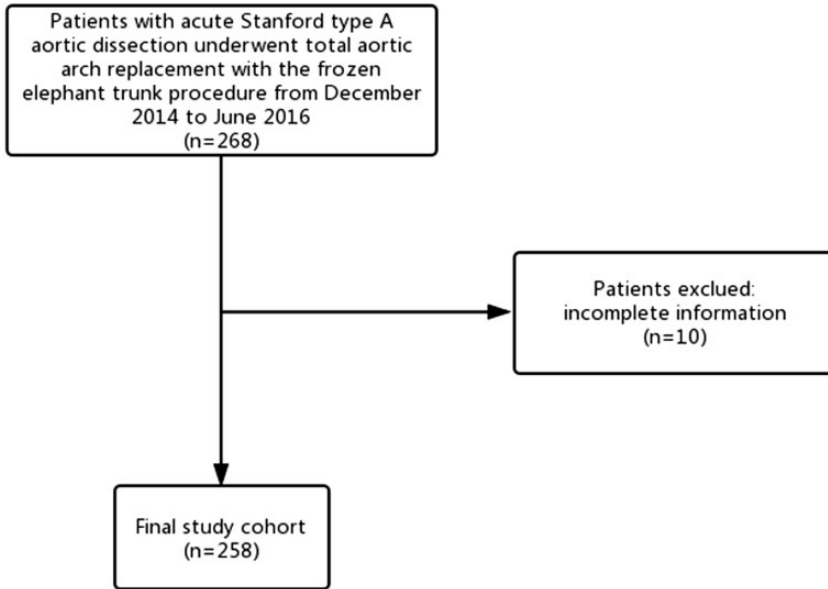
in parallel. Covariables were adjusted according to previous studies:<sup>8</sup> When variables were added, if the matched odds ratio (OR) changed by  $\geq 10\%$ , adjustments were performed. Generalized additive models were applied for identifying linear relationships. Stratified and interaction analyses were performed according to sex, age (aged younger or older than 48 years), BMI ( $<24$  kg/m<sup>2</sup>, 24–28 kg/m<sup>2</sup>, and  $>28$  kg/m<sup>2</sup>), smoking history, hypertension, haemopericardium, preoperative platelet count (higher or lower than  $162 \times 10^9$ /L), aortic cross-clamp duration (longer or shorter than 120 minutes), and duration of circulatory arrest (longer or shorter than 21 minutes).

The PS matching method was performed to adjust for intergroup differences between the non-AO and AO groups. PS was used for matching of variables (adjusted for age, sex, BMI, haemopericardium, preoperative haemodynamic instability, and preoperative platelet count). Matching was performed at a ratio of 1:1 using a greedy matching algorithm,<sup>9</sup> with a calliper width of 0.05 of the standard deviation of the logit. Patients' characteristics within two groups were compared using the paired McNemar test and t-test. Baseline covariates were assessed with standardized differences.

Data were analysed with the R package and Empower Stats (<http://www.empowerstats.com>, X&Y Solutions, Inc., Boston, MA, USA). All assessments were two-sided. *P* values  $<0.05$  were considered statistically significant.

## Results

From December 2014 to June 2016, 268 patients who underwent TAR with FET were eligible for the study. Ten patients were excluded because of incomplete information (final cohort: 258 patients). The screening procedure used in this study is outlined in Figure 1.



**Figure 1.** Flow chart of the patients.

### *Demographics and characteristics of the patients*

Patients had a mean age of  $47.9 \pm 10.6$  years and 196 (76.0%) participants were men. A history of hypertension was present in 181 (70.2%) patients. The Bentall procedure was carried out in 113 (43.8%) patients and ascending aortic replacement was performed in 145 (56.2%) patients. Twenty-eight concomitant procedures were performed in 102 (10.9%) patients, including CABG in 20 (9.4%), mitral valve replacement in 5 (1.9%), and aortic bypass surgery in 3 (1.2%). The overall incidence of AO was 13.6% (35 patients). The incidence of postoperative stroke was 9.3% (24 patients) and the overall operative mortality within 30 days was 10.1% (26 patients). Among the patients with postoperative stroke, the 30-day mortality rate was 60% (15 patients). All baseline characteristics are summarized in Table 1.

### *Univariable analysis*

Table 1 shows the results of univariable analysis. Preoperative haemodynamic instability, haemopericardium, aortic cross-clamp duration, preoperative platelet count, and duration of CPB were significantly associated with AO (all  $P < 0.05$ ). Coronary artery disease, BMI, smoking history, prior CVA, hypertension, diabetes mellitus, left ventricular ejection fraction, intraoperative transfusion of PRBCs, intraoperative transfusion of FFP, intraoperative transfusion of platelets, duration of circulatory arrest, and aortic root repair were not associated with an AO.

### *Effect of the duration of CPB on AO*

Multivariable logistic regression analysis models for AO are shown in Table 2. In model I, there was a significant association between the duration of CPB and AO

Table 1. Univariate analysis of risk factors associated with an AO.

Variable	Total (n = 258)	Non-AO (n = 223)	AO (n = 35)	OR (95% CI)	P value
Sex					
Men	196 (76.0)	167 (74.9)	29 (82.9)	1.0	
Women	62 (24.0)	56 (25.1)	6 (17.1)	1.62 (0.64–4.11)	0.309
Age, years	47.9 ± 10.6	47.6 ± 10.1	49.9 ± 13.6	1.02 (0.99–1.06)	0.249
BMI, kg/m <sup>2</sup>	26.1 ± 3.9	26.2 ± 3.6	25.5 ± 3.5	0.94 (0.85–1.05)	0.284
Hypertension	181 (70.2)	158 (70.9)	23 (65.7)	0.79 (0.37–1.68)	0.538
Diabetes mellitus	7 (2.7)	6 (2.7)	1 (2.9)	1.06 (0.12–9.11)	0.955
Coronary artery disease	5 (1.9)	4 (1.8)	1 (2.9)	1.61 (0.17–14.84)	0.674
Marfan syndrome	9 (3.5)	8 (3.6)	1 (2.9)	0.79 (0.10–6.52)	0.827
Smoking history	126 (48.8)	112 (50.2)	14 (40.0)	0.66 (0.32–1.36)	0.263
Prior CVA	9 (3.5)	8 (3.6)	1 (2.9)	0.79 (0.10–6.52)	0.827
Prior PCI	4 (1.5)	3 (1.4)	1 (2.9)	2.16 (0.22–21.34)	0.511
TEVAR history	9 (3.5)	9 (4.0)	0 (0)	<sup>a</sup>	1.0
LVEF, %	61.0 ± 2.7	61.0 ± 2.7	60.6 ± 2.5	0.94 (0.82–1.07)	0.363
Preoperative neurological defect	8 (3.1)	7 (3.1)	1 (2.9)	0.91 (0.11–7.61)	0.929
Preoperative Haemodynamic instability	13 (5.0)	7 (3.1)	6 (17.1)	6.38 (2.01–23.01)	0.002
Haemopericardium	41 (15.9)	29 (13.0)	12 (34.3)	3.49 (1.57–7.76)	0.002
Emergency	226 (87.6)	194 (87.0)	32 (91.4)	1.59 (0.46–5.54)	0.463
Preoperative platelet count (10 <sup>9</sup> /L)	162 (126–197)	165 (130.5–198)	130 (92.5–179.5)	0.99 (0.98–1.00)	0.011
Preoperative ALT (U/L)	21 (14–37)	21 (14.5–36.5)	23 (14–39.8)	1.00 (0.99–1.01)	0.812
Preoperative AST (U/L)	25 (19–34)	25 (19–34)	28.5 (21–38.5)	1.00 (1.00–1.01)	0.164
Aortic root repair					
Ascending aorta replacement	145 (56.2)	126 (56.5)	19 (54.3)	1.0	
Bentall procedure	113 (43.8)	97 (43.5)	16 (45.7)	1.09 (0.53–2.24)	0.806
Concomitant CABG	20 (7.8)	15 (6.7)	5 (14.3)	2.31 (0.78–6.82)	0.129
Concomitant MVR	5 (1.9)	4 (1.8)	1 (2.9)	1.61 (0.17–14.84)	0.674
Concomitant aortic bypass surgery	3 (1.2)	2 (0.9)	1 (2.9)	3.25 (0.29–36.82)	0.341
Lowest nasopharyngeal temperature (°C)	23.4 ± 1.3	23.4 ± 1.3	23.2 ± 1.5	0.90 (0.70–1.16)	0.423
CPB duration (minutes)	224.3 ± 58.7	218.6 ± 49.2	260.7 ± 93.2	1.01 (1.00–1.02)	0.001
Aortic cross-clamp duration (minutes)	124.6 ± 33.7	122.4 ± 31.2	138.9 ± 44.4	1.01 (1.00–1.02)	0.009

(continued)

**Table 1.** Continued.

Variable	Total (n = 258)	Non-AO (n = 223)	AO (n = 35)	OR (95% CI)	P value
Circulatory arrest duration (minutes)	22.2 ± 6.6	22.2 ± 6.6	22.2 ± 6.9	1.00 (0.95–1.06)	0.991
Intraoperative transfusion of PRBCs	166 (64.3)	143 (64.1)	23 (65.7)	1.07 (0.51–2.27)	0.855
Intraoperative transfusion of FFP	185 (71.7)	161 (72.2)	24 (68.6)	0.84 (0.39–1.82)	0.658
Intraoperative transfusion of platelets	46 (17.8)	42 (18.8)	4 (11.4)	0.56 (0.19–1.66)	0.293

Continuous data are presented as the mean ± standard deviation or median (interquartile range), and categorical data as number (%).

<sup>a</sup>No result because of the small sample size.

AO, adverse outcome; OR, odds ratio; CI, confidence interval; BMI, body mass index; CVA, cerebrovascular accident; PCI, percutaneous transluminal coronary intervention; TEVAR, thoracic endovascular aortic repair; LVEF, left ventricular ejection fraction; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CABG, coronary artery bypass grafting; MVR, mitral valve replacement; CPB, cardiopulmonary bypass; PRBCs, packed red blood cells; FFP, fresh-frozen plasma.

**Table 2.** Multivariable analysis of the independent effect of the duration of CPB on an adverse outcome in patients with acute type A aortic dissection using a model with no adjustment and fully adjusted logistic regression models.

Variable	Model I		Model II		Model III		Model IV	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
CPB (min/10)	1.098 (1.041–1.158)	0.001	1.095 (1.038–1.156)	0.001	1.091 (1.024–1.163)	0.001	1.101 (1.003–1.208)	0.042

Model I: unadjusted.

Model II: adjusted for age and sex.

Model III: adjusted for age, sex, body mass index, diabetes mellitus, emergency surgery, stroke history, coronary artery disease, haemopericardium, preoperative neurological defect, preoperative haemodynamic instability, and preoperative platelet count.

Model IV: adjusted for age, sex, body mass index, diabetes mellitus, emergency surgery, stroke history, coronary artery disease, haemopericardium, preoperative neurological defect, preoperative haemodynamic instability, preoperative platelet count, concomitant coronary artery bypass grafting, aortic cross-clamp duration, duration of circulatory arrest, nasopharyngeal temperature (°C) at circulatory arrest, intraoperative transfusion of packed red blood cells, intraoperative transfusion of fresh-frozen plasma, and intraoperative transfusion of platelets.

CPB, cardiopulmonary bypass; OR, odds ratio; CI, confidence interval; min/10, 10-minute extension in the CPB procedure.

(OR 1.098, 95% confidence interval [CI] 1.041–1.158;  $P=0.001$ ). In model II, the relationship between the duration of CPB and AO remained unchanged (OR 1.095, 95% CI 1.038–1.156;  $P=0.001$ ). In model III, patients with a longer duration of CPB still had a higher incidence of an AO (OR 1.091, 95% CI 1.024–1.163;  $P=0.001$ ). To avoid a large deviation result caused by the relatively small sample size, we added some further covariates to form model IV. In model IV, the results remained significant (OR 1.101, 95% CI 1.003–1.208;  $P=0.042$ ). A 10-minute extension in the CPB procedure increased the risk of an AO by 10.1%.

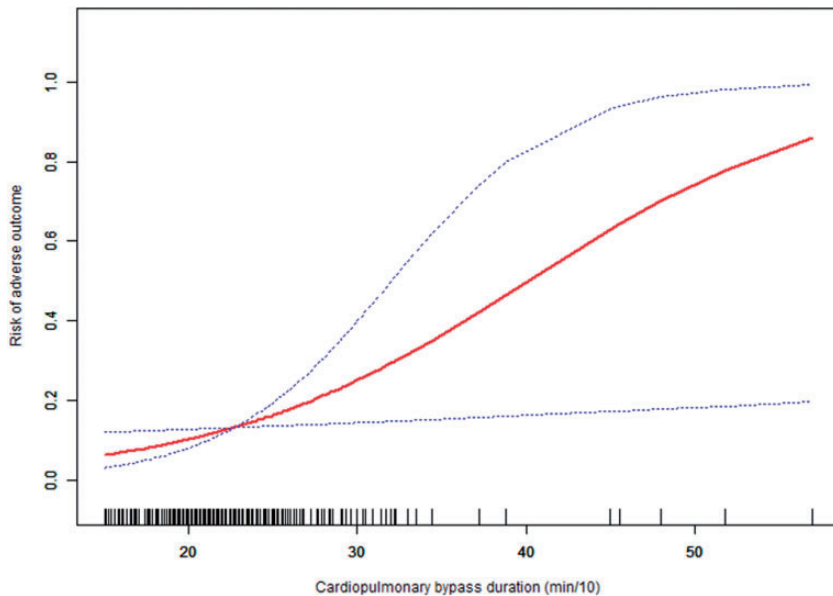
### Linear relationship between the duration of CPB and AO

We used spline smoothing via generalized additive models to define the association

between the duration of CPB and AO after adjusting for sex, age, BMI, diabetes mellitus, emergency surgery, prior CVA, coronary artery disease, haemopericardium, preoperative neurological defect, preoperative haemodynamic instability, preoperative platelet count, concomitant CABG, aortic cross-clamp duration, duration of circulatory arrest, the lowest nasopharyngeal temperature ( $^{\circ}\text{C}$ ), intraoperative transfusion of PRBCs, intraoperative transfusion of FFP, and intraoperative transfusion of platelets. Figure 2 shows that there was a linear association between the duration of CPB and AO.

### Stratified analysis

We performed stratified analyses including sex, age, BMI, preoperative platelet count, aortic cross-clamp duration, duration of



**Figure 2.** Linear relationship between the duration of cardiopulmonary bypass and an adverse outcome. This relationship was adjusted for age, sex, body mass index, diabetes mellitus, emergency surgery, stroke history, coronary artery disease, haemopericardium, preoperative neurological defect, preoperative haemodynamic instability, preoperative platelet count, concomitant coronary artery bypass grafting, aortic cross-clamp duration, duration of circulatory arrest, nasopharyngeal temperature ( $^{\circ}\text{C}$ ) at circulatory arrest, intraoperative transfusion of packed red blood cells, intraoperative transfusion of fresh-frozen plasma, and intraoperative transfusion of platelets. The red solid line shows the fitting spline. The blue dashed lines show the 95% confidence interval.

circulatory arrest, hypertension, smoking history, and haemopericardium. In these analyses, the duration of CPB remained an independent predictor of postoperative AO in the high-risk subgroups. None of those sub-groups showed an interaction with AO. The details of these results are shown in Figure 3.

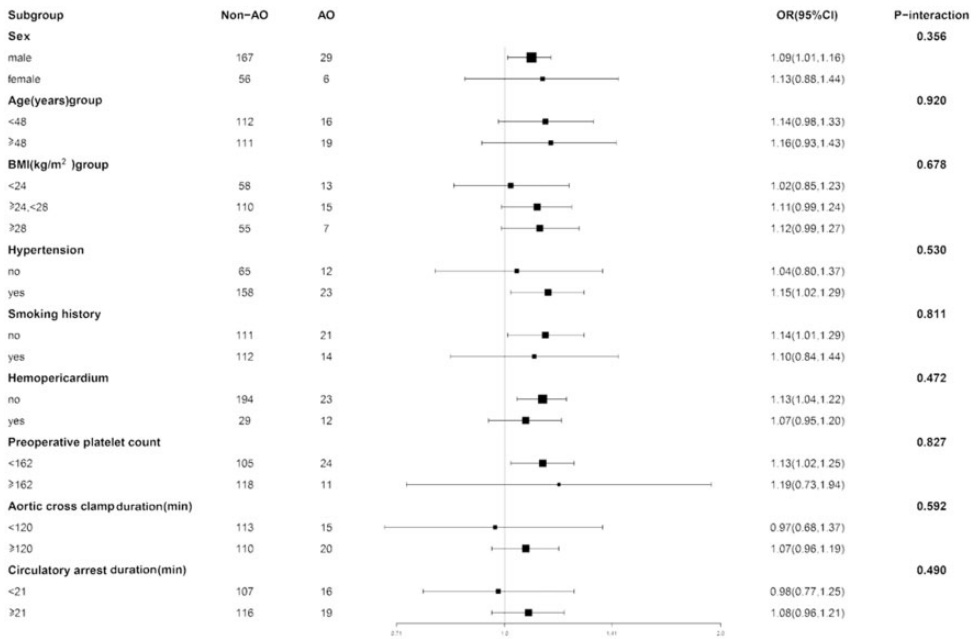
**Characteristics of PS matching**

Derived PS values were used to match 35 patients in the AO group with patients in the non-AO group to reduce the effect of confounding factors (Figure 4). Finally, 33 matched pairs were created (Table 3). AO and the duration of CPB remained

significantly associated (OR 1.178, 95% CI 1.032–1.345;  $P=0.015$ ).

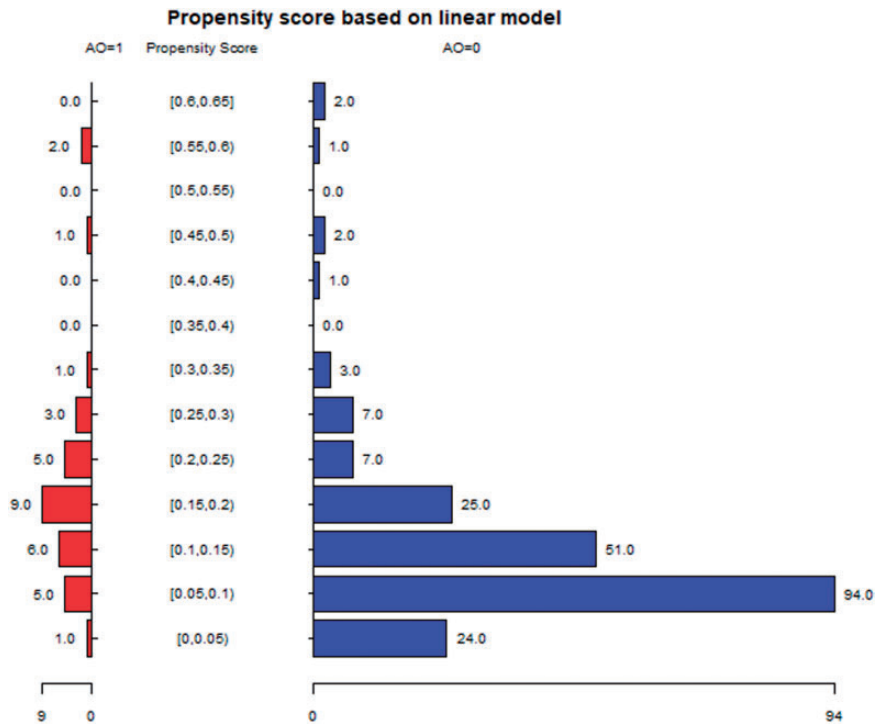
**Discussion**

In this retrospective study, data from 258 patients with ATAAD who underwent TAR with FET were analysed. There was a strong correlation between the duration of CPB and AO, even after adjustment for other risk factors. A 10-minute extension in the CPB procedure increased the risk of AO by 10.1%. Moreover, although age, sex, BMI, preoperative platelet count, preoperative haemodynamic instability, and haemopericardium were adjusted by PS, the duration of CPB remained an



**Figure 3.** Subgroup analysis of the association between the duration of cardiopulmonary bypass and an AO in patients with acute type A aortic dissection. Each stratification was adjusted for all of the factors (age, sex, BMI, diabetes mellitus, emergency surgery, stroke history, coronary artery disease, haemopericardium, preoperative neurological defect, preoperative haemodynamic instability, preoperative platelet count, concomitant coronary artery bypass grafting, aortic cross-clamp duration, duration of circulatory arrest, nasopharyngeal temperature (°C) at circulatory arrest, intraoperative transfusion of packed red blood cells, intraoperative transfusion of fresh-frozen plasma, and intraoperative transfusion of platelets), except for the stratification factor itself. AO, adverse outcome; OR, odds ratio; CI, confidence interval; BMI, body mass index.





**Figure 4.** Propensity score matching map.

Matching variables: age, sex, body mass index, preoperative platelet count, preoperative haemodynamic instability, and haemopericardium. AO, adverse outcome.

**Table 3.** Characteristics of the patients at baseline after propensity score matching.

Variable	Non-AO	AO	Std diff	P value
Age, years	49.7 ± 9.3	49.1 ± 13.5	0.047	0.849
Sex			0.000	1.000
Men	28 (84.8)	28 (84.8)		
Women	5 (15.2)	5 (15.2)		
BMI, kg/m <sup>2</sup>	25.1 ± 3.0	25.4 ± 3.6	0.084	0.734
Preoperative platelet count	139.6 ± 45.2	140.5 ± 76.4	0.014	0.954
Preoperative haemodynamic instability	4 (12.1)	6 (18.2)	0.167	0.731
Haemopericardium	13 (39.4)	11 (33.3)	0.126	0.798
CPB duration (min/10)	21.7 ± 4.1	26.8 ± 9.1	0.721	0.005

For continuous variables, data are presented as the mean ± standard deviation. For categorical variables, data are presented as number (%).

Matching variables: age, sex, BMI, preoperative PLT, preoperative haemodynamic instability, and haemopericardium; AO, adverse outcome; Std diff, standardized difference; BMI, body mass index; CPB, cardiopulmonary bypass.

independent predictor of an AO, which confirmed an association between the duration of CPB and AO.

Postoperative stroke often leads to a low quality of life and early mortality.<sup>10,11</sup> As previously described,<sup>12,13</sup> we defined an AO as stroke or 30-day mortality to increase the sensitivity of risk factors. Similar studies have been performed in patients who had aortic surgery. Ehrlich and colleagues<sup>12</sup> analysed patients who underwent ATAAD repair under deep hypothermic circulatory arrest and found that only preoperative haemodynamic instability was associated with postoperative AO (OR 6.0, 95% CI 2.7–13.4;  $P < 0.0001$ ). No other alterations in patients' characteristics were observed, most likely due to confounding factors in their cohort. A retrospective study by Liu and co-workers<sup>14</sup> identified variables that were associated with an AO after adjustment for other risk factors, including stroke (OR 7.846, 95% CI 2.737–22.489;  $P < 0.001$ ), emergency surgery (OR 2.198, 95% CI 1.019–4.740;  $P = 0.045$ ), PRBCs (OR 1.113, 95% CI 1.038–1.193;  $P = 0.003$ ), concomitant CABG (OR 2.613, 95% CI 1.066–6.405;  $P = 0.036$ ), and CPB time (minutes) (OR 1.009, 95% CI 1.004–1.014;  $P < 0.001$ ). Preventza and colleagues<sup>15</sup> reported that CPB time (minutes) was a significant risk factor for AO (OR 1.01, 95% CI 1.00–1.01;  $P < 0.001$ ). Nakamura and co-workers<sup>16</sup> analysed 119 patients who underwent surgical treatment for aortic disease and found that the duration of CPB was an independent risk factor for an AO. In our centre, Ma and colleagues<sup>17</sup> analysed 803 patients with ATAAD in whom a duration of CPB  $> 180$  minutes was a risk factor for intraoperative mortality, which is consistent with other studies.<sup>18,19</sup> Relatively long CPB times may be due to technical difficulties, dissection-related complications, or the conduct of inexperienced surgeons.

The mechanisms underlying the association between the duration of CPB and AO remain unknown. The disadvantage of CPB is its association with respiratory failure, myocardial, renal, and neurological dysfunction, and eventual organ failure.<sup>3,20</sup> Various measures to reduce damage from CPB to the body have been used over the past decades and have dramatically improved patients' survival and reduced the incidence of other systemic complications. However, the incidence of complications related to the nervous system has remained consistent. The mechanism of brain injury after CPB is complex with major causes that include cerebral emboli (gas, liquid, or solid), cerebral ischaemic injury (e.g., vascular embolism, hypoperfusion, and hypoxia), and inflammatory responses.<sup>3,21</sup> During CPB, stimulation by surgical trauma, blood contact with foreign bodies, body endotoxins, and a low temperature activate non-infectious systemic inflammatory response syndromes.<sup>4</sup> Therefore, a large number of inflammatory cytokines enter the brain, leading to brain damage.

We believe that this is the largest study to assess the effects of the duration of CPB on AO in patients undergoing TAR with FET for ATAAD in Asia. Our cohort differed from studies in other European countries because the mean age of the patients was 48 years, which is lower than that reported in the International Registry of Acute Aortic Dissection.<sup>22</sup> These differences may be due to the frequent aetiology of hypertension. The incidence of hypertension is high in China.<sup>23</sup> However, awareness and control rates are inadequate, resulting in severe complications, such as aortic dissection, which threatens the lives of relatively young patients. The incidence rates of diabetes mellitus and coronary heart disease were also lower in our study than in studies performed in European countries.<sup>12,19,22</sup> Although several studies have shown that

an emergency aortic operation is associated with a high mortality,<sup>14,24,25</sup> it was not a predictor in this study. Because many patients die in ATAAD, emergency surgery benefits more patients than conservative treatment does. The duration of circulatory arrest was also not associated with an AO in our study, which indicated that a lack of cerebral protection did not contribute to development of an AO. Additionally, selective cerebral perfusion significantly extended the safe arch intervention time and increased brain tissue tolerance. This result is consistent with the observations of previous authors.<sup>11,26</sup>

Our clinical results were satisfactory, with a 30-day mortality rate of 10.8% and a stroke rate of 9.3%, which are better than those in other studies.<sup>12,13</sup> Ehrlich and colleagues<sup>12</sup> reported an incidence of AO following ATAAD surgery of 30.5%, which is much higher than the incidence found in this study. These differences between studies are most likely due to the young age of the patients in our cohort and the extensive experience of surgeons who performed the procedures. Studies have shown that advanced age is an independent risk factor for death or neurological outcomes.<sup>18,19</sup> Additionally, the inclusion of a low-risk cohort may explain the low AO rate obtained in this study. A portion of our patients were diagnosed at peripheral or primary hospitals and died of malperfusion, tamponade, or aortic rupture during long-distance transfer. Additionally, some patients or their family members refused an operation owing to a relatively high risk or any other reasons. Thirty-day mortality rates of up to 16.4% and postoperative stroke rates were previously reported in 122 patients with ATAAD.<sup>13</sup> Another study reported a stroke incidence rate of 13% and an intraoperative mortality rate of 17% in 7353 patients following ATAAD repair.<sup>27</sup> In those patients, TAR was associated with a higher risk of stroke than was

associated with the hemi-arch technique. Considering that our patients underwent TAR with FET as a result of ATAAD, the incidence of an AO (13.6%) in our population is acceptable.

There are several ways to shorten the duration of CPB and lower the AO rate. First, we have started to attempt performing surgery at mild hypothermia (28°C or higher), which results in less cooling time and rewarming time. Second, we have been adding more monitoring devices in operations to lower the occurrence of brain malperfusion, such as using transcranial Doppler to detect cerebral blood flow velocity and near-infrared spectroscopy to monitor cerebral oxygen saturation. Additionally, we are striving to set up aortic surgical training centres across China, so that patients will not have to travel such a long distance to receive appropriate surgical management with a relatively short duration of CPB.

### *Strengths and limitations*

This study has several strengths. All operations were performed in the same centre and the study groups were comparable. This study also has some limitations. Because of the retrospective nature of the study, we identified associations as opposed to causalities for all of the evaluated relationships. Second, in our centre, TAR with FET is the method of choice for ATAAD, but this may not be the case in other centres. Therefore, this may have led to discrepancies in outcomes. Third, the mean age of patients was much younger compared with that in Western series.<sup>22</sup> Finally, long-term outcomes were lacking, and therefore, further investigations are required.

### **Conclusions**

This study shows that the duration of CPB is an independent predictor of AO in patients undergoing TAR with FET for

ATAAD. Understanding the molecular mechanism of this association is critical for improving early diagnosis and preventing disease.

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### Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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