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

Acute type A aortic dissection (ATAAD) is a life-threatening condition that requires surgical intervention. This study investigated the relationship between cardiopulmonary bypass (CPB) duration and stroke or early death in ATAAD patients receiving total aortic arch replacement with the frozen elephant trunk procedure (TAR with FET).

Methods

A retrospective cohort study was conducted at the Beijing Anzhen Hospital from December 2014 to June 2016. Patients receiving TAR with FET for ATAAD were included. CPB duration was recorded during the operation. Adverse outcome (AO) was defined as 30-day mortality or stroke. In total, 258 consecutive patients were ultimately analysed. In addition, as the primary outcome, AO was compared using propensity-matched scoring (PS).

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 ± 10.6 years old and were predominantly male (76.0%). The average CPB duration was 224.3 ± 58.7 min. The duration of CPB was an independent predictor of AO occurrence after adjusting for confounding factors through multivariable logistic regression analysis (OR 1.101, 95% CI 1.003–1.208; P = 0.042). After PS matching, 33 matched pairs were created. In the matched analysis, CPB duration remained an AO risk factor (OR 1.178, 95% CI 1.032–1.345; P = 0.015).

Conclusions

CPB duration is an independent predictor of adverse outcome in surgical repair for ATAAD. The underlying mechanisms of this association are key for the development of improved prevention strategies.

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 [1, 2]. The occurrence of stroke after ATAAD leads to higher mortality rates, increased hospital stays, and reduced long-term survival. Adverse outcome (AO) was defined as either early death or stroke since a successful operation should result not only in survival but also in good quality of life. Identifying risk factors and preventing AO following complex aortic arch procedures are necessary to improve outcomes.

Cardiopulmonary bypass (CPB) is an indispensable procedure for the surgical treatment of ATAAD. CPB can, however, induce oxidative stress reactions and systemic inflammation, leading to multi-organ failure. Little is known about the influence of CPB duration on AO in ATAAD patients. This study used multivariable logistic regression models and propensity score (PS) matching method to explore the correlation between AO and the duration of CPB in ATAAD patients who underwent total aortic arch replacement with the frozen elephant trunk procedure (TAR with FET). Our hypothesis was that the risk of AO would increase as CPB duration increased.

Materials And Methods

Patients

This retrospective study was performed at the Beijing Anzhen Hospital between December 2014 and June 2016 and was approved by our Ethics Committee (2019030X). The Ethics Committee waived the need for individual informed consent. All protocols conformed to the 1975 Declaration of Helsinki. All patients with ATAAD who underwent TAR with FET were enrolled. Ten patients lacked complete information and were excluded. In total, 258 consecutive patients were included. Data for baseline variables, peri-operative factors and postoperative outcomes were collected by trained staff for the patients recruited at our medical centre.

Definitions

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

Surgical technique

All operations were performed through a median sternotomy. Briefly, this procedure is performed using right axillary artery cannulation for CPB and selective cerebral perfusion (SCP) [5–10 mL/(kg•min)] under moderate hypothermic circulatory arrest (MHCA). 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 [3, 4]. The procedure involves the 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). Distal reperfusion was initiated upon the 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 treated last.

Statistical analysis

Categorical variables are presented as frequency (percentage); continuous variables are presented as the mean ± standard deviation (SD) or the median (interquartile range, IQR), as appropriate. To determine the causes of AO, univariable logistic regression analysis was used. Multivariable logistic regression was used to assess the relationship between CPB duration and AO. Four models were constructed: (I) not adjusted; (II) sex and age adjusted; (III) sex/ age/ BMI/ diabetes mellitus/ emergency surgery/ prior cerebrovascular accident (CVA)/ coronary artery disease/ haemopericardium/ preoperative neurological defect/ preoperative haemodynamic instability/ preoperative platelet count adjusted; and (IV) 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/ circulatory arrest duration/ lowest nasopharyngeal temperature (°C)/ intraoperative transfusion of packed red blood cells (PRBCs)/ intraoperative transfusion of fresh-frozen plasma (FFP)/ intraoperative transfusion of platelets adjusted. All protocols conformed to the Strengthening the Reporting of Observational Studies in Epidemiology statement [5]. The four models were analysed in parallel. Covariables were adjusted according to previous studies [6]: When variables were added, if the matched odds ratio changed by ≥ 10%, adjustments were performed. Generalized additive models (GAMs) were applied for the identification of linear relationships. Stratified and interaction analyses were performed according to sex, age (aged younger or older than 48 years old), BMI (≤ 24 kg/m^2, 24–28 kg/m^2, ≥ 28 kg/m^2), smoking history, hypertension, haemopericardium, preoperative platelet count (higher or lower than 162), aortic cross clamp duration (longer or shorter than 120 min) and circulatory arrest duration (longer or shorter than 21 min). The PS matching method was performed to adjust intergroup differences between non-AO and AO groups. For variable matching, PS was employed (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 [7] with a calliper width of 0.05 of the SD of the logit. Patient characteristics within two groups were compared using paired McNemar's and t-tests. Baseline covariants 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). All assessments were 2-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. Ten patients were excluded for incomplete information (final cohort: 258 patients). The screening procedure used in this study is outlined in Fig. 1.

Demographics

Patients were aged 47.9 ± 10.6 years old, and 196 (76.0%) participants were males. A history of cerebrovascular accident was present in 3.5% of the patients; 1.9% had coronary artery disease, and 3.5% had Marfan syndrome. History of hypertension was present in 181 of the patients (70.2%). Preoperative neurological defect was found in only 8 of the patients (3.1%), and preoperative haemodynamic instability was present in 13 of the patients (5.0%). Severe haemopericardium was documented in 15.6% of the patients. The Bentall procedure was carried out in 113 of the patients (43.8%), and ascending aorta replacement was performed in 145 of the patients (56.2%). In total, 28 concomitant procedures were performed in 102 patients (10.9%), including coronary artery bypass grafting in 20 (9.4%), mitral valve replacement in 5 (1.9%), and aortic bypass surgery in 3 (1.2%). The average CPB duration was 224.3 ± 58.7 min. The overall AO incidence 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.

Table 1
Univariate analysis of risk factors associated with AO.

Variable	Total (n = 258)	Non-AO (n = 223)	AO (n = 35)	OR(95%CI)	*P*-value
Sex					
male	196 (76.0)	167 (74.9)	29 (82.9)	1.0	
female	62 (24.0)	56 (25.1)	6 (17.1)	1.62 (0.64–4.11)	0.309
Age	47.9 ± 10.6	47.6 ± 10.1	49.9 ± 13.6	1.02 (0.99–1.06)	0.249
BMI	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%)	a	1.0
LVEF(%)	61.0 ± 2.7	61.0 ± 2.7	60.6 ± 2.5	0.94 (0.82–1.07)	0.363

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

Abbreviations: AO, adverse outcome; OR, odd ratio; 95% CI, 95% 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.

[a]The result failed because of the small sample size

Variable	Total (n = 258)	Non-AO (n = 223)	AO (n = 35)	OR(95%CI)	*P*-value
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 (10^9/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

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

Abbreviations: AO, adverse outcome; OR, odd ratio; 95% CI, 95% 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.

[a]The result failed because of the small sample size

Variable	Total (n = 258)	Non-AO (n = 223)	AO (n = 35)	OR(95%CI)	P-value
CPB duration(min)	224.3 ± 58.7	218.6 ± 49.2	260.7 ± 93.2	1.10 (1.04–1.16)	0.001
Aortic cross clamp duration (min)	124.6 ± 33.7	122.4 ± 31.2	138.9 ± 44.4	1.01 (1.00-1.02)	0.009
Circulatory arrest duration (min)	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(percentage).					
Abbreviations: AO, adverse outcome; OR, odd ratio; 95% CI, 95% 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.					
[a]The result failed because of the small sample size					

Univariable analysis

Table 1 reveals the results of the univariable analyses. Preoperative haemodynamic instability, haemopericardium, aortic cross clamp duration, preoperative platelet count, and CPB duration were correlated with AO. 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, circulatory arrest duration and aortic root repair were not associated with AO.

Influence of CPB duration on AO

The multivariable logistic regression analysis models for AO are shown in Table 2. In model I, there was a significant correlation between CPB duration and AO [odds ratio (OR) 1.098, 95% CI 1.041–1.158; P = 0.001]. In model II (adjusted for age and sex), the relationship between CPB duration and AO remained unchanged (OR 1.095, 95% CI 1.038–1.156; P = 0.001). When adjusted for age, sex, BMI, diabetes mellitus, emergency surgery, prior CVA, coronary artery disease, haemopericardium, preoperative neurological defect, preoperative haemodynamic instability, and preoperative platelet count, patients with longer CPB durations still had a higher AO incidence (OR 1.091, 95% CI 1.024–1.163; $P = 0.001$). In order to avoid the result deviation caused by the relatively small sample size, etc., We add some covariates mentioned by other documents to form Model IV. In model 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 CABG, aortic cross clamp duration, circulatory arrest duration, lowest nasopharyngeal temperature (°C), intraoperative transfusion of PRBCs, intraoperative transfusion of FFP, intraoperative transfusion of platelets), the results remained significant (OR 1.101, 95% CI 1.003–1.208; $P = 0.042$).

Table 2
Multivariable analysis to assess the independent impact of CPB duration on AO in patients with ATAAD using none adjusted and fully adjusted logistic regression model.

Variable	Model I OR (95% CI)	*P*-value	Model II OR (95% CI)	*P*-value	Model III OR (95% CI)	*P*-value	Model IV 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

Abbreviations: CPB, cardiopulmonary bypass; AO, adverse outcome; ATAAD, acute type A aortic dissection; OR, odd ratio; 95% CI, 95% confidence interval.

Model I: unadjusted.

Model II: adjusted for age and sex.

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

Linear relationship between CPB duration and AO

We used spline smoothing via GAMs to define the association between CPB duration 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, circulatory arrest duration, lowest nasopharyngeal temperature (°C), intraoperative transfusion of PRBCs, intraoperative transfusion of FFP, intraoperative transfusion of platelets. Figure 2. shows that there was a linear association between CPB duration and AO.

Stratified analysis

We performed stratified analyses according to sex, age, BMI, preoperative platelet counts, aortic cross clamp duration, circulatory arrest duration, hypertension, smoking history, and haemopericardium. In these analyses, CPB duration remained an independent predictor of postoperative AO in the high-risk subgroups. In addition, none of those groups showed an interaction with AO. The details of these results are summarized in Fig. 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 influence of confounding factors (Fig. 4). Finally, 33 matched pairs were created (Table 3). AO and CPB duration remained significantly associated (OR 1.178, 95% CI 1.032–1.345; $P = 0.015$) (Table 4).

Table 3
Characteristics of the study patients at baseline after PS matching.

Variable	**Non-AO**	**AO**	**Std diff**	***P*-value**
Age	49.7 ± 9.3	49.1 ± 13.5	0.047	0.849
Sex			0.000	1.000
male	28 (84.8)	28 (84.8)		
female	5 (15.2)	5 (15.2)		
BMI	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, Standardized difference = abs (Mean1-Mean0)/sqrt((S1 ± S2)/2).				
For categorical variables: Data are presented as the number(percentage), Standardized difference = abs(P1-P0)/sqrt((P1*(1-P1) ± P0*(1-P0))/2).				
Matching variable: age, sex, BMI, preoperative PLT, preoperative haemodynamic instability, haemopericardium.				
Abbreviations: PS, propensity score; AO, adverse outcome; BMI, body mass index; CPB duration, cardiopulmonary bypass time.				

Table 4
Multivariable analysis to assess the independent impact of CPB duration on AO in patients with ATAAD after PS matching.

Variable	PSM OR (95%CI)	*P*-value
CPB duration (min/10)	1.178 (1.032, 1.345)	0.015
Abbreviations: CPB, cardiopulmonary bypass; AO, adverse outcome; ATAAD, acute type A aortic dissection; BMI, body mass index; PS, propensity score; OR, odd ratio; 95% CI, 95% confidence interval.		
Matching variable: age, sex, BMI, preoperative platelet count, preoperative haemodynamic instability, haemopericardium.		
Adjust for: PP. SCORE		

Discussion

In this retrospective study, data from 258 ATAAD patients 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 (OR 1.101, 95% CI 1.003–1.208; P = 0.042). In total, a 10-min 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, CPB duration remained an independent predictor of AO, confirming an association between CPB duration and AO.

Postoperative stroke often leads to a low quality of life and early mortality [8, 9]. As previously described [10, 11], we defined AO as stroke or 30-day mortality to increase the sensitivity of risk factors. Similar studies have been performed in aortic surgery patients. Ehrlich and colleagues [10] analysed patients who underwent ATAAD repair under deep HCA 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 patient characteristics were observed, most likely due to confounding factors in the cohort. Retrospective studies by Liu and co-workers [12] identified variables that were associated with 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 (min) (OR 1.009, 95% CI 1.004–1.014; $P <$ 0.001). Preventza and colleagues [13] reported that CPB time (min) was a significant risk factor for AO (OR 1.01, 95% CI 1.00-1.01; $P < 0.001$). Nakamura and co-workers [14] analysed 119 patients who underwent surgical treatment for aortic disease and found that CPB duration was an independent risk factor for AO. In our centre, Ma and colleagues [15] analysed 803 ATAAD patients in which CPB duration > 180 min was a risk factor for intraoperative mortality, consistent with previous studies [16, 17]. Relatively long CPB times may be due to technical difficulties, dissection-related complications, or the conduct of inexperienced surgeons.

The mechanisms underlying the correlation between CPB duration and AO remain unknown. The disadvantage of CPB is its known association with respiratory failure, myocardial, renal and neurological dysfunction and eventual organ failure [18, 19]. Various measures to reduce CPB damage to the body have been employed over the past decades and have dramatically improved patient 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 including cerebral emboli (gas, liquid, or solid), cerebral ischaemic injury (such as vascular embolism, hypo perfusion, and hypoxia), and inflammatory responses [19, 20]. During CPB, stimulation by surgical trauma, blood contact with foreign bodies, body endotoxins, and a low temperature activate non-infectious systemic inflammatory response syndromes [21]. Thus, 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 CPB duration on AO in patients undergoing TAR with FET for ATAAD in Asia. Our cohort differed from those studies in other European countries as the mean patient age of 48 years old was lower than that reported in the International Registry of Acute Aortic Dissection [22]. These differences may be due to the frequent etiology of hypertension. The incidence of hypertension is very high in China [23]; however, awareness and control rates are inadequate, resulting in severe complications, such as aortic dissection threatening the lives of relatively young patients. The incidence rates of diabetes mellitus and coronary heart disease were also lower in this study than in studies performed in European countries [10, 17, 22]. Although several studies have shown that emergency aortic operation is associated with high mortality [12, 24, 25], it was not a predictor in this study. Because many patients die in the acute phase of type A aortic dissection, emergency surgery benefits more patients than conservative treatment does. Circulatory arrest duration was also not associated with AO in this study, indicating that a lack of cerebral protection did not contribute to AO development. In addition, SCP significantly extended the safe arch intervention time and increased brain tissue tolerance. This result was consistent with the observations of previous authors [9, 26].

Our clinical results were satisfactory, with a 30-day mortality rate of 10.8% and a stroke rate of 9.3%, showing improvement compared to other studies [10, 11]. Ehrlich and colleagues [10] reported an AO incidence following ATAAD surgery of 30.5%, which was much higher than the incidence this study. These differences are most likely due to the young ages of the patients in our cohort and the extensive experience of surgeons who performed the procedures. Studies have revealed that advanced age is an independent risk factor for death or neurological outcomes [16, 17]. In addition, 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 mal-perfusion, tamponade, or aortic rupture during long-distance transfer. In addition, some patients or their family members refused operation due to a relative high risk or any other reasons. Thirty-day mortality rates of up to 16.4% and postoperative stroke rates were previously reported in 122 ATAAD patients [11]. Another study reported a stroke incidence rate of 13% and an intraoperative mortality rate of 17% in 7353 patients following ATAAD repair. In those patients, TAR was associated with a higher risk of stroke than was associated with the hemi-arch technique [27]. Considering that our patients underwent TAR with FET as a result of ATAAD, the AO incidence (13.6%) in our population was acceptable.

This study has several strengths. All operations were performed in the same centre, and the study groups were comparable. The identification of the duration of CPB as a risk factor for AO could improve intraoperative management strategies, including the development of surgical techniques and efforts to minimize CPB time to reduce the risk of surgery. First, we have started to try to do surgery at mild hypothermia (28 °C or higher), which results in less cooling time and rewarming time. Second, we add 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 monitoring cerebral oxygen saturation. In addition, 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 within a relatively shorten CPB duration.

Limitations

This study has some limitations. Due to the retrospective nature of the study, we identified associations as opposed to causalities for all 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, and this may lead to discrepancies in outcomes. Third, the average age of patients was much younger compared to Western series. Finally, long-term outcomes were lacking, and further investigations are therefore required.

Conclusions

We identified the duration of CPB as an independent predictor of AO in patients undergoing TAR with FET for ATAAD. Understanding the molecular mechanism governing this association is critical for the improvement of early diagnosis and disease prevention.

List of abbreviations

Acute type A aortic dissection, ATAAD; Adverse outcome, AO; Cardiopulmonary bypass, CPB; propensity score, PS; total aortic arch replacement with the frozen elephant trunk procedure, TAR with FET; computed tomography, CT; selective cerebral perfusion, SCP; moderate hypothermic circulatory arrest, MHCA; standard deviation, SD; interquartile range, IQR; prior cerebrovascular accident, CVA; coronary artery bypass grafting, CABG; packed red blood cells, PRBCs; fresh-frozen plasma, FFP; generalized additive models, GAMs.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the ethics committee at Anzhen Hospital (Institutional Review Board File 2019030X), and all experimental methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Consent was obtained from the patients or their relatives.

Availability of data and materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Competing interests

The authors have declared that no interest.

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Authors' contributions

(I) Conception and design: K Zhang, X Pan, L Sun; (II) Administrative support: L Sun; (III) Provision of study materials or patients: L Sun; (IV) Collection and assembly of data: K Zhang, X Pan, S Dong, K Zhu; (V) Data analysis and interpretation: K Zhang, X Pan, S Dong; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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