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Original Article

Application of Aortic Balloon Occlusion in Total Aortic Arch Replacement with Frozen Elephant Trunk on Clinical Endpoints for Aortic Dissection Patients

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Purpose: Total aortic arch replacement (TAR) with frozen elephant trunk (FET) is the standard operation for treating aortic dissection (AD) patients involving aortic arch with high operative risk due to long circulatory arrest (CA). We used aortic balloon occlusion technique that safely reduced the CA time to 5 min in average and investigated whether it can improve the clinical endpoints.
Methods: All patients diagnosed with AD and underwent TAR with FET operation (123 with aortic balloon occlusion and 221 with conventional method) in Fuwai Hospital during August 2017 and February 2019 was reviewed in this retrospective observational study.
Results: After propensity score matching, the 30-day mortality of aortic balloon occlusion group and conventional group was 4.88% and 11.38% (*P* = 0.062), respectively. In multivariate analysis, aortic balloon occlusion is one of the factors that reduced the risk for renal and hepatic injury, shortened postoperative conscious revival time, and reduced red blood cell (RBC) transfusion during operation.
Conclusions: The aortic balloon occlusion technique, as a perfusion strategy during operation, could alleviate postoperative complication. This method deserves further attention in future clinical practice for its value in treating patients with higher operative risks.

Keywords: total aortic arch replacement, frozen elephant trunk, aortic dissection, hypothermic circulatory arrest, aortic balloon occlusion

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Introduction

Total aortic arch replacement (TAR) with frozen elephant trunk (FET) is a surgical technique that facilitates extensive repair of complex aortic arch pathologies. By current standard, the safety and efficacy of the TAR with FET approach has proven to be acceptable in mortality and morbidity risks and achieved satisfactory results.[1] However, in exchange for a more reliable extensively aortic repair, the lower body must undergo hypothermic circulatory arrest (CA). Conventionally, lower body CA is imposed when a Cronus stent elephant trunk (Cronus, MicroPort Endovascular Shanghai Co., Ltd., Shanghai, China) was released in the descending thoracic aorta (DTA) and the tetrafurcated graft was anastomosed end-to-end to the DTA. With this surgical pattern, lower body CA time is 17 min in average in our hospital, the target nadir temperature for CA is set at 26°C, during which time femoral perfusion is halted and continuous antegrade selective cerebral perfusion (ASCP) through right axillary cannulation is used at the rate of 5–10 mL/(kg/min). This lower body CA temperature level is considered sufficient for abdominal end organ protection[2] and this ASCP rate is considered safe for the brain.[3]

We have recently applied aortic balloon occlusion technique that has evolved from conventional TAR with FET we used to perform over the past several years.[4] This new method could consistently shorten average lower body CA time to 5 min. The rationales of the aortic balloon occlusion technique are as follows. After the Cronus stent elephant trunk is inserted in DTA, the aortic balloon (40 ml Coda Balloon Catheter, Cook Incorporated, Bloomington, IN, USA), matching the size of DTA, is adequately inflate to occlude the stent graft, resulting in the same effect of clamping. The aortic balloon occlusion technique provides continuous lower body perfusion through femoral cannulation while ASCP through right axillary cannulation is used during the time point when the femoral perfusion of lower body was discontinued until left common carotid artery is anastomosed to branch of tetrafurcate graft. With the average lower body CA time shortened to 5 min, the target nadir temperature for CA is raised to 28°C. The aortic balloon occlusion technique offers continuous perfusion to abdominal end organ, a more solid protective factor than hyperthermia, and guaranteed a longer operative time windows for previous procedures performed during CA. With the higher CA target temperature, the risk of the operation might decrease to a lower level than ever before. The aortic balloon occlusion technique is one of the major technical improvements in TAR with FET in the treatment of complex thoracic aortic disease. It inherited the advantage of reliable extensively aortic repair and overcame its weakness of requiring lower body CA. The present study investigated how the application of aortic balloon occlusion had affected the clinical endpoints for aortic dissection (AD) patients. By retrospectively reviewing the all consecutive patients who underwent TAR and FET operation, we aimed to investigate the current status of TAR with FET in real-world clinical practice, in particular to compare the strength of the protective effect of aortic balloon occlusion technique against the other preoperative risk factors statistically. This study explored what risk factors affect different clinical endpoints and revealed which subset of patients may benefit more with the aortic balloon occlusion approach.

Materials and Methods

Patient selection

All consecutive patients who were diagnosed with AD using computed tomography (CT) and underwent TAR and FET operation in Fuwai Hospital between August 2017 and February 2019 were retrospectively reviewed. Institutional review board approval for this study was obtained from Ethics Committee of Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College. We reviewed the in-hospital record of all these patients, which are the routine parameters from our institution that did not constitute any additional burden for the patients. The first case utilized the aortic balloon occlusion technique was explored in August 2017. After ensuring its safety in the next 2 months by testing on more cases, it gradually became the routine method of TAR with FET for more surgeons in our hospital. By February 2019, 344 AD patients were operated with TAR and FET, 123 of which with the new aortic balloon occlusion technique and the rest 221 with conventional method.

Procedure of aortic balloon occlusion technique

The tetrafurcated graft (Terumo, Vascutek Limited, Renfrewshire, Scotland, UK) was trimmed, and 40-mL aortic balloon in a 18F Gore sheath (W.L. Gore & Associates, Inc., Flagstaff, AZ, USA) was passed through the graft before it was employed in the procedure. Arterial cannulation was achieved using the right axillary and femoral arteries of bifurcated arterial line from one central perfusion. Systemic cooling was discontinued at 28°C of target nasopharyngeal temperature. Then lower body CA and could be started if necessary. After clamping the proximal innominate artery, the ASCP was obtained at a rate of 5–10 mL/(kg/min) through the right axillary artery cannula. After Cronus stent elephant trunk was released in the true lumen of the DTA, the aortic balloon in a sheath was deployed into metal part of the stent graft, and inflated by injection of 40 mL saline to compress the stent graft. Immediately after the balloon was fixed, perfusion of the lower body was then resumed through the right femoral artery cannula along with ASCP through the right axillary artery cannula from the single

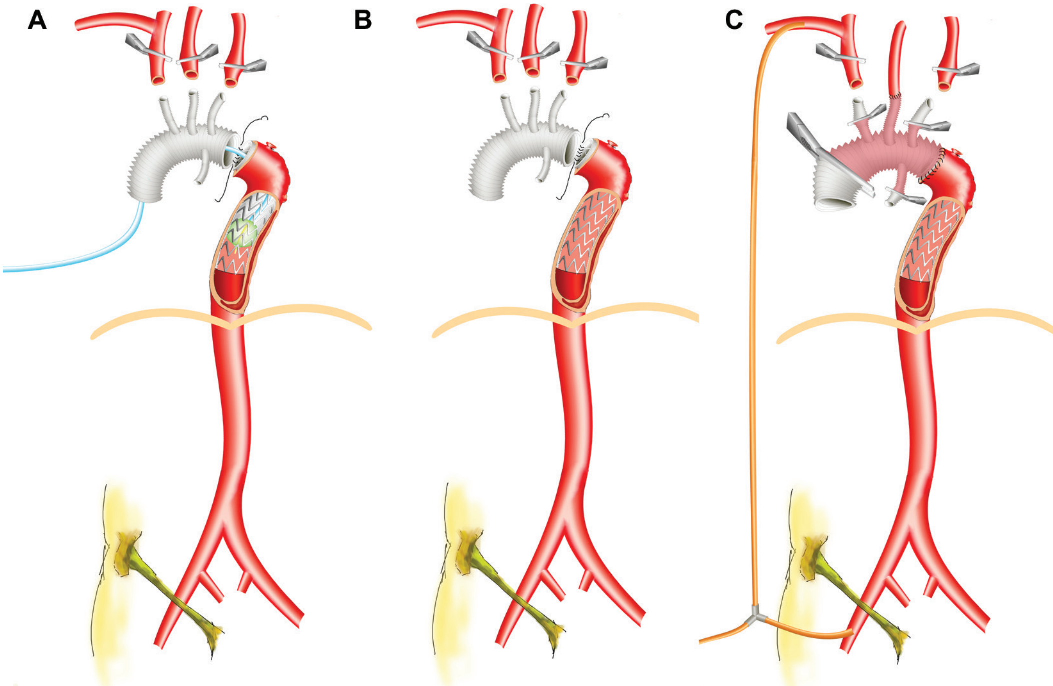

Fig. 1 Illustration of surgical technique: (**A**) aortic balloon occlusion, (**B**) conventional method, and (**C**) rewarming began (perfusion through carotid arteries achieved).

central perfusion. The cardiopulmonary bypass (CPB) flow was restarted and gradually increased to 1/2 of total flow. The lower body CA was about 5 min (**Fig. 1a**). The left common carotid artery was anastomosed first, after which the perfusion through both carotid arteries could be obtained. Then, rewarming for the patient was started with the CPB flow gradually increased to total flow (**Fig. 1c**).

Data processing and statistical analysis

The data of aortic balloon occlusion group (N = 123) and conventional group (N = 221) were reported separately. Continuous variables are presented as median and interquartile range (IQR) and categorical variables are presented as number of cases (N) and percentage (%). Then the two groups underwent direct univariate comparison. Normally distributed continuous variable was evaluated with Student's *t*-test, non-normally distributed continuous variable was evaluated with Mann–Whitney U test, and categorical variables were compared using χ^2 test. The early clinical outcomes were reported according to the consensus statement from the International Aortic Arch Surgery Study Group,[5] in which acute kidney injury (AKI) was defined in Grade I postoperative examination serum creatinine (Scr) was 1.5–2 times of normal baseline values or oliguria 6–12 h, Grade II postoperative Scr was 2–3 times of normal baseline values or oliguria 12–24 h, Grade III postoperative Scr was >3 times of normal baseline values or oliguria >24 h or anuria >12 h, Grade IV requiring ongoing dialysis; and hepatic injury was defined as elevated hepatic enzymes by 1.5 times of the upper range of normal and considered as Grade I if it lasts <48 h or Grade II if it lasts >48 h, Grade III when requiring surgical consultation, and Grade IV when requiring surgical intervention. The preoperative and operative details had some heterogeneity between the two groups. Thus, we performed 1:1 propensity score match on age, sex, concomitant coronary artery bypass grafting (CABG), cardiac surgery history, emergency operation (the situation that surgery must be performed on admission day or next morning if admission at night), preoperative Scr, and total CPB time, which were preoperative factors either statistically different between two groups or very important in affecting clinical results. Propensity score matching was used to reduce the potential bias of baseline characteristics between the two groups. Even though propensity score matching may increase the statistic power of univariate comparison, the matched univariate comparison only revealed impact of aortic balloon occlusion technique alone on TAR with FET. We next combined all cases (N = 344) to perform multivariate analysis, which could not only reflect all factor's significance in affecting different clinical endpoints but also the strength of the protective effect of aortic balloon occlusion technique against the other risk factors statistically. Binary logistic regression was performed on none-graded clinical events (30-day mortality and severe lung infection) and checked with Hosmer–Lemeshow fitness before drawing conclusion. If the Hosmer–Lemeshow fitness failed, some risk factors were removed from consideration until the fitness was more than 0.05. Binary logistic regression calculated odds ratio (OR), which is the relative risk for the specific factor and OR >1 suggests the factor is a positive risk. Graded clinical endpoints or parameters, including renal system endpoint, hepatic system endpoint, conscious revival time, mechanical ventilation time, and transfusion requirement, were tested by ordinal logistic regression and checked with test of parallel to validate its fitness. Ordinal logistic regression calculated the regression coefficient (Co) of the specific factor to the progression of the endpoint, and Co >0 suggests the factor is a positive risk. The Co value is served as the rake ratio between the grades, which is predicated on the progression of the endpoint between the grades were arithmetic. Thus, when test of parallel failed, grading definition is modified to make the gaps between grades in arithmetic progression (listed in **Supplementary Table 1**. Supplementary Tables are available online). The statistical analysis was performed using SPSS (Version 22.0, IBM-SPSS Inc., Armonk, NY, USA).

Results

Baseline characteristics of the patients

The consecutive patients who were diagnosed with AD using CT scan upon admission and underwent TAR with FET were selected in the study. The baseline demographic and clinical characteristics of the patients of the two groups are separately listed in **Table 1**. Their mean age was 51 (42–58) and 47 (40–55) years, and 77.24% and 75.11% of them were men. From symptom onset to operation, 69.11% and 75.11% of the AD cases were classified into acute stage (<72 h). The patients had similar smoking history (58.54% vs 56.56%), cardiovascular disease history (9.76% vs 9.50%), stroke history (8.94% vs 9.50%), and thoracic endovascular aortic repair (TEVAR) history (8.13% vs 5.88%). For segmental distribution of AD, all AD were involved in aortic arch (total or distal part) with proximal extension to aortic root (43.09% vs 42.08%) and/or distal extension to iliac arteries (59.35% vs 61.09%). If proximal endoleak from TEVAR exist, TAR was still performed despite only distal part of the arch was involved by AD according to the surgical protocol described in a previous research.[6] In addition to TAR with FET as the main operation, the concomitant aortic root operation and CABG were performed according to indications. With the aortic balloon occlusion approach, a different cerebral protection paradigm was used as the duration of lower body CA and ASCP was significantly shortened from 17 (14–20) min to 5 (3.5–7) min (*P* <0.001) and CA nasal temperature rose from 25.40 (24.90–26.00)°C to 27.60 (27.05–28.00)°C.

The early outcomes

The early clinical outcomes of the two groups are listed in **Table 2**. The 30-day mortality rate was 4.88% and 11.38% in aortic balloon occlusion group and conventional TAR with FET group with no statistical difference (*P* = 0.062). These cases consist of failed operation that did not undergo subsequent intensive care unit (ICU) treatment (0% vs 3.25%, *P* = 0.090), fail to survive before revival from anesthesia and withdraw from mechanical ventilation support (1.63% vs 4.88%, *P* = 0.839), and fail to survive after mechanical ventilation support (1.54% vs 3.25%, *P* = 0.675). There was only a trend that aortic balloon occlusion reduced 30-day mortality but could not reach statistic significant. Multivariable analyses of clinical endpoints are listed in **Table 3**. Multivariable binary logistic regression showed that heavy smoker (OR 8.208, 95% confidence interval [CI] 1.711–39.367, *P* = 0.008)], emergency operation (OR 45.906, CI: 4.455–472.994, *P* = 0.001), preoperative percentage of neutrophil (OR 1.099 per %, CI: 1.008–1.119, *P* = 0.033), and CPB time (OR 1.010 per min, CI: 1.005–1.015, *P* <0.001) were independent risk factors for 30-day mortality for AD patients after operation. The protective effect of aortic balloon occlusion relatively scarce compared these risks in associating with in-hospital mortality, suggesting its utilization did not affect 30-day mortality. The ICU stay time (90.53 [59.33–132.75] h vs 89.47 [62.77–139.32] h, *P* = 0.886) and postoperative in-hospital stay time (11 [8–14] d vs 10 [8–14] d, *P* = 0.748) was similar between the groups.

The incidence of stroke and paraplegia was similar between the groups. Stroke was a more serve complication that manifested as failed revival with prolonged mechanical ventilation, which was potentially contributed by their burden of vascular diseases history due to

Table 1 Preoperative and operative details

Variables	Aortic balloon occlusion (N = 123)	Conventional before matching (N = 221)	*P*	Conventional after matching (N = 123)	*P*
Preoperative details					
Age (years)	51 (42–58)	47 (40–55)	0.058	47 (41–58)	0.392
Body mass (kg)	75 (68–85.5)	75 (68–86)	0.953	75 (69–85)	0.955
Body height (cm)	171 (169.5–175)	167 (172–176)	0.779	172 (165–175)	0.413
Male	95 (77.24)	166 (75.11)	0.659	93 (75.61)	0.764
Smoker	72 (58.54)	125 (56.56)	0.723	71 (57.72)	0.897
Coronary artery disease history	12 (9.76)	21 (9.50)	0.939	12 (9.76)	1
Stroke history	11 (8.94)	21 (9.50)	0.864	11 (8.94)	1
Thoracic endovascular aortic repair history	10 (8.13)	13 (5.88)	0.424	7 (5.69)	0.451
Cardiac surgery history	2 (1.63)	13 (10.57)	0.064	3 (2.33)	0.651
Classification based on chronicity N (%)					
Acute, <7 d (h)	85 (69.11)	166 (75.11)	0.229	93 (75.61)	0.254
Subacute, 7–30 d (d)	23 (18.70)	20 (9.05)	0.009**	13 (10.57)	0.071
Chronic, >30 d (d)	15 (12.20)	35 (15.84)	0.358	17 (13.82)	0.705
Aortic dissection involvement					
Root	53 (43.09)	93 (42.08)	0.910	54 (43.90)	0.898
Ascending	105 (85.37)	208 (94.12)	0.010*	112 (91.06)	0.166
Arch	123 (100)	221 (100)	/	123 (100)	/
Total/proximal	116 (94.31)	217 (98.19)	0.060	119 (95.12)	0.355
Left subclavian artery or distal	7 (5.69)	4 (1.81)		4 (3.25)	
Thoracic descending	115 (93.50)	207 (93.67)	1	115 (93.50)	1
Abdominal	82 (66.67)	142 (64.25)	0.653	77 (62.60)	0.505
Iliac	73 (59.35)	135 (61.09)	0.818	74 (60.16)	0.897
Operative details					
Aortic root operation					
None	36 (29.27)	90 (40.72)	0.130	50 (40.65)	0.264
Repair or plasticity	52 (42.28)	68 (30.77)		44 (35.77)	
Bentall	26 (21.14)	51 (23.08)		25 (20.33)	
Wheat	8 (6.50)	9 (4.07)		3 (2.44)	
David	1 (0.81)	3 (1.36)		1 (0.81)	
Concomitant coronary artery bypass graft	17 (13.82)	29 (23.58)	0.050	22 (17.89)	0.383
Require secondary cardiopulmonary bypass to maintain circulation	5 (4.07)	29 (23.58)	<0.001***	19 (15.45)	0.003**
Require extracorporeal membrane oxygenation to maintain circulation	0 (0)	4 (1.74)	0.133	4 (3.25)	0.044*
Operation time (min)	380 (338–436.5)	394.5 (330–463.25)	0.539	391.5 (323.25–462.25)	0.547
Cardiopulmonary bypass	180 (149.5–202.5)	164 (141–209.5)	0.124	172.5 (141.25–210.5)	0.585
Clamp	115 (94–144)	109.5 (89–131.25)	0.055	113.5 (90–134.75)	0.294
Circulatory arrest	5 (3.5–7)	17 (14–20)	<0.001***	16 (14–19.75)	<0.001***
Post cardiopulmonary bypass	119 (97.5–136)	156.5 (112.75–199)	<0.001***	155 (125–192.5)	<0.001***
Temperature when circulatory arrest was commenced (°C)					
Nasal	27.60 (27.05–28.00)	25.40 (24.90–26.00)	<0.001***	25.40 (24.90–26.00)	<0.001***
Rectal	28.70 (28.00–29.75)	28.00 (26.70–30.03)	0.016*	28.00 (26.73–29.88)	0.010*

Values are expressed as median and inter-quartile range (IQR) or number (%). Percentage is expressed compared with the total population (123 for aortic balloon occlusion and matched group and 221 for conventional group).
**P* <0.05, ***P* <0.01, ****P* <0.001.

the deficit in the construct of blood vessel. All the paraplegia cases were temporal and recover before discharge. Incidence of stroke and paraplegia were relatively lower than other outcomes and were more affected by the vasculature rather than age or sex, thus we could not find risk factors for them this quantity of patients with these considered factors. The incidence of delirium, which manifested as mania or depression, failed to make

Table 2 Postoperative details

Variables	Aortic balloon occlusion (N = 123)	Conventional before matching (N = 221)	*P*	Conventional after matching (N = 123)	*P*
30-day mortality	6 (4.88)	18 (8.14)	0.254	14 (11.38)	0.062
Failed operation	0 (0)	5 (2.26)	0.382	4 (3.25)	0.148
Fail to revive	4 (3.25)	8 (3.62)		6 (4.88)	
After mechanical ventilation	2 (1.63)	5 (2.26)		4 (3.25)	
Redo thoracotomy to control bleeding	7 (5.69)	9 (3.17)	0.515	6 (4.88)	0.776
Conscious revival (h)	8.12 (4.92–13.14)	11.75 (7.80–18.83)	<0.001***	13.38 (9.33–23.93)	<0.001***
Mechanical ventilation (h)	18.67 (13.27–36.31)	21.92 (13.50–47.17)	0.139	23.06 (14.31–59.50)	0.040*
ICU stay (h)	90.53 (60.54–132.98)	86.91 (60.82–134.24)	0.440	89.47 (62.77–139.32)	0.886
Postoperative in-hospital stay (d)	11 (8–14)	11 (9–14)	0.541	10 (8–14)	0.748
Neurological System					
Stroke	2 (1.63)	7 (3.17)	0.391	5 (4.07)	0.250
Temporal paraplegia	3 (2.44)	9 (4.07)	0.429	6 (4.88)	0.308
Delirium	4 (3.25)	15 (6.78)	0.169	11 (8.94)	0.062
Severe lung infection	3 (2.44)	12 (5.43)	0.064	10 (8.13)	0.046
Oliguria or anuria	10 (8.13)	20 (9.05)	0.772	17 (13.82)	0.153
Renal system	20 (16.26)	60 (27.15)	0.022*	41 (33.33)	0.002**
I. Scr 1.5–2 times	4 (3.25)	22 (9.95)	0.024	22 (17.89)	<0.001***
II. Scr 2–3 times	6 (4.88)	13 (5.88)	0.696	6 (4.88)	1
III. Scr >3 times	0 (0)	3 (1.36)	0.194	2 (1.63)	0.156
IV. Ongoing CRRT	10 (8.13)	22 (9.96)	0.577	19 (15.45)	0.075
Hepatic system	33 (26.83)	100 (45.25)	0.001**	62 (50.41)	<0.001***
I. Hepatic enzymes >1.5 times, <48 h	24 (19.51)	60 (27.15)	0.114	34 (27.64)	0.133
II. Hepatic enzymes >1.5 times, >48 h	9 (7.32)	40 (18.10)	0.006**	28 (32.52)	<0.001***
III. Hepatobiliary ischemia requiring general surgeon consultation	0 (0)	0 (0)	/	0 (0)	/
IV. Hepatobiliary ischemia requiring surgical intervention	0 (0)	0 (0)	/	0 (0)	/
Transfusion requirement (quantity if used and percentage of usage)					
Red blood cell (u) total	4 (4–10)	6 (4–10)	0.616	6 (4–11.5)	0.169
	81 (65.85)	166 (75.11)	(0.067)	95 (77.24)	(0.048*)
Operative	4 (4–6)	4 (2–8)	0.307	4 (4–8)	0.219
	53 (43.09)	110 (49.77)	(0.234)	68 (55.28)	(0.056)
Postoperative	4 (2–8)	4 (2–6)	0.719	4 (2–8)	0.606
	64 (52.03)	127 (57.47)	(0.331)	72 (58.54)	(0.305)
Plasma (mL) total	600 (400–800)	700 (600–1200)	0.008**	800 (600–1200)	0.002**
	80 (65.04)	132 (59.73)	(0.332)	69 (56.10)	(0.151)
Operative	400 (400–600)	600 (400–800)	0.001**	600 (400–800)	0.001**
	69 (56.10)	116 (52.49)	(0.520)	61 (49.59)	(0.307)
Postoperative	400 (400–650)	600 (400–800)	0.120	600 (400–1200)	0.024*
	40 (35.52)	68 (30.77)	(0.737)	38 (30.89)	(0.784)
Platelets (u) total	1 (1–2)	1 (1–2)	0.433	1 (1–2)	0.278
	98 (79.67)	181 (81.90)	(0.613)	104 (84.55)	(0.318)
Operative	1 (1–1)	1 (1–1)	0.817	1 (1–1)	0.464
	89 (72.36)	164 (74.21)	(0.709)	92 (74.08)	(0.664)
Postoperative	1 (1–3)	1 (1–3)	0.294	1 (1–4)	0.794
	18 (14.63)	48 (21.72)	(0.110)	33 (36.83)	(0.018*)

CRRT: continuous renal replacement therapy; Scr: serum creatinine

*P <0.05, **P <0.01, ***P <0.001. Values are expressed as median and interquartile range (IQR) or number (%).

Table 3 Multivariable analysis of clinical endpoints

Risk factors (Hosmer–Lemeshow fitness for binary regression)*	Odds ratio	95% confidence interval	*P*
30-day mortality (0.610)			
Heavy smoker	8.208	1.711 to 39.367	0.008
Emergency operation	45.906	4.455 to 472.994	0.001
Preoperative percentage of neutrophil (%)	1.099	1.008 to 1.119	0.033
CPB time (min)	1.010	1.005 to 1.015	<0.001
Severe lung infection (0.176)			
Female	135	1.36 to 13401	0.037
Heavy smoker	34.028	2.063 to 561.198	0.014
CPB time (min)	1.013	1.005 to 1.021	0.002
Postoperative Scr1 (μmol/L)	1.013	1.003 to 1.024	0.015
Postoperative hemoglobin 0 (g/L)	1.066	1.012 to 1.122	0.016
Risk factors (test of parallel for ordinal regression)	**Correlation**	**95% confidence interval**	***P***
Endpoints of renal system (0.088)			
Conventional group	1.011	0.530 to 1.491	<0.001
Age (years)	0.030	0.006 to 0.055	0.016
Height (cm)	–0.046	–0.085 to –0.007	0.022
Preoperative Scr (μmol/L)	0.016	0.009 to 0.023	<0.001
Preoperative leukocyte count (10^9/mL)	0.114	0.038 to 0.189	0.003
CPB time (min)	0.008	0.005 to 0.012	<0.001
Conscious revival time (0.998)			
Conventional group	0.674	0.246 to 1.101	0.002
Female	1.369	0.724 to 2.014	<0.001
Emergency operation	0.714	0.148 to 1.281	0.013
Age (years)	0.025	0.003 to 0.046	0.023
Height (cm)	0.021	0.001 to 0.041	0.037
Preoperative ALT (U/L)	0.008	0.000 to 0.015	0.042
Preoperative AST (U/L)	–0.007	–0.014 to –0.001	0.025
Preoperative Scr (μmol/L)	0.009	0.003 to 0.016	0.004
CPB time (min)	0.007	0.003 to 0.010	<0.001
Mechanical ventilation time (0.321)			
Female	0.355	0.043 to 1.820	0.002
Height (cm)	0.022	0.002 to 0.043	0.035
CPB time (min)	0.011	0.007 to 0.015	<0.001
Postoperative hemoglobin 0 (g/L)	0.020	0.003 to 0.037	0.018
Postoperative Leukocyte count 0 (10^9/mL)	0.055	0.001 to 0.109	0.047
Postoperative platelet count 0 (10^9/mL)	–0.006	–0.011 to –0.001	0.014
Endpoints of hepatic complication (0.846)			
Conventional group	0.835	0.305 to 1.366	0.002
Preoperative AST (U/L)	0.043	0.020 to 0.066	<0.001
Preoperative leukocyte count (10^9/mL)	0.152	0.066 to 0.238	0.001
Preoperative percentage of neutrophil (%)	–0.049	–0.083 to –0.015	0.005
Preoperative Platelet count (10^9/mL)	–0.005	–0.083 to –0.015	0.014
Preoperative D-dimer (μg/mL)	0.047	0.001 to 0.092	0.044
Preoperative FDP (μg/mL)	–0.007	–0.012 to –0.002	0.006
CPB time (min)	0.011	0.007 to 0.015	<0.001

ALT: alanine transaminase; AST: aspartate transaminase; CPB: cardiopulmonary bypass; FDP: fibrinogen degradation product; Scr: serum creatinine

*30-day mortality and severe lung infection are binary multivariable analysis (odds ratio >1 for positively related) and endpoints of renal and hepatic system are ordinal multivariable analysis (correlation >0 for positively related).

statistical difference between the groups. Even though it is not a serious complication, application of aortic balloon occlusion did not affect its incidence nor did we find risk factors to delirium.

Renal system outcomes

Scr was used as the only indicator to define AKI in this study instead of urine output because all oliguria or anuria lasted more than 24 h and they were treated with continuous renal replacement therapy (CRRT). The application of aortic balloon occlusion significantly decreased the incidence of AKI (16.26% vs 33.33%, $P = 0.002$), but did not significantly decrease the incidence of CRRT (8.13% vs 15.45%, $P = 0.075$). Multivariable ordinal logistic regression revealed that being in conventional group (longer CA and lower nadir temperature) is a risk factor for more severe renal outcome (regression coefficient [Co] 1.011, CI: 0.530 to 1.491, P <0.001). In addition, older age, higher preoperative Scr, higher preoperative leukocyte count, and longer CPB time are risks factor for more severe renal outcome.

Respiratory system outcomes

The patient must revive from anesthesia before withdrawal of mechanical ventilation. The conscious revival time from anesthesia was much shorter in aortic balloon occlusion group (8.12 [4.92–13.80] h vs 13.38 [9.33–23.93] h, P <0.001), suggesting the potential central nervous system protection by aortic balloon occlusion. The mechanical ventilation support time was also statistically shorter (18.67 [13.30–36.87] h and 23.06 [14.31–59.50] h, $P = 0.040$). Severe lung infection stands for delayed mechanical ventilation prolonged despite with prolonged strong antibiotics usage, in which situation surgical or endoscopic intervention was used. Incidence of severe lung infection was lower in aortic balloon occlusion group (2.44% vs 8.13%, $P = 0.046$). However, multivariable ordinal logistic regression suggested that being conventional group only increased conscious revival time (Co 0.674, CI: 0.246–1.101, $P = 0.002$), but did not statistically affect mechanical ventilation time or severe lung infection. In addition, longer CPB time and being female are risk factors to increase conscious revival time, mechanical ventilation time, and severe lung infection.

Hepatic system outcomes

The application of aortic balloon occlusion significantly decreased the incidence of postoperative hepatic enzyme elevation (26.83% vs 50.41%, $P = 0.001$). Multivariable ordinal logistic regression suggested that being conventional group increased the risk for hepatic injury (Co 0.835, CI: 0.305–1.366, $P = 0.002$). In addition, only aspartate transaminase (AST), but not alanine transaminase (ALT) was calculated as the risk for hepatic injury by the current definition (Co 0.043 per U/L, CI: 0.020–0.066, P <0.001). In fact, previous studies have found AST is much more sensitive than ALT in reflecting postoperative hepatic injury.[7] Although hepatic injury is a sensitive reflection for continuous perfusion provided with aortic balloon occlusion, it only appeared as a subclinical event resolved by routine practice.

Blood transfusion

Univariable comparison suggested that aortic balloon occlusion decreased the percentage of red blood cell (RBC) transfusion during operation, platelet transfusion after operation, but did not affect average quantity if used. Aortic balloon occlusion also decreased average quantity of plasma transfusion but did not affect percentage of usage. Multivariable ordinal logistic regression suggested that aortic balloon occlusion had some hematological protection effect. Being in conventional group increased quantity of operative transfusion (Co 0.453, CI: 0.011–0.895, $P = 0.045$), which also translated into more total RBC transfusion during in-hospital stay (Co 0.529, CI: 0.114–0.944, $P = 0.012$). Plasma and platelets transfusion were not affected by aortic balloon occlusion, but were both risked from longer CPB time. Other blood examination related to hepatic function and coagulation function (such as fibrinogen degradation product) also affected quantity of transfusion (**Supplementary Table 2**).

Discussion

The TAR with FET operation in our hospital has progressively evolved along with the improvement of surgical skills and perioperative management. Not until the application of aortic balloon occlusion technique, could we overcome its weakness of requiring lower body CA. This surgical method greatly improved operative protection and postoperative recovery of these patients. When reporting the prevalence of clinical endpoint after aortic arch surgery, we used to feel most postoperative complications came out randomly. This was because we had somewhat perfunctory understanding of the link of commonly recognized risk factors to the major complications. The present study aims to compare clinical outcome of aortic balloon occlusion with its conventional form and investigate the risk factors for each clinical outcome to provide a clear reference to the whole demography of the cases in assessment of the operative of each patient.

The application of aortic balloon occlusion technique to TAR with FET provided an opportunity to greatly facilitate TAR with FET for us to handle more complicated aortic arch diseases, with possible wider surgical indications and less cost. The rationale for this balloon device is that it provides continuous blood supply of the lower body with the much higher CPB temperature that would offer better organ protection to the patients. This surgical approach requires only simple procedure to set up and can provide sufficient time to perform the distal anastomosis for the surgeon. The aortic balloon occlusion not only simplified the CPB management for TAR with FET with higher hypothermic setting point and less lower body CA but also reduced the difficulty of the operation for the surgeon in a sense because after the balloon has been properly set up and blocked the refluxing blood in the stent graft, the surgeon can perform distal anastomosis much more smoothly instead of racing against the clock to shorten the time of lower body CA. This modification of the operation can inherit all the advantages of TAR with FET while avoiding the shortcomings of TAR with FET involving DHCA. Its combined major advantages gave promises to improve the clinical outcomes and quality of life for patients with complex aortic diseases.

By analyzing the risk factors for TAR and FET with multivariable analysis, the hematological, hepatic, and renal factors were intertwined and mutually affected each other. For example, the high postoperative Scr was an independent risk factor for more platelet transfusion, while higher preoperative and lower postoperative platelet count was a risk factor for AKI. This mutual relationship of platelet count and renal function was observed in a previous study.[8] We believe the difference of preoperative and postoperative platelet count sensitively reflected the operative harm to the hematological system, which may also sensitively predict the postoperative AKI. The real strong factors affecting postoperative complication are CPB time (reflecting the time needed for completing the operation procedure) and aortic pathology (reflected by AD involvement and preoperative biochemical tests), both of which represented the severity of the disease and could only be partially relieved by the protective effect of aortic balloon occlusion technique. In the present study, with the CPB time, aortic clamp time, and aortic pathology being similar between groups, application of aortic balloon occlusion technique is safe and it showed notable advantages in preventing postoperative complications.

There were several limitations of this study. This is only a retrospective study presented the data within a short era (since the invention of the technique in Aug 2017). As aortic balloon occlusion gradually spread during the study period, there is also a potential bias as they appeared in relatively later period of this study with better standard of ICU care. Using propensity score matching only favored univariate comparisons. Thus, we used all consecutive to perform multivariate analysis and reported both results together. As a result, the number of patients was enough to find risk factors for many, but not all kinds of clinical results. We did not find risk factors for postoperative stroke or paraplegia.

Conclusion

The aortic balloon occlusion technique, as a perfusion strategy during operation, served an adjuvant factor for alleviating postoperative complication. The protective effect of aortic balloon occlusion technique is limited, but still apparent on clinical blood examination. It is a very feasible approach that is recommended for patients who carried more risks for complications and may not survive aortic operation with prolonged CA. Despite we only primarily investigated its effect on clinical outcomes, this method deserves further attention in future clinical practice.

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Disclosure Statement

The authors declare no conflicts of interest.

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