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1 Department of Cardiovascular Surgery, Beijing Anzhen Hospital, Capital Medical

CLINICAL RESEARCH

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Authors' Contribution:

Manu

ABE 1 Guanglong Sun

Efficacy of Total Aortic Arch Replacement Combined with Frozen Elephant Trunk in Aortic Reoperation

| Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G | | Lizhong Sun Junming Zhu Yongmin Liu Yipeng Ge Shijun Xu | University, Beijing, P.R. China 2 Department of Cardiovascular Surgery, Beijing Aortic Disease Center, Beijing Anzhen Hospital, Capital Medical University, Beijing Institute of Heart, Lung, and Blood Vessel Disease, Beijing, P.R. China |
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| Correspondir Source o | ng Author: of support: | Lizhong Sun, e-mail: lizhongsun@foxmail.com Departmental sources | |
| Bacl Material/N | kground: Methods: | the frozen elephant trunk (TAR+FET) technique for ac We performed TAR+FET for 118 patients for major ve dian sternotomy incision. All patients were divided i aortic valve replacement (AVR); in group B, the prior ment; in group C, the prior major procedure was aorti | efficacy of total aortic arch replacement combined with ortic disease following a prior cardiac surgery procedure. ssel disease following a prior cardiac procedure with me- nto 5 groups: in group A, the prior major procedure was r major procedure was isolated ascending aorta replace- ic root replacement; in group D, the prior major procedure group E, the prior major procedure was 'other' cardiac op- |
| | Results: | erative procedure. The long-term follow-up visit resu The 30-day mortality rate after the operation was 13.6 4 in group D, and 1 in group E. Follow-up visits were was 47.6±36.3 months and 12 patients had died by f One-year survival rates of the 5 groups were 85% (gr | |
| Con | clusions: | The TAR+FET technique is feasible and efficacious for | aortic reoperation in patients who previously underwent ients with recurrent aortic arch disease after cardiac sur- |
| MeSH Ke | eywords: | Aortic Diseases • Reoperation • Treatment Outcor | ne |
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Background

There are many reasons for aortic reoperation after cardiac surgery, including: planned second-stage surgery, aneurysm and anastomotic leakage due to re-expansion of the proximal or distal end of the operation site, new aortic dissection or aneurysm, and artificial blood vessel infection [1,2]. TAR+FET is usually used for patients of type A aortic dissection (AD) and has gradually become the "standard technique" [3,4]. Although our previous study confirmed the efficacy and durability of TAR+FET for type A AD after Bentall procedure in Marfan syndrome [5], there is scant data on the results on TAR+FET for patients who had a previous cardiac operation. The aim of the present retrospective study was to investigate the early and late outcomes in a cohort of 118 patients who needed aortic reoperations with TAR+FET technique following cardiac surgery.

Material and Methods

We included a total of 118 patients undergoing TAR+FET after the first cardiac surgery for major vascular disease from January 2009 to December 2017 in the Department of Cardiac Surgery, Beijing Anzhen Hospital, Capital Medical University. This study was approved by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University. Signed written informed consent was obtained from all participants before the study. Inclusion criteria were: (1) The first operation participants underwent was cardiac surgery via a transthoracic midline incision, and (2) the reoperation was TAR+FET or concurrent with other operations. Patients were divided into 5 groups according to the last operation type: in group A, the previous major procedure was aortic valve replacement (AVR) (n=20, 16.9%); in group B, the previous major procedure was isolated ascending aorta replacement (n=16, 13.6%); in group C, the previous major procedure was a ortic root replacement (n=62, 52.5%); in group D, the previous major procedure was aortic arch replacement or intervention (n=12, 10.2%); and in group E, the previous major procedure was other cardiac operative procedure (n= 8, 6.8%). The mean age of patients undergoing TAR+FET was 44.7 years (range, 16-68 years). Marfan syndrome was diagnosed in 30 patients (25.4%) and hypertension was diagnosed in 74 (62.7%). The interval between the initial operation and TAR+FET averaged 6.3±4.8 years. The preoperative clinical profile is summarized in Table 1.

Primary indications for reoperation included: (1) The new aortic dissection involved the arch; (2) The aortic arch was severely expanded to a diameter of more than 5 cm; (3) Severe inner leakage or anastomotic leakage occurred at the proximal end of the descending aortic stent after the arch surgery; and (4) The artificial blood vessel of the previous arch surgery was infected.

Table 1. Clinical characteristics of 118 patients.

| Variable | Case (percentage)/ mean (SD) | | | |
|---|---------------------------------|---------|--|--|
| Demographic information | | | | |
| Sex (male) | 97 | (82.2%) | | |
| Age (years) | 44.7 | (11.9) | | |
| BMI | 24.2 | (3.4) | | |
| Smoking | 41 | (34.7%) | | |
| Emergency operation | 9 | (7.6%) | | |
| Interval from the initial operation (years) | 6.3 | (4.8) | | |
| Comorbidities | | | | |
| Hypertension | 74 | (62.7%) | | |
| Marfan disease | 30 | (25.4%) | | |
| Acute myocardial infarction within 3 weeks | 3 | (2.5%) | | |
| Initial operation type | | | | |
| AVR (group A) | 20 | | | |
| Isolate AVR | 17 | (85%) | | |
| AVR+MVR | 3 | (15%) | | |
| AAR (group B) | 16 | | | |
| Isolate AAR | 13 | (81.3%) | | |
| AAR+AVP | 3 | (18.7%) | | |
| ARR (group C) | 62 | | | |
| ARR | 5 | (8.1%) | | |
| Bentall | 48 | (77.4%) | | |
| Bentall+other | 7 | (11.3%) | | |
| David | 2 | (3.2%) | | |
| TAR (group D) | 12 | | | |
| Bentall+FET | 1 | (8.3%) | | |
| Bentall+TAR+FET | 4 | (33.3%) | | |
| AAR+TAR | 2 | (16.7%) | | |
| AAR+FET | 2 | (16.7%) | | |
| AAR+TAR+FET | 2 | (16.7%) | | |
| FET | 1 | (8.3%) | | |
| Others (group E) | 8 | | | |
| ASDR | 1 | (12.5%) | | |
| CABG | 2 | (25%) | | |
| MVR | 3 | (37.5%) | | |
| Carbol | 1 | (12.5%) | | |
| Exploratory thoracotomy | 1 | (12.5%) | | |

Surgical technique

All patients underwent TAR+FET technique through a redo median sternotomy. Before sternotomy, the free femoral artery and vein were preserved for later use, and the sternum was then sawed by a swing saw through the original incision approach. If there was major bleeding during the sternotomy, the skin incision was quickly sutured and compressed, and the femoral artery and vein were intubated and transferred to cool down after heparinization. The cardiopulmonary bypass (CPB) was generally established as follows: femoral artery+2-step drainage tube into the right atrium, right axillary artery+2-step drainage tube into the right atrium or femoral artery+intubation through femoral vein. The single-pump double-tube technique was used in arteries with one branch of cardiopulmonary bypass and the other branch of cervical vascular intubation for cerebral protection perfusion. The circulation was stopped when the temperature of the nasopharyngeal dropped to 25°C, and then the selective cerebral perfusion was performed. The aortic arch was cut open after blocking the 3 branch vessels of the arch. After the FET (Cronus[®], MicroPort Medical, Shanghai, China), a 4-branched vascular graft (Maquet, Rastatt, Germany) was used to complete the TAR, and 1 branch of the 4-branched vascular graft was used to start the CPB. The corresponding artificial branched vessel was anastomosed with the left common carotid artery, after which rewarming was started and the brain was perfused bilaterally, followed by the ascending aorta, and then we resumed the myocardial perfusion and anastomosed the left subclavian artery and innominate artery. After heart fibrillation, defibrillation was performed with an electrode defibrillator to restore the heartbeat. The anastomosis of the aortic arch and ascending aorta was wrapped with autologous pericardium or bovine pericardium and shunted with the right atrium.

Follow-up visit

The primary outcome examined was 30-day mortality after the operation, and the secondary outcome was long-term survival (1, 3, and 5 years) estimated using the Kaplan-Meier method. Follow-up was completed in 99.2% (117/118) of patients by June 2018, for a mean duration of 47.6 ± 36.3 months (range, 0.1–113 months).

Statistical analysis

Statistical analysis was performed using Statistical Product and Service Solutions (SPSS) for Windows 19.0 (SPSS, Inc., Chicago, IL, USA). P<0.05 was considered statistically significant. All measurement data are expressed as the mean \pm standard deviation or number (percentage), and comparisons between groups were conducted using the *t* test and multivariate analysis of variance. Enumeration data are expressed by frequency, and comparison between groups was performed by χ^2 test. Postoperative survival was analyzed using Kaplan-Meier survival analysis.

Results

Operative data

The main reasons for this group of patients undergoing secondary TAR+FET were: (1) new aortic dissection or aneurysm; (2) residual dissection or aneurysm, and persistent expansion in the later stage; (3) anastomotic leakage, including aortic paravalvular leakage, coronary anastomotic leakage, proximal and distal aortic leakage; and (4) aortic dissection or aneurysm combined with anastomotic leakage.

Type A AD was found in 79 (66.9%) patients, type A AD+root aneurysm was found in 1 (0.8%), type A AD+arch aneurysm was found in 3 (2.5%), type A AD+anastomotic leakage was found in 10 (8.5%), type B AD was found in 9 (7.6%), type B AD+root aneurysm was found in 1 (0.8%), type B AD+arch aneurysm was found in 1 (0.8%), type B AD+anastomotic leakage was found in 4 (3.4%), arch aneurysm was found in 6 (5.1%), root combined arch aneurysm was found in 2 (1.6%), arch aneurysm+anastomotic leakage was found in 1 (0.8%) patient.

The times of CPB, cross-clamping, and low flow infusion were 194.9 \pm 61.2 min, 98.5 \pm 37.8 min, and 27.0 \pm 13.1 min, respectively. The CPB time was longer in group E than in other groups, but without significant differences among the 5 groups. The intraoperative bleeding volumes were 1735.0 \pm 689.2 ml, 1812.5 \pm 1434.7 ml, 1869.4 \pm 962.6 ml, 2800.0 \pm 1492.4 ml, and 1837.5 \pm 1788.8 ml, respectively. The bleeding volume of group D was more than in other groups and it was significantly different between group D and other groups (group D *vs.* A, *P*=0.011; D *vs.* B, *P*=0.024; D *vs.* C, *P*=0.010; D *vs.* E, *P*=0.044). The operative data are listed in Table 2 and the comparison of operative data among the 5 groups is listed in Table 3.

30-day mortality and morbidity after surgery

The 30-day mortality was 13.6% (16/118), with deaths occurring in 2 patients in group A, 1 in group B, 8 in group C, 4 in group D, and 1 in group E. The causes of death were multiple organ failure, low cardiac output syndrome, vessel rupture, cardiac shock, and infection. The main causes of postoperative morbidity were renal insufficiency, hepatic insufficiency, delirium, delay of recovery, delayed paraplegia, and low cardiac output. The 30-day mortality and morbidity rates are listed in Table 4.

Table 2. Operative profile in the 5 groups.

| | Group A | Group B | Group C | Group D | Group E |
|---|--------------|---------------|--------------|---------------|---------------|
| Case | 20 | 16 | 62 | 12 | 8 |
| Cardiopulmonary bypass (CPB) time | 200.7±57.2 | 178.8±49.9 | 189.0±61.2 | 216.4±69.1 | 226.0±75.8 |
| Aortic cross-clamp time (min) | 104.9±32.7 | 86.9±23.9 | 96.5±40.1 | 100.8±30.4 | 117.3±56.1 |
| Intraoperative low flow time | 25.5±9.9 | 25.2±13.5 | 27.4±14.1 | 31.5±15.3 | 24.1±7.8 |
| Intraoperative bleeding volume (mL) | 1735.0±689.2 | 1812.5±1434.7 | 1869.4±962.6 | 2800.0±1492.4 | 1837.5±1788.8 |
| Bleeding volume 24 h after operation | 762.0±572.9 | 1164.4±1370.1 | 781.5±754.3 | 1208.3±1014.1 | 761.3±761.1 |
| Postoperative mechanical ventilation time (h) | 65.1±61.9 | 40.3±60.8 | 67.2±147.0 | 98.8±169.4 | 65.0±75.5 |
| ICU stay time (d) | 3.4±2.9 | 2.3±2.8 | 2.9±4.3 | 4.9±7.4 | 5.1±4.6 |
| Postoperative survival time (m) | 48.6±34.3 | 62.2±36.5 | 48.8±34.0 | 33.6±24.4 | 51.9±41.9 |

Table 3. P-values of comparison in operative profiles among the 5 groups.

| | A <i>vs</i> . B | A <i>vs</i> . C | A vs. D | A vs. E | B vs. C | B vs. D | B vs. E | C vs. D | C <i>vs</i> . E | D vs. E |
|---|-----------------|-----------------|---------|---------|---------|---------|---------|---------|-----------------|---------|
| Cardiopulmonary bypass (CPB) time | 0.285 | 0.456 | 0.48 | 0.322 | 0.551 | 0.108 | 0.076 | 0.155 | 0.108 | 0.73 |
| Aortic cross-clamp time (min) | 0.156 | 0.387 | 0.766 | 0.437 | 0.363 | 0.335 | 0.065 | 0.718 | 0.146 | 0.342 |
| Intraoperative low flow time | 0.944 | 0.573 | 0.216 | 0.804 | 0.548 | 0.214 | 0.853 | 0.33 | 0.508 | 0.224 |
| Intraoperative bleeding volume (mL) | 0.838 | 0.644 | 0.011* | 0.828 | 0.857 | 0.024* | 0.959 | 0.010* | 0.94 | 0.044* |
| Bleeding volume 24 h after operation | 0.168 | 0.93 | 0.16 | 0.998 | 0.117 | 0.894 | 0.284 | 0.12 | 0.951 | 0.26 |
| Postoperative mechanical ventilation time (h) | 0.613 | 0.87 | 0.425 | 0.953 | 0.451 | 0.229 | 0.653 | 0.43 | 0.963 | 0.559 |
| ICU stay time (days) | 0.48 | 0.713 | 0.328 | 0.333 | 0.612 | 0.121 | 0.14 | 0.153 | 0.185 | 0.917 |
| Postoperative survival time (months) | 0.258 | 0.987 | 0.046* | 0.652 | 0.181 | 0.006* | 0.191 | 0.033* | 0.608 | 0.028* |

* *P*<0.05, statistically significant difference.

Long-term survival

Late death occurred in 12 patients: 1 in group A, 7 in group C, 2 in group D, and 2 in group E. The main causes of death were hemorrhage, low cardiac output, cerebral hemorrhage and respiratory failure, and non-cardiac causes in 1 patient. Survival was 85%, 93.8%, 82.3%, 50%, and 50%, respectively, at 1 year, and 85%, 93.8%, 80.6%, 50%, and 50%, respectively, at 5 years (Table 5). At 9 years after TAR + FET, survival was different among the 5 groups, and survival in group D was lower than in the other groups, with a significant difference. The survival times of different groups are listed in Figure 1.

Discussion

There are many factors associated with aortic reoperation after cardiac surgery. Some cardiac centers have reported that the main causes of redo intervention are: planned second-stage surgery, aneurysm and anastomotic leakage due to re-expansion of the proximal or distal end of the operation site, new aortic dissection or aneurysm, and artificial blood vessel infection [1,2], but few studies have reported on this topic in China. Professor Sun Li-zhong studied a group of patients undergoing secondary and multiple aortic operations, and found the main causes of reoperation were development of residual dissection or aneurysm and new dissection. Recently, Luo et al. [3] reported on a group of 51 patients with Stanford type A AD who underwent the TAR+FET procedure, finding that all patients avoided reoperation caused by dilation of the aorta, but the study had a small sample size and low power. Among the 118 patients in the present study, most of their previous surgeries were operations on the great artery, and some patients received aortic valve replacement and other operations, including valve replacement, congenital heart surgery, and bypass surgery. In these 118 patients undergoing secondary TAR+FET procedures, aortic root

Table 4. Postoperative complications and mortality.

| | Group A | Group B | Group C | Group D | Group E |
|-------------------------|----------|----------|----------|----------|----------|
| 30-day mortality | 2 (1.7%) | 1 (0.8%) | 8 (6.8%) | 4 (3.4%) | 1 (0.8%) |
| Postoperative mortality | - | _ | _ | _ | - |
| Renal insufficiency | 3 | _ | 4 | 3 | 2 |
| Hepatic insufficiency | 7 | 2 | 15 | 5 | 1 |
| Delirium | 1 | - | - | _ | - |
| Delay of recovery | 3 | 1 | 5 | 1 | 4 |
| Cerebral infarction | - | _ | _ | 1 | - |
| Cerebral hemorrhage | - | _ | 1 | _ | - |
| Coma | - | _ | 5 | 2 | 1 |
| Delayed paraplegia | 1 | 1 | | 1 | |
| Low cardiac output | 3 | - | 5 | 3 | 1 |
| IABP | - | - | - | _ | 1 |
| ECMO | - | - | 2 | - | - |
| Hemorrhage | - | - | 5 | _ | - |
| Tracheotomy | - | - | 4 | 1 | 1 |
| Thoracotomy | - | _ | _ | 3 | 1 |
| Incision infection | _ | _ | _ | | 1 |

IABP - intra-aortic balloon pump; ECMO - extracorporeal membrane oxygenation

Table 5. Long-term survival in the 5 groups.

| | Group A | Group B | Group C | Group D | Group E |
|---------|-------------|---------------|---------------|------------|-----------|
| 1 year | 85% (17/20) | 93.8% (15/16) | 82.3% (51/62) | 50% (6/12) | 50% (4/8) |
| 5 years | 85% (17/20) | 93.8% (15/16) | 80.6% (50/16) | 50% (6/12) | 50% (4/8) |
| 9 years | 85% (17/20) | 93.8% (15/16) | 77.4% (48/62) | 50% (6/12) | 50% (4/8) |

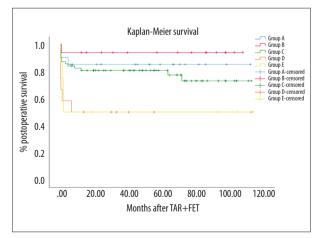


Figure 1. Survival curve after TAR+FET.

replacement was the previous operation in 62 patients, which is more than 50% of the total number of patients. All of these 62 patients were diagnosed with aneurysms or aortic dissection, suggesting that the main reasons for the secondary aortic arch replacement were: (1) Progression of the dissection or aneurysm, and the aortic arch is involved, and (2) Improper choice of the initial surgical method. For example, when aortic dissection or aneurysm involved a wide range of lesions, simplified surgery or the total arch replacement of the fast branch vessels were performed, resulting in residual dissection or severe internal leakage. The best surgical choice for type A AD treatment has previously been controversial, but studies [4,5] have shown that (TAR+FET) has become the 'standard procedure' for the treatment of type A AD. Although operation on the great artery can currently be done by many hospitals in China, primary hospitals conduct ascending aortic replacement or root replacement instead of more thorough surgical methods only for patients with acute type A aortic dissection, due to technical conditions

and hardware factors, which will lead to reoperation in the future. The literature has reported that the 5-year survival rate for type A AD patients receiving simple ascending aortic replacement or root replacement for the first time is only 70-80%, the 10-year reoperation rate is more than 10% [6-9], and the average age of Chinese patients is around 45 years old. These results are unacceptable, since the average age of the patients in this study was 44.7 years old. Furthermore, the expansion of residual dissection after type A dissection is also responsible for reoperation. In general, the proximal end of the aortic arch and descending aorta is the most easily dilated part of the aorta. Immer et al. [10] found that 86% of the aortic long-term expansion occurred in the aortic arch and proximal to the descending aorta. Some studies reported that aortic arch surgery is considered only when its inner diameter reaches 5-6 cm or the expansion speed exceeds 0.5 mm/year. In China, type A AD occurs mostly in young and middle-aged patients. For this reason, Professor Sun et al. [11] initiated TAR+FET ("Sun's procedure"), which greatly reduced the need for aortic arch reoperation. The indications include: retrograde aortic dissection, primary endometrial rupture at the aortic arch or distal end, aortic aneurysm or occlusion in branches of iocephalic arteries, aneurysm in the arch or the descending aortic arch, and Marfan syndrome.

In this study, the number of patients who underwent AVR for the first time in the aortic arch intervention was second only to those who underwent root replacement, accounting for 16.9% of the total number. The main reason was the new onset of type A AD after AVR. Previous studies have shown that the incidence of AD after AVR is about 0.6% [12,13]. For patients with aortic valve disease combined with ascending aortic dilatation, the choice of AVR or AVR+ascending aortoplasty or valve replacement has a crucial impact on the prognosis, directly determining whether secondary aortic intervention will be needed in the future. For patients with aortic insufficiency (AI) combined with ascending aortic dilatation, occult lesions often occur in the aortic wall [14]. For these patients, the initial surgery of AVR or AVR+ascending aortoplasty may lead to persistent expansion of the ascending aorta and development of aortic dissection. Aortic stenosis (AS) patients combined with ascending aortic dilatation are often complicated with lesions in the aortic wall if the etiology lies in the bicuspid aortic valve. AVR without the ascending aortic replacement may cause the persistent expansion of arteries after surgery, leading to development of type A AD, resulting in reoperation [15,16]. In addition, improper surgical procedure can also lead to need for reoperation. Some studies have found that in patients with AD after AVR and requiring reoperation, some patients developed endometrial rupture originated from the aortic sinus at the annulus because of tearing of the aortic wall caused by the suture needle being inserted too close to the sinus wall [17].

Another cause of aortic arch reoperation is the various anastomotic leakages that occur after dissection or aneurysm surgery, including coronary anastomotic leakage, paravalvular leakage, proximal anastomotic leakage, and distal anastomotic leakage. Some anastomotic leakage enters into the mediastinum or the thoracic cavity to form a pseudoaneurysm. If anastomotic leakage enters the wrapping cavity of the ascending aorta, it may cause a large number of left-to-right shunts, which results in heart failure. A study [18] reported that the occurrence of anastomotic leakage may be associated with aortic dissection infection and a combination of autoimmune diseases. Studies performed outside China [19,20] have reported that the main causes of anastomotic leakage include: weak vascular tissue at the anastomosis site (dissection, arteritis, and Behcet's disease); poor anastomosis technique; graft infection or mediastinal infection; and aortic tissue necrosis due to the intraoperative use of biological glue. In the present study, GRF glue was not used, so we considered that the cause of anastomotic leakage may due to the weakening of the aortic wall and anastomotic techniques. For patients with simple anastomotic leakage, re-anastomosis is generally not required. The anastomotic leakage that occurred in this group was the development of a new arterial lesion or an old lesion, so a secondary TAR+FET was performed.

Among the patients undergoing a secondary TAR+FET procedure, the mortality rate within 30 days after operation was 13.6%, and the long-term mortality rate was 23.7%, which is generally equivalent to the in-hospital mortality rates of 9–25% in other studies [21–23]. Thus, TAR+FET is feasible for use in treating macrovascular disease after cardiac surgery and does not increase the risk of mortality.

This study found that patients who had previously undergone arch surgery had significantly greater intraoperative bleeding volume and shorter survival time than did those undergoing other surgeries. The reason for this may be that arch surgery is more complicated than others, and techniques including deep hypothermic circulatory arrest, arch reconstruction, branch vessel revascularization and brain protection used during the operation have great impacts on the heart and other organs. Therefore, aortic arch reoperation is more difficult in patients whose previous surgery was arch surgery than in those undergoing other surgeries, and resulting in a difficult operation that leads to increases in the operation time and intraoperative bleeding volume. On the other hand, a larger bleeding volume will have a greater impact on the systemic organs of patients after the operation, resulting in an increase in the incidence of complications and shorter long-term survival. The preoperative conditions are more complicated in patients who previously underwent arch surgery than in those undergoing other surgeries. Since there are various complications and residual problems of the first operation, reoperation may result in increased complexity of the secondary arch surgery and

decreased survival rate. A limitation of this study is its small sample size, which cannot reflect the real situation of patients, and further studies on this topic are warranted.

Conclusions

The main causes of aortic reoperation are new dissection or aneurysm, progression of dissection and aneurysm, and anastomotic leakage. The TAR+FET technique was feasible and

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efficacious for aortic reoperation with prior cardiac operation since the short-term mortality in patients with recurrent aortic arch disease after cardiac surgery is not high. The bleeding volume was significantly increased and the long-term survival time was significantly shorter during the reoperation after the aortic arch surgery than that in other operations.

Conflict of interest

The authors declared no conflict of interest.

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