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Challenges and outcomes of complex endovascular aortic repair

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Challenges and outcomes of complex endovascular aortic repair

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Table of contents

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Editorial: Challenges and outcomes of complex endovascular aortic repair

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Editorial on the Research Topic
Challenges and outcomes of complex endovascular aortic repair

Aortic disease constitutes an important spectrum of arterial diseases including aortic aneurysms (aortic arch, thoracoabdominal and abdominal aorta), acute aortic syndromes (aortic dissection, intramural hematoma, penetrating ulcer and aortic injury), as well as genetic diseases and congenital pathologies (Marfan syndrome, coarctation of the aorta etc.). Endovascular aortic repair has gained wide acceptance in treating patients with complex aortic pathology and has been established as the treatment of choice for most patients with suitable anatomy.

Type A aortic dissection is an acute condition that should be treated by emergent operation immediately after the diagnosis (1). Open repair has been the treatment of choice for most patients. In recent years, hybrid methods have been introduced as a simpler and safer alternative approach. Liu et al. examined the use of ministernotomy in comparison to total arch replacement with frozen elephant trunk in patients with type A aortic dissection. Liu et al. They found that total arch replacement via ministernotomy was safe, feasible, with similar short-term prognosis and also reduced ICU and hospital stay. Patients with type A dissection have a high complication risk. Without intervention, the risk of death raises 1%–2% per hour, while half of patients die within the first 24 h after diagnosis (1). Several biomarkers have been related to higher in-hospital mortality for patients with aortic dissection, showing an incremental prognostic value that can aid in decision making (2). Xie et al. explored the predictive value of preoperative nutritional index (PNI) combined with D-dimer in patients with acute type A dissection. Both markers were independent predictive factors for adverse events during hospitalization. Additionally, Miao et al. found an increase in a certain secreted frizzled-related protein in patients with acute aortic dissection that also may affect the prognosis of the disease.

Long term durability of thoracic endovascular repair depends on the preservation of an adequate proximal sealing zone. The 2020 SVS guidelines support that preoperative or concurrent left subclavian artery (LSA) revascularization is necessary for elective TEVAR (3). Ye et al. reported 83 patients undergoing fenestration or chimney technique to preserve LSA during zone 2 TEVAR for dissection. Complete thrombosis

in the aorta distal to the stent graft was above 60% in both techniques with high technical success Ye et al. One of the worst complications after TEVAR is the occurrence of retrograde type A aortic dissection (RTAD) (4). RTAD may occur rarely but may be associated with a high mortality rate (5). Wang et al. reported on 1688 TEVAR patients and found that RTAD occurred in 1. 1% of the patients during the procedure, at early and at late postoperative periods. Stent graft oversizing ratio was the only relevant risk factor for RTAD Wang et al. Additionally, aberrant right subclavian artery (ARSA) constitute the most common congenital anomaly of the aortic arch, arising from the proximal portion of the descending thoracic aorta and affecting 0.5%–1% of the population (6). The presence of an aberrant right subclavian artery in patients with type B aortic dissection undergoing TEVAR may affect outcome as the primary tear is often located near the aortic isthmus and the ARSA. Zeng et al. reported their experience in 9 cases and found excellent technical success rate and minimum complications with a mean follow-up period of three years.

The presence of intramural hematoma (IMH) in the proximal sealing zone has also been associated with a worse outcome. Lescan et al. examined two groups of 84 patients with and without intramural hematoma at the proximal landing zone undergoing TEVAR for acute and subacute type B dissections. Migration >10 mm and bird-beaks (failure to achieve a complete proximal seal on the inner curvature of the aorta presenting as a wedge-shaped gap between the stent graft and the aortic wall) (7) were comparable in both groups, while the presence of the IMH may not be relevant to the occurrence of the retrograde type A dissection as a complication after TEVAR Lescan et al.

In complex aortic repair, fenestrated and branched endovascular aortic repair (F/BEVAR) have been efficient and safe in treating patients with supra/pararenal aneurysms (8, 9). However, further advances are needed to decrease the associated morbidity and mortality that accompanies these complex procedures. Kapalla et al. showed that inner-branch technology may provide a feasible therapeutic option in these patients, depicting a high technical success (100%), excellent estimated survival (95%) and branch patency (98%) during a 1-year mean follow-up. Additionally target vessel patency after the procedure is an important factor contributing to the technical and clinical success of F/BEVAR. Loss of patency especially for the superior mesenteric artery (SMA) may become fatal. Gallitto et al. reported their experience with the fate of SMA incorporated during complex aortic procedures. Relining of the SMA stent graft was necessary in 21% of the cases, while SMA orientation determines the necessity of such approach. An aortic diameter >35 mm at the SMA level predicted SMA related adverse events.

Type II endoleak (ET II) has been defined as collateral retrograde flow from the aortic branches. Although half of ET II will spontaneously resolve during follow-up, the sac will increase in up to 25% of patients (10). ET II is considered a benign condition in most cases, however its persistence has been associated with sac expansion and adverse events during the follow-up period (10). Chen et al. examined the association between ETII and the iliolumbar artery and identified the number of lumbar arteries and inferior mesenteric artery diameter as independent risk factors for ET II. Reinterventions for the persistent ET II did not affect long term survival or increased aneurysm related mortality after EVAR.

Coarctation of the aorta is a congenital pathology that has been associated with severe cardiac complication if left untreated. Patients with coarctation of the aorta should be followed on a regular basis despite surgical repair. Zhao et al. identified several risk factors for recurrence after surgical repair including preoperative z-score of the ascending aorta and transverse aortic arch, an arm-leg systolic pressure gradient. Patients with these factors may need close surveillance especially within the first postoperative year.

Advanced endovascular techniques and specialized devices are making endovascular repair a viable option in treating complex aortic pathology. As those techniques and experience with the endografts progress, and the durability of the repair is established and improved upon, we expect that endovascular means will be used more frequently as the treatment of choice for patients with any complex aortic disease.

Author contributions

GK: Conceptualization, Writing – original draft, Writing – review & editing. KS: Writing – review & editing. W-HE: Writing – review & editing. TK: Writing – review & editing.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Risk factors for recurrence after surgical repair of coarctation of the aorta in children: a single-center experience based on 51 children

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Background: Coarctation of the aorta (CoA), is a congenital malformation, often combined with several cardiac abnormalities. At present, the operation effect is satisfactory, but postoperative restenosis is still a matter. Identification of risk factors for restenosis and prompt therapy adjustments may improve patient outcomes.

Materials and methods: A retrospective clinical study of patients under 12 who had CoA repair in 2012–2021, with a randomized cohort population of 475 patients.

Results: A total of 51 patients (M/F: 30/21) with a mean age of 5.33 (2.00–15.00) months and a median weight of 5.60 (4.20–10.00) kg. The mean follow-up was 8.93 (3.77–19.37) months. Patients were divided into 2 groups: no-restenosis (n-reCoA) (G1, 38 patients) and restenosis (reCoA) (G2, 13 patients). ReCoA was defined as a restenosis requiring interventional or surgery or a pressure gradient >20 mmHg at the repair site as reported by B-ultrasound with the presence of an upper and lower limb blood pressure gradient or growing dysplasia. The overall reCoA incidence was 25% (13/51). In multivariate COX regression, smaller preoperative z-score of the ascending aorta ($P = 0.009$, HR = 0.68) and transverse aortic arch ($P = 0.015$, HR = 0.66), arm-leg systolic pressure gradient ≥12.5 mmHg at discharge ($P = 0.003$, HR = 1.09) were independent risk factors for reCoA.

Conclusion: The overall outcome of CoA surgery is successful. Smaller preoperative z-score of the ascending aorta and transverse aortic arch, and an arm-leg systolic pressure gradient ≥12.5 mmHg at discharge increase reCoA risk, and closer follow-up for such patients are required especially within 1 postoperative year.

KEYWORDS

coarctation of the aorta (COA), congenital heart disease - cardiac, pediatrics - children, risk factor, surgical treatment

Introduction

Coarctation of the aorta (CoA), a congenital abnormality, often occurs in the arterial catheter or arterial ligament region, which has an incidence rate of about 0.287‰ and accounts for 3.57% of all congenital cardiovascular malformations (1). It can be isolated or with additional cardiac abnormalities such as ventricular septal defect and patent ductus arteriosus (2). End-to-end anastomosis (EEA) was first proposed by Crafoord and Nylin in 1945 (3), but with a significant rate of restenosis (reCoA) (4–6). People have used a variety of methods to reduce postoperative mortality and restenosis rate to improve patient survival time and quality, including patch aortoplasty (PAP), subclavian artery valvuloplasty, expanded end-to-end anastomosis (EEEA), end-to-side anastomosis (ESA), and balloon angioplasty. Advancements in science and technology have dramatically reduced mortality (7), therefore reCoA has attracted more focus. Several studies have shown contradictory outcomes on age and weight at the surgical procedure and other variables (8–12). This research aimed to collect data and examine risk factors of reCoA to guide clinical practice.

Materials and methods

Study population

This is a retrospective study of patients who underwent CoA surgical procedures at the Children's Hospital of Chongqing Medical University between 2012 and 2021. Patients were eligible if they met the following criteria: (1) age ≤12 years old, (2) had preoperative echocardiography and cardiac CT scan and three-dimensional reconstruction, (3) CoA is the main diagnosis, and (4) successful follow-up after discharge. Evaluate available data (all obtained by gathering clinical records, surgery reports, and discharge records) to detect reCoA risk factors. A total cohort population of 51 people was enrolled randomly from 475 patients. Demographic data (such as gender, age, and weight at the time of surgical procedure), perioperative data [such as whether cardiotonic agents were used before surgery, operation procedures, time of cardiopulmonary bypass (CPB), and so on], and follow-up data were gathered. The surgical treatment was considered a success if patients did not die after the operation, the Doppler pressure gradient across the repair site <20 mmHg during the follow-up, and the blood pressure of the upper limb was lower than that of the lower limb, and no evidence of hypertension. The hypertension diagnostic criteria were based on the China Guidelines for Prevention and Treatment of Hypertension, the systolic blood pressure (mmHg) for boys over 100 + 2× age (years), and girls over 100 + 1.5× age (years), or taking antihypertensive agents. When the z-score of the transverse arch < −2, hypoplastic aortic arch (HAA) can be diagnosed. The pressure gradient obtained by echocardiography varies depending on the location of the constriction. Use echocardiography to determine the flow rate at the constriction, and the pressure was estimated using the simplified Bernoulli equation $P = 4V^2$. The Children's Hospital of Chongqing Medical University's Ethics Committee authorized the study, and all patients signed the informed consent form.

Surgical technique

The suitable surgical technique was chosen based on the patient's clinical state, including combined intracardiac malformations, preoperative cuff blood pressure, medical imaging data such as ultrasonic cardiogram and CT scan, and requests of their parents. A median sternotomy method is chosen for patients with intracardiac abnormalities that require simultaneous repair and CPB. A lateral thoracotomy method is chosen for patients with intracardiac abnormalities that can be treated minimally invasively without CPB. EEEA, ESA, and PAP are the three main categories of surgical techniques. The anastomotic strain encountered throughout the procedure determines the use of certain surgical techniques. In general, patients with simple isthmus aortic coarctation are treated with EEEA, whereas those with hypoplastic aortic arch may be treated with ESA and PAP. It should be highlighted that SAR was chosen by two patients. After performing SAR on the two patients during the operation, the surgeon noticed that the invasive systolic blood pressure difference between the brachial artery and the femoral artery had returned to normal (upper limb < lower limb). The surgeon then immediately informed the patients' families of this finding and they decided to change the preoperatively decided surgical plan and adopt SAR.

Statistical methods

Kolmogorov-Smirnov test examines the normality of continuous variables. Normal distribution variables were shown as mean ± standard deviation (SD), compared by Student's t-test or ANOVA. The skewed distribution variables were shown as medians (P25, P75), compared by the Wilcoxon signed-rank test. Chi-square test, corrected Chi-square test, or Fisher exact test compared rates or component ratios. Echocardiographic data and demographics were potential predictors. Only variables ($P < 0.2$) with univariate COX regression were included in multivariable COX regression operated by stepwise regression. ROC curve was used to determine the best cutoff (Jordan index-based) with the maximum sensitivity and specificity for a critical continuous risk factor. AUC measured accuracy. ReCoA-free survival rate was conducted by Kaplan–Meier curve. The log-rank test compared patient subgroups' differences in freedom from event (reCoA vs. n-reCoA) rates. The statistically significant difference was defined as $P < 0.05$, and all statistical analyses were performed using SPSS26.0 software.

Results

The study cohort included 51 patients (30 males, 21 females) with a 25% (13/51) incidence of reCoA. The median weight was 5.60 kg (interquartile range, 4.20–10.00 kg) and the mean age was 5.33

months (interquartile range, 2.00–15.00 months). The mean follow-up was 8.93 months (interquartile range, 3.77–19.37 months). Patients were divided into two groups: n-reCoA (G1, 38 patients) and reCoA (G2, 13 patients). Table 1 compares demographics and surgical variables. Concomitant hypoplastic aortic arch appeared to be a reCoA risk factor with 10 patients (26%) in G1 and 8 patients (62%) in G2, respectively ($P = 0.050$). As for gender, 10 males and 3 females had reCoA ($P = 0.125$). And 6 of 26 VSD patients (23%) and 7 of 25 non-VSD patients (28%) had ReCoA ($P = 0.687$). Surgical age shows no significant difference in <1 month compared with the other two groups ($P = 0.751$). Variables including surgical weight and CPB time did not statistically differ ($P > 0.05$).

Table 2 shows the relationship between surgical protocol and reCoA. The six surgical regimens were statistically comparable ($P > 0.05$) (Figure 1A). We may hypothesize that selecting the optimal surgical strategy for each case is acceptable since reCoA rates after surgery are not significantly different. Meantime, in certain patients, simple aorta releasing (SAR) may achieve the therapeutic goal (1/2, 50%), highlighting the importance of fluid dynamics even with Artificial Intelligence technology in CoA diagnosis and therapy (Figure 2).

Figure 3 compares data for different time nodes of G1 and G2. Preoperatively, the mean gradient of G1 was slightly higher than

TABLE 1 Demographic and perioperative variables.

Variable	G1 no-reCoA ($n = 38$)	G2 reCoA ($n = 13$)	P value
Age at operation			
<1 mo	6	2	0.751
1–12 mo	22	6	
1–12 yrs	10	5	
Weight at operation (kg)	5.05 (4.07–8.75)	9.00 (4.70–10.00)	0.173
Incision (median sternotomy/ lateral chest)	19/19	7/6	0.811
Crossclamp time (min)	43.31 (24.79–83.00)	54.93 ± 7.23	0.681
CPB time (min)	108.49 ± 7.59	117.42 ± 10.28	0.536
Operation time (min)	212.50 (113.75–250.75)	193.62 ± 17.78	0.991
Extubation time (d)	5.50 (4.00–8.50)	6.08 ± 0.65	0.896
ICU time (d)	9.00 (4.00–13.00)	8.04 ± 1.17	0.690
Hospitalization time (d)	25.46 ± 1.42	20.69 ± 1.92	0.079
Congenital heart malformation, *n* (%)			
VSD	20 (53)	6 (46)	0.687
ASD	23 (61)	6 (46)	0.366
PDA	29 (76)	8 (62)	0.502
BAV	3 (8)	2 (15)	0.808
HAA	10 (26)	8 (62)	0.050
Mitral stenosis	3 (8)	0	0.561
PLSVC	3 (8)	2 (15)	0.808
Congenital extracardiac malformation	7 (18)	1 (8)	0.634

Comparison of demographic and surgical variables. Values are shown as mean ± standard deviation (SD), median (P25-P75), or number (percent %). CPB, cardiopulmonary bypass; ICU, intensive care unit; VSD, ventricular septal defect; ASD, atrial septal defect; PDA, patent ductus arteriosus; BAV, bicuspid aortic valve; HAA, hypoplastic aortic arch; PLSVC, persistent left superior vena cava.

TABLE 2 Relationship between surgical protocol and reCoA.

	EEEA ($n = 30$)	ESA ($n = 10$)	PAP ($n = 9$)	SAR ($n = 2$)	Total ($n = 51$)	P value
reCoA, *n* (%)	8 (27)	2 (20)	2 (22)	1 (50)	13 (25)	0.809

The relationship between surgical protocol and reCoA. Values are shown as number (percent %). EEEA, extended end-to-end anastomosis; ESA, end-to-side anastomosis; PAP, patch aortoplasty; SAR, simple aorta releasing; reCoA, recurrent coarctation.

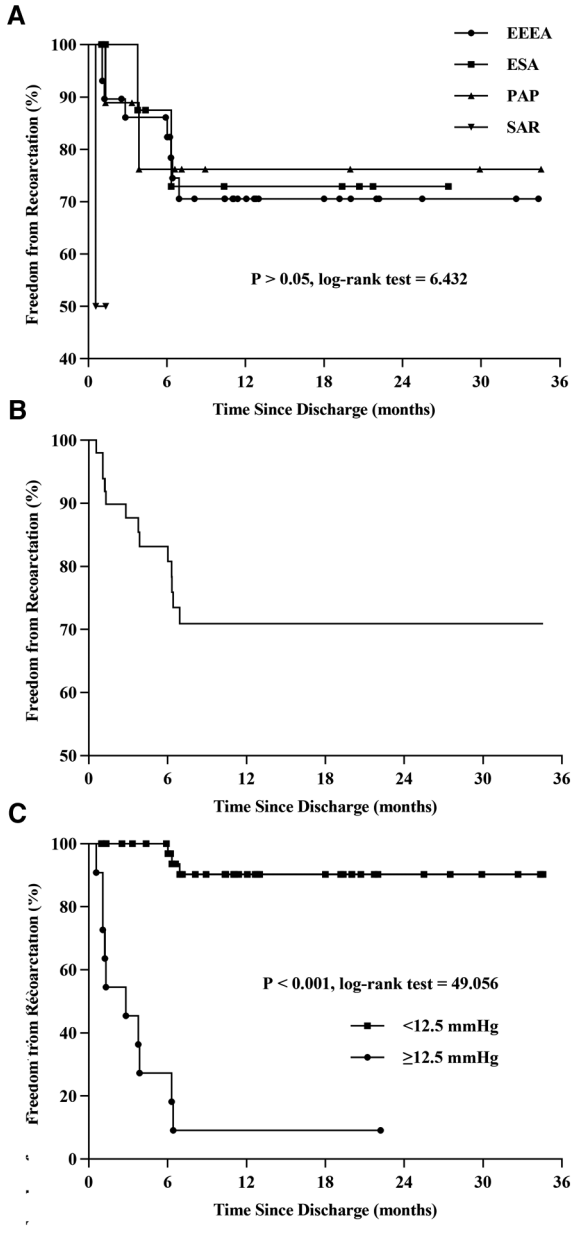

FIGURE 1
Kaplan-Meier curve. Compare the differences of reCoA among the six surgical options (A). Freedom from reCoA after discharge (B). Patients with a blood pressure gradient ≥12.5 mmHg at discharge have a significantly higher rate of reCoA (C). EEEA, extended end-to-end anastomosis; ESA, end-to-side anastomosis; PAP, patch aortoplasty; SAR, simple aorta releasing; reCoA, recurrent coarctation.

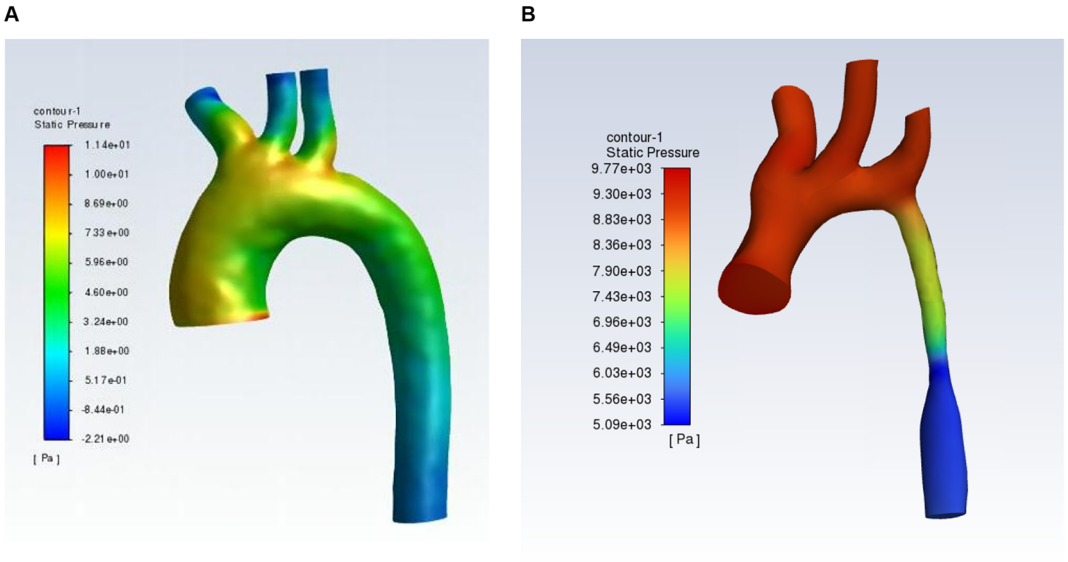

FIGURE 2
Hydrodynamics shows normal aortic arch (A) and coarctation of the aorta (B).

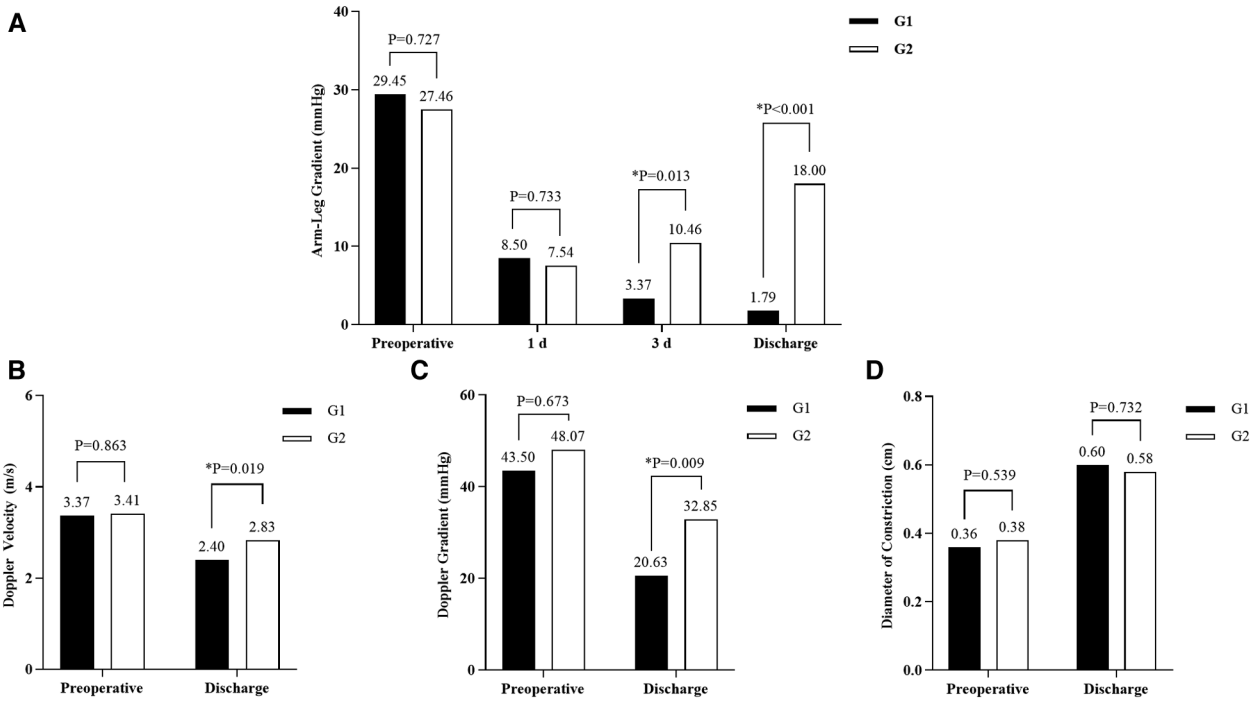

FIGURE 3
Changes in patient data from postoperative to discharge. Systolic blood pressure gradient (arm-leg) (A). Doppler peak flow velocity across the repair site (B). The Doppler pressure gradient across the repair site (C). Diameter of constriction (D). *Statistical significance.

that of G2 (29.45 ± 2.87 vs. 27.46 ± 4.81, $P = 0.727$). Although the mean gradient of G1 was almost identical to that of G2 one day after surgery (8.50 ± 2.49 vs. 7.54 ± 1.30, $P = 0.733$), it was significantly higher in G2 than G1 three days after surgery (10.46 ± 2.06 vs. 3.37 ± 1.45, $P = 0.013$) and at discharge (18, 11.5–21 vs. 1.79 ± 1.12, $P < 0.001$). The gradient of G2 at discharge was about 9 times that of G1 and gradually increased during the period (1 d after surgery, 3 d after surgery, and at discharge), while the gradient of G1 at discharge was lower than that during hospitalization (Figure 3A).

The mean peak Doppler flow velocity at the repair site: G1 was significantly lower than G2 at discharge (2.40 ± 0.09 vs. 2.83 ± 0.14,

$P = 0.019$) while almost similar preoperatively (3.37 ± 0.14 vs. 3.41 ± 0.17, $P = 0.863$). Both groups had significantly lower velocity after the operation (G1: $P < 0.001$; G2: $P = 0.006$) (**Figure 3B**).

G1 had a significantly lower mean pressure gradient at the repair site than G2 at discharge (20.63, 16.24–30.30 vs. 32.85 ± 3.14, $P = 0.009$), which was almost comparable to G2 before surgery (43.50, 32.00–62.25 vs. 48.07 ± 4.52, $P = 0.673$). Gradient made a significant reduction in both groups (G1: $P < 0.001$; G2: $P = 0.009$) (**Figure 3C**).

The average diameters of repair site in G1 and G2 were almost identical before and after surgery (Preoperative: G1: 0.36 ± 0.02, G2: 0.38 ± 0.03, $P = 0.539$; Postoperative: G1: 0.60 ± 0.03, G2: 0.58 ± 0.03, $P = 0.732$). The diameter increased significantly in both groups at discharge (G1: $P < 0.001$; G2: $P = 0.001$) (**Figure 3D**).

Use ROC curve to determine which time point between pre-surgery and discharge most affected reCoA and was then included in COX regression. The arm-leg systolic blood pressure gradient, Doppler peak blood flow velocity, and pressure gradient across the repair site (at discharge) were all well affected (**Table 3**).

The multivariate COX regression includes variables with $P < 0.2$ in univariate COX regression (**Table 4**). Among the variable examined, the smaller preoperative z-score of the ascending aorta, the smaller preoperative z-score of the transverse aortic arch, and the higher arm-leg systolic blood pressure gradient at discharge were independent risk factors for reCoA ($P < 0.05$).

The Kaplan-Meier curve predicted freedom from reCoA was 70.9% after an average follow-up of 8.93 months (interquartile range, 3.77–19.37 months) (**Figure 1B**).

The median time from discharge to reCoA was 3.77 months (interquartile range, 1.15–6.32 months). All 13 patients had reCoA within one year, 1 had balloon angioplasty one year after discharge, and 1 is taking antihypertensive agents now, the other 11 patients are currently under close follow-up at the discretion of their parents.

The optimum cutoff for arm-leg systolic pressure gradient at discharge, based on the ROC curve and AUC area, was 12.5 mmHg, with a sensitivity of 76.9% (G2: 10/13) and specificity of 97.4% (G1: 1/38). Thus, patients with a gradient of 12.5 mmHg or higher at discharge had a significantly increased risk of reCoA during follow-up (**Figure 1C**, log-rank = 49.06, $P < 0.001$).

Discussion

Coarctation of the aorta (CoA), the sixth most common CHD (13), may occur anywhere in the aorta, mainly distal to the left subclavian artery (14, 15). Morgagni reported CoA in 1760. It could be isolated or related to long-segment stenosis or hypoplastic aortic arch (16). Various CoA treatments now exist, including balloon angioplasty reported by Singer in the 1980s (17). With the decline in surgical mortality, reCoA has received increasing attention with a rate of 5.9–46.6% (18). ReCoA risk factor analysis provides conflicting findings. Young age, low weight, hypoplastic aortic arch, and pressure gradient may increase risk (8–11, 19). In this study, 13 of 51 children developed reCoA within a year, and 1 got balloon angioplasty with satisfactory results. The smaller preoperative *z*-score of the ascending aorta, the smaller preoperative *z*-score of the transverse aortic arch, and the arm-leg systolic blood pressure gradient ≥12.5 mmHg at discharge have an increased risk of reCoA in our patients.

Our research found no significant difference between gender and reCoA ($P = 0.249$), which consists of multiple studies (9, 20, 21). In a study of 167 patients by Burch (10), female showed significant difference ($P = 0.04$, HR = 2.77). 11 females had reCoA (1 Turner's syndrome), which they considered difficult to explain. It has been reported that 7%–12% of Turner syndrome girls in childhood have COA (22). Gene loss on the short arm of the X chromosome may cause isolated CoA (23).

Age and weight at surgery did not increase the risk of reCoA. This finding matched Adamson's study (age, $P = 0.73$) (19). Bacha showed that surgical weight <1.5 kg increased the risk of reCoA (24). It has previously been argued that delaying surgery properly may lower the risk in well-controlled patients. That may be because the aortic arch and constrictions expand steadily as the patient ages, making it easier to detect and remove aberrant areas during operation. With the improved surgical ability and perioperative control, we believe age and weight have lessened their effect on reCoA.

PGE1 has been proven to keep arterial ducts even constrictions open to sustain life. Liberman found ectopic ductal-like tissue in the aorta may induce CoA (25). PGE1 relieves blockage even arterial catheter is closed. Ajay suggested that high-dose PGE1 may treat serious patients with CoA who were unsuccessful in the standard dose (26). However, Burch found that 14 of 105 PGE1-treated patients had reCoA, compared to 1 of 41 non-PGE1-treated

TABLE 3 Accuracy in predicting reCoA.

Variable	Arm-leg gradient			Doppler velocity			Doppler gradient		
Time point	AUC	95% CI	*P* value	AUC	95% CI	*P* value	AUC	95% CI	*P* value
Preoperative	0.432	0.25–0.61	0.469	0.554	0.37–0.73	0.567	0.539	0.36–0.72	0.673
1 d	0.432	0.28–0.58	0.469	/			/		
3 d	0.705	0.56–0.85	0.028	/			/		
Discharge*	0.935	0.86–1.00	<0.001	0.740	0.58–0.90	0.010	0.743	0.59–0.90	0.009

Comparison data for different time nodes of G1 and G2. AUC, the area under the curve; CI, confidence interval; reCoA, recurrent coarctation.
*Data at the time point are included for further analysis.

TABLE 4 COX regression of reCoA affecting variables.

Variable	*P* value, Exp (b), 95% CI	
	Univariate	Multivariate
Gender: male/female	0.249, 2.14 (0.59–7.76)	
Age at operation	0.137, 1.02 (0.99–1.05)	0.054, 1.04 (1.00–1.07)
Weight at operation	0.101, 1.08 (0.99–1.19)	
Preoperative cardiotonic agents (with or without)	0.173, 0.24 (0.03–1.86)	
Surgery option (radical vs. SAR)	0.042, 0.10 (0.01–0.92)	0.103, 0.01 (0–2.80)
Preoperative ascending aorta, *z*-score	<0.001, 0.59 (0.49–0.71)	0.009, 0.68 (0.51–0.91)
Preoperative transverse aortic arch, *z*-score	<0.001, 0.62 (0.50–0.76)	0.015, 0.66 (0.47–0.92)
Preoperative descending aorta, *z*-score	0.278, 0.84 (0.62–1.15)	
Peak Doppler flow velocity across the repair site at discharge	0.014, 3.23 (1.27–8.24)	
The pressure gradient across the repair site at discharge	0.016, 1.05 (1.01–1.09)	
Arm-leg systolic blood pressure gradient at discharge	<0.001, 1.10 (1.06–1.14)	0.003, 1.09 (1.03–1.15)

The multivariate COX regression includes variables with $P < 0.2$ in univariate COX regression. CI, confidence interval; reCoA, recurrent coarctation.

patients ($P = 0.07$) (10). We did not use PGE1 preoperatively, thus this factor has not been studied in this study and may be explored in the future. Similar to our findings, reCoA has not been connected to cardiac abnormalities (8, 9, 19, 27).

We believed preoperative cardiotonic agents do not increase the risk of reCoA. But Truong found that did ($P = 0.04$, HR = 5.57), while multivariate analyses did not (12). We hypothesized that probably because most young PGE1 recipients were treated with cardiotonic agents preoperatively.

Many studies have examined how surgery option affects reCoA. Several procedures have been developed to reduce risk. However, the optimal one is still debated (28, 29). Crafoord proposed EEA in 1944 (3), despite a decreased mortality (6), the reCoA rate was high (4–6), probably because of incomplete resection of the catheter tissue, which partially grow into the normal-appearing aorta wall, lack of growth at the circular anastomosis and the hypoplastic aortic arch. Thus, patch aortoplasty has gradually replaced EEA (30). Patches materials include artificial materials, allogeneic blood vessels, autologous pulmonary artery, or pericardium. The anastomotic stoma is tension-free, collateral vessels do not need to be ligated or disconnected, and the hypoplastic region of the arch can be extended at the same time. But Adamson linked patch material to reCoA ($P = 0.014$, OR = 9.26) (19), and long-term patch's contralateral aortic posterior wall aneurysm is another potential risk (31). EEEA can better manage remaining catheter tissue, protect the left subclavian artery, avoid artificial materials, retain natural vascular architecture, lower aneurysm risk, and repair transverse arch and isthmus dysplasia (32). Meantime, EEEA reduces mortality and reCoA rate (33, 34) and promotes long-term aortic compliance (35), so it may be the best potential surgery. Patients with other CHD may accept one-period surgery through median sternal, with satisfactory outcomes (36, 37). Results from the analysis of ESA were similar (33, 37, 38). Balloon angioplasty can cure reCoA well (10, 17, 39), with a 93% success rate (40). One reCoA patient in this study got balloon angioplasty without any additional intervention.

Each strategy has pros and cons. EEEA or ESA may cause patients to suffer from large-scale surgery, which is psychologically and financially taxing. Nearly 60% of patients in this research had successful EEEA. Meantime, if we took EEEA, ESA, and PAP as radical surgery whereas SAR was considered a relative surgery. Neither was proven to be reCoA risk factor ($P = 0.075$). Although fewer patients had SAR, we assumed that careful selection of operation according to ease patients may even prevent major surgery. Therefore, in the future, we may take more in-depth research on the morphology and hydrodynamics of the aortic arch during the perioperative period, and even pre-do the operation with Virtual Reality (VR), to allow surgeons to better determine the therapy for patients.

Multiple studies have explored aortic arch morphology and whether systolic blood pressure gradient affects reCoA. We found that the preoperative *z*-score of the ascending aorta impacted reCoA ($P = 0.009$), which matched Kumar (34). In this 10-variable research, reCoA was only associated with a small preoperative ascending aorta ($P < 0.01$). McElhinney agreed ($P = 0.02$, HR = 2.1), but disagreed when body weight was the indicator ($P = 0.48$, HR = 1.34) (9). This may be because children with lower body weight in cohorts of patients had a lesser ascending aorta. Unfortunately, maybe because of the limited sample size in the cohort, we could not identify an optimal cutoff for the ascending aorta z-score linked with reCoA. Future research in larger cohorts is conceivable.

A smaller preoperative z-score of the transverse aortic arch increased the risk of reCoA ($P = 0.015$). Burch found that for every 1 mm increase in aortic arch transverse diameter, reCoA risk was reduced ($P = 0.04$, RR = 0.57) (10). However, Kumar (34) cannot relate transverse arch dysplasia to reCoA. Truong found that preoperative aortic arch measurements and transverse aortic arch abnormalities were not reCoA risk factors in thoracotomy patients (12). We believe our findings are reliable, cardiac surgeons should choose the approach carefully for patients with smaller preoperative z-score of the transverse aortic arch to improve their outcomes.

Arm-leg systolic blood pressure gradient ≥12.5 mmHg at discharge affected reCoA ($P < 0.001$, log-rank = 49.06). Kumar examined blood pressure gradients at 24 h, 48 h, and 72 h following surgery and at discharge, finding that the gradient at discharge was significant compared with other points (34), reCoA was more likely in patients with a gradient >13 mmHg ($P < 0.001$, log-rank = 19.49). Although we considered that in the

early postoperative stage, blood pressure was unstable due to operation, anesthesia, and other factors, we think the conclusion is reliable. In the future, more precise pressure measurements can help further explore its relationship with reCoA.

About 60% (8/13) developed reCoA within 6 postoperative months, and all within one year. Therefore, we suggested that closer follow-up is necessary for the first year postoperatively.

Limitations

This work is unusual because we evaluated the impacts of several parameters on reCoA and found the blood pressure cutoff and its specificity and sensitivity to better predict reCoA, which has great practical application. However, our study had several limitations. This is a retrospective study that has the inherent limitations of any retrospective study. Five congenital cardiac surgeons operated the surgical procedures and at least three different echocardiography specialists were included to take the measurements of aortic arch morphology preoperatively and postoperatively. Meanwhile, several issues need to be explored, including the best preoperative z-score cutoff of the ascending aorta and transverse aortic arch, which may be examined in a larger sample cohort. For reCoA, because the follow-up did not exactly follow the plan, the accurate reCoA time may be earlier, but all reCoA can be found within 1 year after the surgical procedure, so we think it does not affect the study results.

Conclusion

In conclusion, the smaller preoperative *z*-score of the ascending aorta, the smaller preoperative *z*-score of the transverse aortic arch, or the discharge arm-leg systolic blood pressure gradient ≥12.5 mmHg make an increased risk of reCoA. We suggested more active follow-up for such patients, especially within 1 postoperative year, to detect reCoA timely.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Institutional Review Board of Children's Hospital of Chongqing Medical University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

ZZ, ZP, and XJ contributed to the conception and design of the study and the critical revision of the manuscript. ZZ and ZP contributed to the interpretation of the data. ZZ and CW contributed to the manuscript draft. JT, JQ, and YZ contributed to the acquisition and analysis of the data. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Homemade fenestration and chimney techniques for the left subclavian artery revascularization during zone 2 thoracic endovascular aortic repair

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Background: To investigate the safety and efficacy of homemade fenestration and chimney techniques for the left subclavian artery (LSA) revascularization during zone 2 thoracic endovascular aortic repair (TEVAR).

Methods: From February 2017 to February 2021, 41 patients undergoing fenestration technique (group A) and 42 patients undergoing chimney technique (group B) to preserve the LSA during zone 2 TEVAR were enrolled in the present study. The procedure was indicated for dissections with unsuitable proximal landing zone with refractory pain and hypertension, rupture and malperfusion, and high-risk radiographic features. The baseline characteristics, peri-procedure, and follow-up clinical and radiographic data were recorded and analyzed. The primary endpoint was clinical success, and the secondary endpoints were rupture-free survival, LSA patency, and complications. Aortic remodeling, defined as patency, partial and complete thrombosis of the false lumen, was also analyzed.

Results: Technical success was achieved in 38 and 41 patients in groups A and B, respectively. Four intervention-related deaths were confirmed, two in each group. Immediate post-procedural endoleaks were detected in two and three patients in group A and B, respectively. No other major complications were found in either group, except for one retrograde type A dissection in group A. During follow-up, the initial clinical success rates were 90.24% and 92.86% in groups A and B, respectively. The primary and secondary mid-term clinical success rates were 87.5% and 90% in group A, and both of them were 92.68% in group B. Rupture-free survival and LSA patency were not significantly different between the two groups. The incidence of complete thrombosis in the aorta distal to the stent graft was 67.65% and 61.11% in groups A and B, respectively.

Conclusions: Apart from the lower clinical success rate of fenestration technique, both physician-modified techniques are available for LSA revascularization during zone 2 TEVAR and significantly promote favorable aortic remodeling.

KEYWORDS

aortic dissection, endovascular therapy, fenestration, chimney, left subclavian artery, zone 2 thoracic endovascular aortic repair

Introduction

Thoracic endovascular aortic repair (TEVAR) is routinely accepted as the first-line therapeutic option for type B aortic dissections (TBADs) with a lower incidence of morbidity and mortality than open surgery (1, 2). Despite the application of TEVAR has extended from the descending thoracic aorta to arch pathologies, an increasing risk of posterior circulation and upper extremity ischemia is considered to be associated with coverage of the left subclavian artery (LSA) during zone 2 TEVAR (3, 4). A meta-analysis reported that stroke has been a common finding after TEVAR, especially with LSA coverage without revascularization (5). TEVAR for thoracic aortic pathologies without a healthy proximal landing zone remains a challenge. Therefore, several commercially available devices and physician-modified techniques, including single-branched stent-graft, fenestration, and chimney techniques, have been introduced for LSA revascularization during zone 2 TEVAR (6–10).

According to previous studies, the issue of fenestrated endograft integrity may be related to long-term outcomes (8, 11), and the chimney technique is considered to increase the risk of endoleaks (12, 13). Therefore, selection criteria for different physician-modified techniques for LSA revascularization during zone 2 TEVAR for TBADs have not been established. In the present study, we aimed to summarize our experience and evaluate the safety and efficacy of the fenestration and chimney techniques for LSA revascularization during zone 2 TEVAR.

Materials and methods

Patient enrollment

From February 2017 to February 2021, 41 patients who underwent the fenestration technique (group A) and 42 patients who underwent the chimney technique (group B) for LSA revascularization during zone 2 TEVAR for TBADs with unsuitable proximal landing zones (entry tear located distal <15 mm to the ostium of the LSA and dissection or intramural hematoma extending proximal to the LSA) were enrolled in this study. The present study was approved by our institutional review board, and the requirement for written informed consent was waived owing to the retrospective design of the study. The indications for TEVAR included recurrent/refractory pain ($n = 55$), visceral/renal/limb ischemia ($n = 6$), hypotension/aortic rupture ($n = 15$), and rapid aortic expansion ($n = 7$). Both techniques were offered without preference, and the patients decided which to undergo. Data related to demographic characteristics and in-hospital and follow-up clinical and radiographic outcomes were recorded and analyzed. A flowchart of patient enrollment is shown in **Figure 1**.

Outcome criteria and definitions

The primary and secondary outcome criteria included the prevention of rupture or significant enlargement of the false lumen (aortic growth >5 mm per year), and death related to the primary pathology and the interventions. Technical success was defined as successful access to the arterial system using a remote site and deployment of the stent-graft at the intended location, absence of a type I or III endoleak and patent endoluminal graft without severe stenosis. TEVAR performed with the absence of type I or III endoleaks, significant enlargement of the false lumen or rupture, conversion to open repair, and death due to the original pathology and management was considered as clinical success. Leak at the proximal or distal graft attachment site, and around a fenestration or chimney stent was defined as type I, and Leak associated with modular disconnect or apposition failure, and fabric tear was considered to be type III. The stent-graft patency was defined as the stenosis should be <50% and the mean pressure gradient should be <10 mmHg (1, 2, 14). Major complications were defined as the requirement for significant re-intervention, prolongation of convalescence, and association with permanent disability and death (15).

Radiographic data evaluation and procedure performance

With the assistance of Endosize software (Therenva SAS, Rennes, France), the perioperative and follow-up radiographic images were evaluated by the same two interventional radiologists with >15 years of experience in TEVAR, and who performed the procedure for all patients.

The fenestration and chimney techniques were performed under general anesthesia with tracheal intubation in all patients. Additionally, cerebrospinal fluid drainage was performed in two patients with the requirement to extend the distal landing zone in group B. Fenestration and chimney techniques were performed according to previous reports (7, 16). An Ankura stent-graft (Life-tech Scientific Co., Ltd., Shenzhen, China) was deployed to exclude the entry tear, and a Zilver bare metal stent (Cook Medical, Bloomington, IL, USA) was selected as chimney stent to preserve the LSA.

Fenestration technique

A 6 Fr sheath (Terumo Corporation, Tokyo, Japan) was inserted in the left brachial artery (LBA), and angiography was performed via a calibrated pigtail catheter (Cook Medical) advanced into the ascending aorta through the 6 Fr sheath. Subsequently, the proximal end of the stent graft (Life-tech Scientific) was unsheathed on the table, and the fenestration was created in linear alignment with the "8"-shaped radio-opaque marker, and a smooth edge was achieved by suturing circularly (**Figure 2**). Clock position was used to determine the LSA position on the reconstructed image. A 4 Fr tapered catheter (Cordis Corporation,

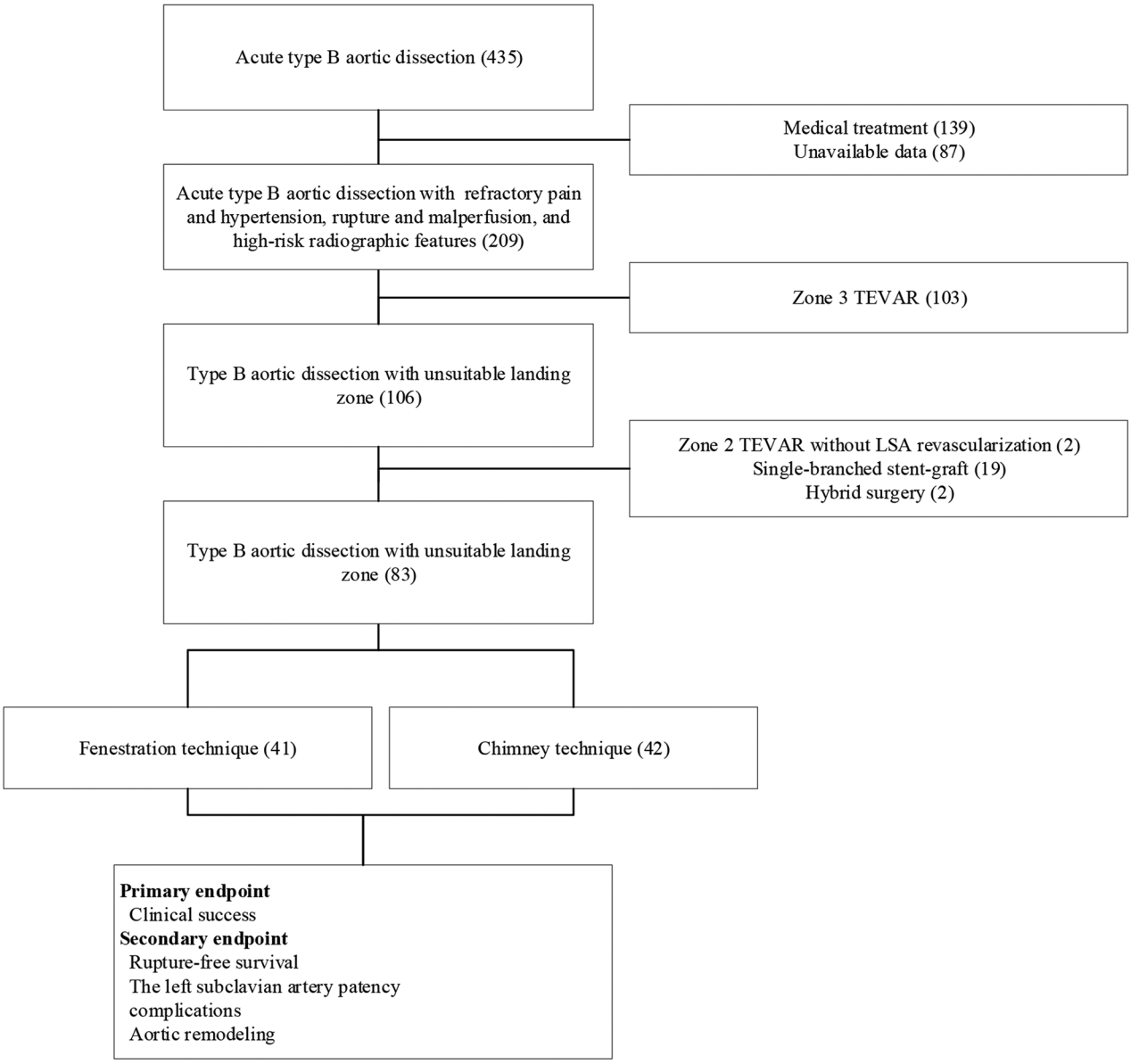


FIGURE 1
Flowchart of patient enrollment.

Miami, USA) along with a 150 cm guidewire was advanced into the ascending aorta via surgically exposed common femoral artery (CFA). An extra stiff guidewire (Cook Medical) was exchanged for better support. Heparin (80 U/kg) was administrated intravenously. Subsequently, the modified stent graft was delivered to the aortic arch along with the extra-stiff guidewire (Cook Medical), and deployed with systolic blood pressure <90 mmHg, and transient apnea. Minor orientation of the stent graft was performed to indicate the accurate position of the fenestration once the first segment was released. Furthermore, a 4 Fr tapered-angle catheter was advanced into the LSA via the 6 Fr sheath to validate the patency of the LSA. An 8/10 mm × 40 mm bare metal stent (Cook Medical) was used to keep the LSA perfusion for those with unintentional covered LSA.

Chimney technique

A 6 Fr sheath (Terumo Corporation) was deployed in the LBA percutaneously. Subsequently, a 5 Fr pigtail catheter (Cook Medical) was advanced over a guidewire into the ascending aorta for angiography. A unilateral CFA was exposed surgically. An extra-stiff guidewire (Cook Medical) was advanced into the ascending aorta along with a 4 Fr tapered catheter. The stent graft (Life-tech Scientific) was advanced into the aortic arch along with the extra stiff guidewire. Heparin (80 U/kg) was administrated intravenously, and the stent graft (Life-tech Scientific) was deployed proximal to the LSA and distal to the left common carotid artery under transient apnea with a systolic blood pressure ≤100 mmHg. A

stiff guidewire (Abbott Medical) was exchanged over the pigtail catheter (Cook Medical), and an 8/10 mm × 40/60 mm bare self-expanded stent (Cook Medical) was introduced parallel to the main stent graft to keep the LSA patent. The proximal segment protruded to the aortic lumen ≥20 mm with the distal end remaining in the LSA.

The follow-up protocols, including clinical and radiographic surveillance, were performed for all patients before discharge, at 3 and 6 months after the procedure, and yearly thereafter (**Figures 3**, **4**).

Statistical analysis

Continuous variables were expressed as mean ± standard deviation and analyzed using Student's *t*-test. Comparisons of categorical variables were performed using the Pearson χ^2 test, continuity-corrected χ^2 test, or Fisher's exact test. Kaplan-Meier curves were calculated when reporting rupture-free survival and LSA patency. The follow-up period was dated to the last clinical and radiographic examination. Statistical significance was set at p value <0.05. The analysis was performed using SPSS version 19 (IBM Corp., Armonk, NY, USA).

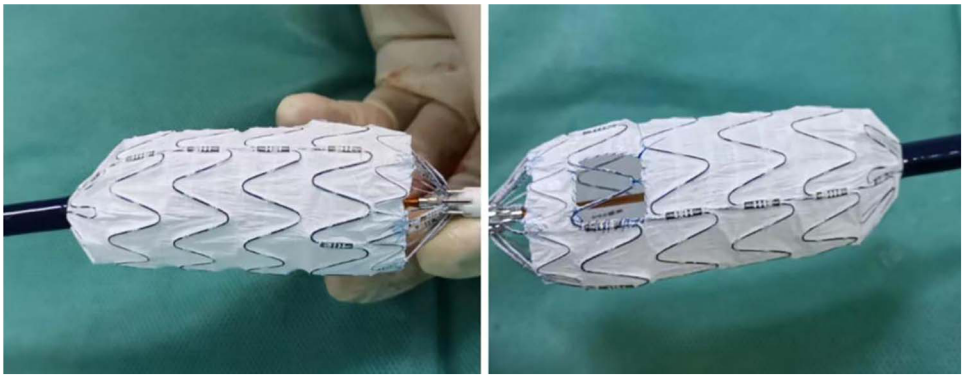


FIGURE 2
The fenestration was created in line with the radio-opaque middle-8-marker of the stent graft.

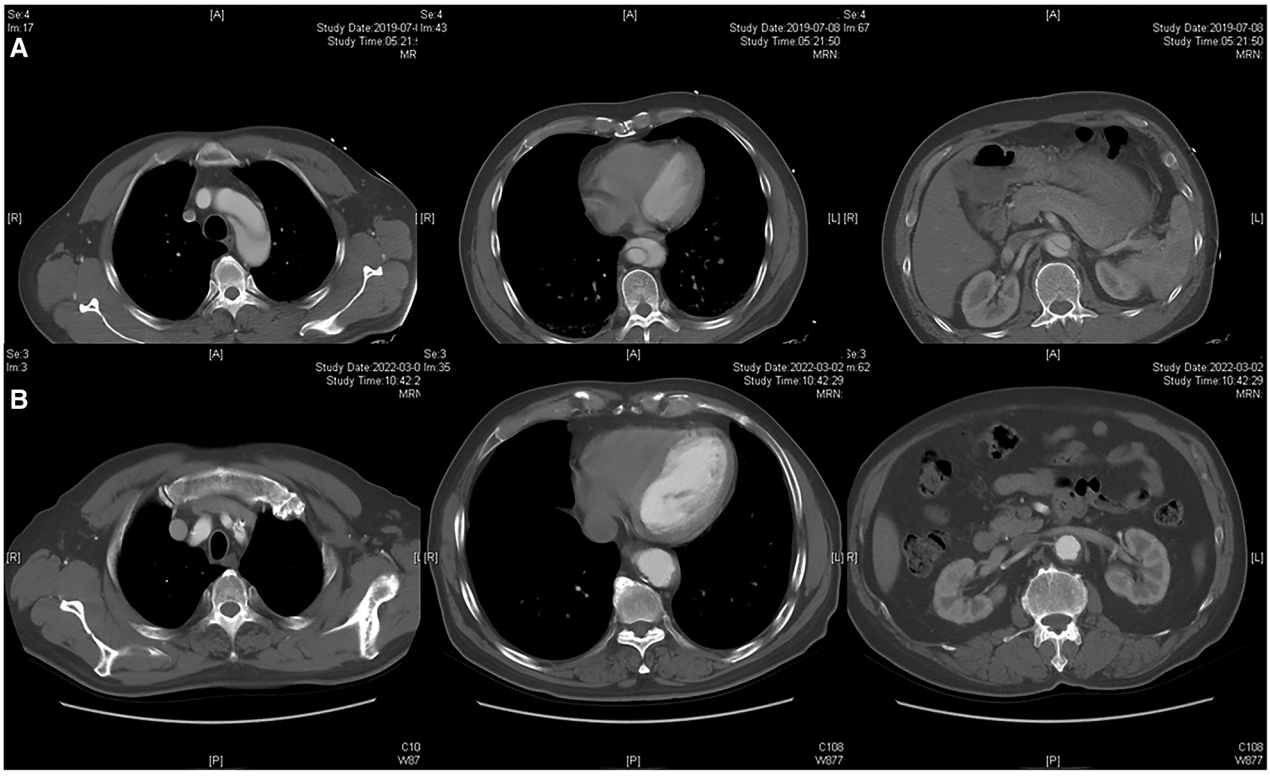


FIGURE 3
Radiographic image of fenestration technique. (**A**) Preoperative CTA showed the dissection involving the distal aortic arch and visceral aortic segment. (**B**) Postoperative CTA indicated the patency of the LSA and complete thrombosis of the visceral aortic segment over 2 years.

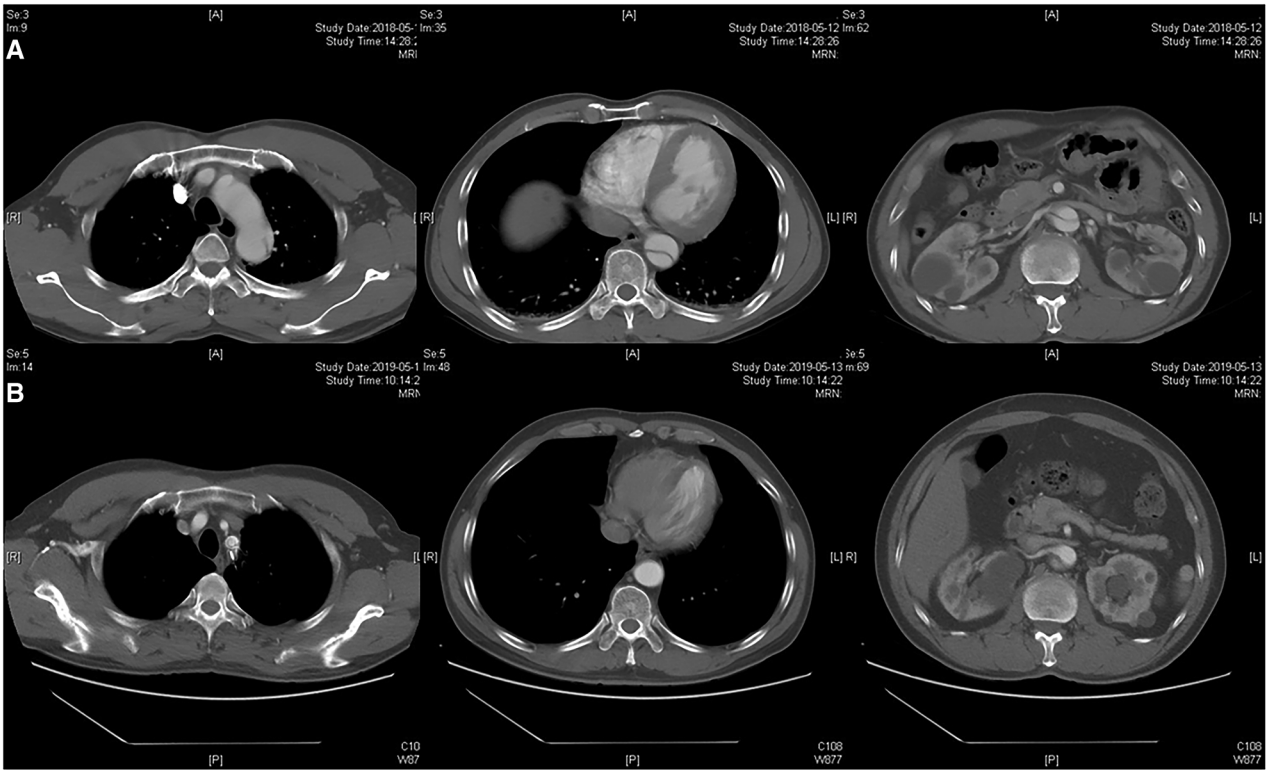


FIGURE 4
Radiographic image of chimney technique. (A) Preoperative CTA showed the dissection involving the distal aortic arch and visceral aortic segment. (B) Postoperative CTA indicated the patency of the chimney stent and partial thrombosis of the visceral aortic segment during 1-year follow-up.

TABLE 1 Baseline characteristics of patients.

	Fenestration ($n = 41$)	Chimney ($n = 42$)	p
Age, year	54.54 ± 11.49	53.98 ± 13.67	0.84
Gender, m	29	31	0.754
Co-morbidity, *n*			
Hypertension	35	36	0.964
CAD	1	1	1
DM	0	2	0.494
Others	3	4	1
Parameters of the thoracic aorta			
Zone 2 diameter, mm	31.05 ± 3.07	30.40 ± 2.91	0.329
Length of the proximal neck, mm	9.61 ± 3.17	9.33 ± 3.32	0.699
Distal attachment zone diameter, mm	23.44 ± 2.97	23 ± 3.19	0.518
Confined to thoracic aorta, *n*	10	11	0.85
Extend proximal to LSA, *n*	6	8	0.591

CAD, coronary artery disease; DM, diabetes mellitus; LSA, left subclavian artery.

TABLE 2 Peri-operative outcome.

	Fenestration ($n = 41$)	Chimney ($n = 42$)	p
Technical success, *n* (%)	38 (92.68)	41 (97.62)	0.591
Secondary technical end points			
Procedure time, minutes	115.37 ± 28.64	117.38 ± 31.38	0.761
Fluoroscopy time, minutes	20.12 ± 3.79	20.57 ± 4.34	0.617
Blood loss, ml	25.73 ± 8.56	31.55 ± 8.94	0.003
Contrast load, ml	104.02 ± 9.50	108.45 ± 12.27	0.07
Hospital length of stay, days	15.29 ± 3.12	16.38 ± 6.02	0.306
TEVAR-related death, *n* (%)	2 (4.88)	2 (4.76)	1
Complications, *n* (%)			
Immediate endoleak	2 (4.88)	3 (7.14)	1
Spinal cord ischemia	0	0	N/A
Stroke	0	0	N/A
Others	3 (7.32)	3 (7.14)	1
Combined complications	5 (12.20)	6 (14.29)	0.779
Parameters of stent-graft			
Numbers of stent-graft, *n*	42	45	
Oversize, %	5.16 ± 1.84	5.06 ± 1.88	0.811
Coverage length, mm	195.61 ± 8.38	201.67 ± 18.73	0.062
Distal to the proximal end, mm	8.14 ± 3.38	9.10 ± 1.96	0.12

TEVAR, thoracic endovascular aortic repair.

Results

The demographic characteristics of patients are presented in Table 1. The mean age was 54.54 and 53.98 years in groups A

and B, and the majority of patients in both groups were male and had a history of hypertension. In group A, there was one patient with atrial septal defect, one patient with cerebral hemorrhage, and one patient with a left renal stone. In group B, one patient had renal atrophy, one patient had cerebral infarction, and two patients had abdominal aortic aneurysms. No significant difference in preoperative comorbidities was detected between the two groups. The parameters of the thoracic aorta pathologies that exhibited no significant difference between the two groups are also described in Table 1.

TABLE 3 The primary and secondary endpoints.

	Fenestration ($n = 41$)	Chimney ($n = 42$)	p
Initial clinical success, n	37	39	0.973
Primary clinical success, n			
Short-term	35	38	0.682
Mid-term	35	38	0.682
Secondary clinical success, n			
Short-term	36	38	0.973
Mid-term	36	38	0.973
Endoleak, n			
Type I or III	2	1	0.983
Type II	0	2	0.494
Stroke	0	0	N/A
Rupture-free survival, n	38	39	0.984
LSA patency, n	37	38	0.553

LSA, left subclavian artery.

Perioperative details are shown in Table 2. The technical success rates were 92.68% and 97.62% in groups A and B, respectively. Except for blood loss, the remaining secondary technical endpoints, including procedure time, fluoroscopy time, contrast load, and hospital length of stay, showed no significant difference between the two groups. TEVAR-related death was found in four patients, two in each group. Immediate post-procedural endoleaks were detected in two (type I) and three patients (one type I and two type II) in groups A and B, respectively. Neither spinal cord ischemia nor stroke was found in either group. Only one transient ischemic attack occurred in group A, and it resolved spontaneously before discharge. The parameters of stent-graft, number of stent-grafts, oversize, coverage length, and distance to the proximal end of the aortic graft trunk were not significantly different between the two groups.

Initial clinical success was achieved in 37 (90.24%) and 39 (92.86%) patients in groups A and B, respectively. During a mean follow-up of 34.88 months in groups A, the primary and secondary mid-term clinical success rates were 87.5% and 90%. Both of them were 92.68% in group B with a mean follow-up of 37.49 months. The mid-term primary and secondary clinical success rates showed no significant difference between the two

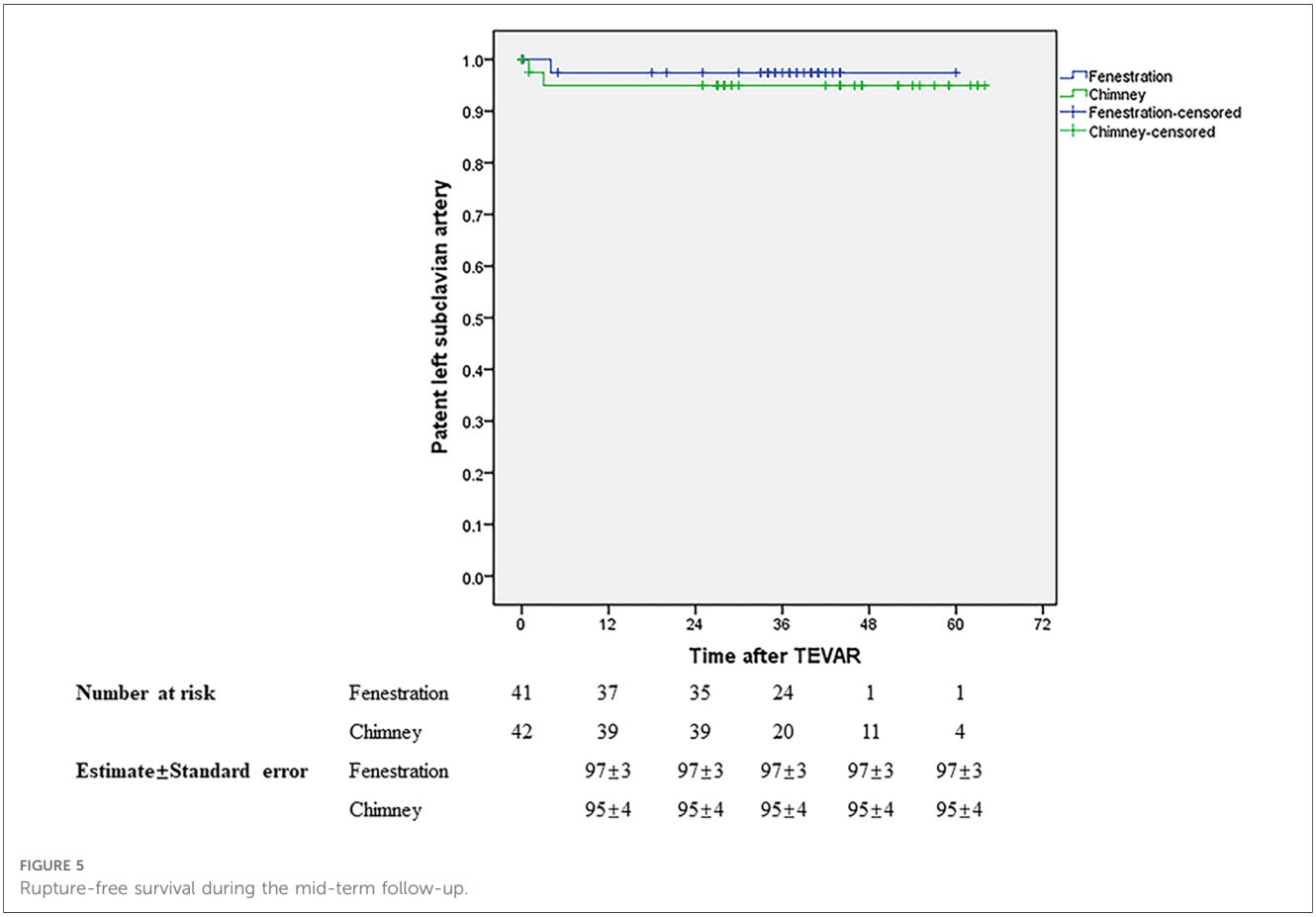


FIGURE 5
Rupture-free survival during the mid-term follow-up.

groups, similar to the short-term outcomes. Table 3 presents the results. During follow-up, one patient died in month 5 due to lung cancer in group A and one patient died 1 month later due to acute upper gastrointestinal bleeding in group B. The LSA was patent in 37 and 38 patients in groups A and B, respectively. No stroke occurred in either group during follow-up. There was no significant difference in rupture-free survival and LSA patency between the two groups during the mid-term follow-up (Figures 5, 6).

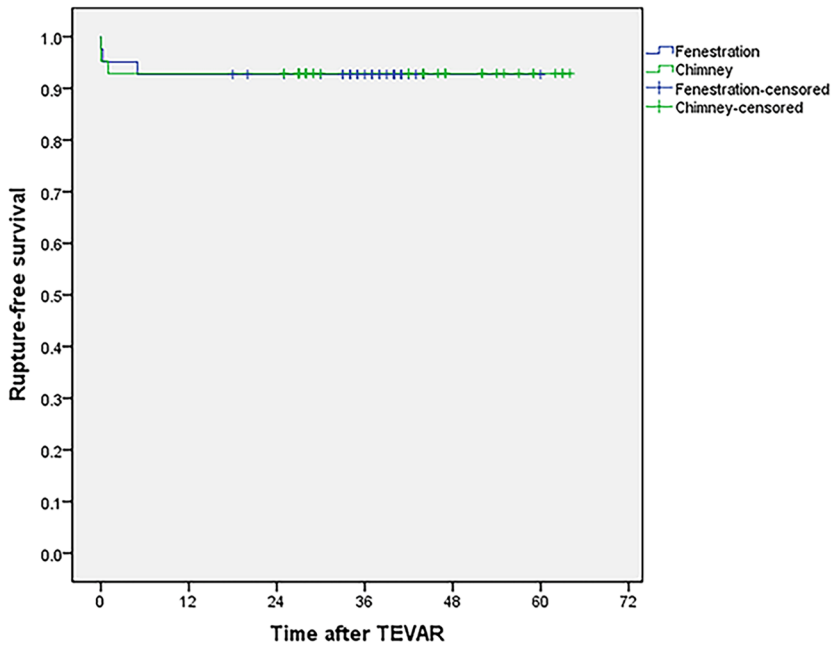
Remodeling of the aorta is shown in Table 4. According to the last CTA, complete thrombosis of the false lumen in the aorta distal to the stent graft was confirmed in 23 and 22 patients in groups A and B, and partial thrombosis was confirmed in 11 and 14 patients at the same level. The incidence of complete thrombosis in the aorta distal to the stent graft was 67.65% and 61.11% in groups A and B, respectively. Eight patients with complete thrombosis and 11 patients with partial thrombosis were detected in the visceral aortic segment in group A, and 10 patients with complete thrombosis and 11 patients with partial thrombosis were found in the visceral aortic segment in group B. The incidence of partial and complete thrombosis of false lumens significantly increased after TEVAR in both groups. Stable and reduced transaortic diameter of the aorta distal to the stent graft and visceral aortic segment were observed in the majority of patients in both groups. No significant enlargement of the false lumen was observed during follow-up. Both physician-modified techniques significantly promoted favorable aortic remodeling with negligible differences.

During follow-up, three complications, including one wound infection, one pulmonary infection, and one retrograde type A dissection (RTAD), were detected in group A. One case of renal insufficiency, one case of celiac thrombosis, and one case of upper extremity ischemia were found in group B. Except for the requirement of open repair for RTAD in group A, the remaining complications resolved with nominal intervention among the two groups.

The last CTA confirmed two residual type II endoleaks during follow-up. However, no re-intervention was required due to clinical silence and no significant enlargement in the false lumen. During follow-up, three residual type I endoleaks disappeared spontaneously (two at 18 months and one at 24 months). No other major complications were detected in either group during follow-up.

Discussion

TEVAR using zone 2 as a proximal landing zone has been performed for pathologies involving the distal aortic arch (17–19). Additionally, several commercially available devices and physician-modified techniques, including single-branched stent-graft, fenestration and chimney technique, and carotid-subclavian



Number at risk	Fenestration	41	38	36	25	1	1
	Chimney	42	39	39	20	11	4
Estimate±Standard error	Fenestration		93±4	93±4	93±4	93±4	93±4
	Chimney		93±4	93±4	93±4	93±4	93±4

FIGURE 6
LSA patency during the mid-term follow-up.

TABLE 4 Aortic remodeling during mid-term follow-up.

	Fenestration		Chimney	
	Pre-TEVAR	Post-TEVAR	Pre-TEVAR	Post-TEVAR
Aorta distal to SG				
Complete thrombosis, *n*	0	23	0	22
Partial thrombosis, *n*	4	11	7	14
Patent, *n*	30	0	29	0
*p**	<0.001		<0.001	
Significant reduction, *n*	10		12	
Significant enlargement, *n*	0		0	
No significant change, *n*	24		23	
*p***	0.664			
Visceral aortic segment				
Complete thrombosis, *n*	0	8	0	10
Partial thrombosis, *n*	4	11	5	11
Patent, *n*	20	5	20	4
*p**	<0.001		<0.001	
Significant reduction, *n*	4		6	
Significant enlargement, *n*	0		0	
No significant change, *n*	20		19	
*p***	0.523			

SG, stent graft; TEVAR, thoracic endovascular aortic repair.
**p*, pre. vs. post.
***p*, fenestration vs. chimney.

artery bypass, have been employed to keep the LSA patent to decrease the risk of posterior stroke and upper extremity ischemia (20–22). However, neither randomized controlled studies nor guidelines have been introduced for choosing different techniques for zone 2 TEVAR. In the present study, we compared fenestration technique with chimney technique for LSA revascularization during zone 2 TEVAR, and introduced our experience.

Although the in-situ fenestration technique is more prevalent in fenestrated zone 2 TEVAR (23, 24), all patients in the present study were treated with the on-the-table fenestration technique according to our experience and previous reports (16, 21, 25). According to previous studies, the technical success rate of fenestration ranges from 90% to 100%, with no significant difference between *in situ* and on-the-table techniques (8, 21, 23, 25). Similar to previous reports, technical success was achieved in 38 (92.68%) patients in group A, and only one LSA occlusion was detected during the mid-term follow-up. Creation of the fenestration in line with the radiopaque middle-8-marker on the proximal end of the stent graft and minor rotation to adjust the fenestration orientation during the procedure are associated with a satisfactory technical success rate and high LSA patency.

Both covered and bare stents are used as chimney stents for LSA revascularization during zone 2 TEVAR (6, 26, 27). According to a previous report, covered stents had better primary patency rates than bare metal stents in aortoiliac occlusive disease (14). Endovascular treatment with primary stenting for LSA stenotic and occlusive lesions results in acceptable long-term patency with a decreased risk of perioperative complications. However, a comparison between different stents has not been performed (28). Currently, neither guidelines nor randomized controlled studies have been performed to establish selection criteria for chimney stents. Despite the use of only self-expanded bare metal stents as chimney stents in our study, LSA patency was achieved in 38 (90.48%) patients during mid-term follow-up, which was comparable to the results in previous reports (27, 29).

Carotid to subclavian bypass has been considered as the standard treatment for LSA revascularization during zone 2 TEVAR (30). However, surgical debranching carries 29% of the early complications, including stroke, phrenic nerve palsy, hematoma, and chyle leak (30, 31). Carotid to subclavian artery bypass was not routinely considered during zone 2 TEVAR at our center. Therefore, a comparison between endovascular repair and hybrid surgery was not conducted.

During the mid-term follow-up, three immediate postoperative type I endoleaks in both groups disappeared spontaneously. Hemodynamic and anatomical changes after stent graft deployment may contribute to false lumen thrombosis and promote favorable aortic remodeling. Two type II endoleaks remained patent in group B during follow-up, and the gutter arising between the proximal landing zone and the stent-graft is considered to be related to this dilemma (32). No major neurological complications were found in our study. LSA revascularization and limited coverage of the thoracic segmental arteries were related to a decreased risk of stroke and spinal cord ischemia (33).

Both techniques contributed significantly to the favorable aortic remodeling with negligible differences during mid-term follow-up. A sufficient proximal seal promoted complete thrombosis of the false lumen in the distal aortic arch and stented segment of the thoracic aorta, and prevented further aortic enlargement and rupture. The variety of thrombosis of the false lumen was confirmed at the level of the aorta distal to the stent graft and visceral aortic segment during follow-up. Further thrombosis of the false lumen and aortic remodeling processes are a matter of time. Retrograde flow from distal entry tears could serve as a predictor of aortic remodeling. Moreover, the outcomes should be interpreted carefully after considering selection biases and a limited number of patients.

The present study has several limitations. First, the outcomes of this retrospective study with a limited number of patients and experience in a single center may not be generally applicable. A larger randomized controlled study with long-term follow-up is required to confirm these findings. Second, only self-expanded bare stents were used as chimney stents in zone 2 TEVAR. Comparisons with other techniques, including covered stents serving as chimney stents and carotid to subclavian artery bypass or transposition, should be performed to establish the selection criteria for choosing different techniques for LSA revascularization during zone 2 TEVAR. Third, the on-the-table modified fenestrated stent-graft required multiview fluoroscopy to confirm insertion orientation. Additionally, deployment of a stent severing as a bailout strategy to maintain the LSA patent may be required.

In conclusion, both fenestration and chimney techniques, with a significantly decreased incidence of stroke and spinal cord

ischemia, are safe and feasible for LSA revascularization during zone 2 TEVAR. Minor orientation of the stent graft is difficult in a tortuous and calcified aorta and iliac artery, and a lower rate of clinical and technical success for the fenestration technique was detected. However, both techniques significantly contributed to favorable aortic remodeling during mid-term follow-up. Long-term clinical and radiographic surveillance are required to confirm these findings.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Second Hospital of Shandong University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

JY, YLL, and HC contributed to conception and design of the study. YL and HC organized the database. BL and HC performed the statistical analysis. JY and HC wrote the first draft of the manuscript. JY, YLL, YL, YW, BL and HC wrote sections of the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Single-center initial experience with inner-branch complex EVAR in 44 patients

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Purpose: The use of inner-branch aortic stent grafts in the treatment of complex aortic pathologies aims at broad applicability and stable bridging stent sealing compared to other endovascular technologies. The objective of this study was to evaluate the early outcomes with a single manufacturer custom-made and off-the-shelf inner-branched endograft in a mixed patient cohort.
Methods: This retrospective, monocentric study between 2019 and 2022 included 44 patients treated with inner-branched aortic stent grafts (iBEVAR) as custom-made device (CMD) or off-the-shelf device (E-nside) with at least four inner branches. The primary endpoints were technical and clinical success.
Results: Overall, 77% ($n = 34$) and 23% ($n = 10$) of the patients (mean age 77 $\pm$ 6.5 years, $n = 36$ male) were treated with a custom-made iBEVAR with at least four inner branches and an off-the-shelf graft, respectively. Treatment indications were thoracoabdominal pathologies in 52.2% ($n = 23$), complex abdominal aneurysms in 25% ($n = 11$), and type Ia endoleaks in 22.7% ($n = 10$). Preoperative spinal catheter placement was performed in 27% ($n = 12$) of patients. Implantation was entirely percutaneous in 75% ($n = 33$). Technical success was 100%. Target vessel success manifested at 99% (178/180). There was no in-hospital mortality. Permanent paraplegia developed in 6.8% ($n = 3$) of patients. The mean follow-up was 12 months (range 0–52 months). Three late deaths (6.8%) occurred, one related to an aortic graft infection. Kaplan–Meier estimated 1-year survival manifested at 95% and branch patency at 98% (177/180). Re-intervention was necessary for a total of six patients (13.6%).
Conclusions: Inner-branch aortic stent grafts provide a feasible option for the treatment of complex aortic pathologies, both elective (custom-made) and urgent (off-the-shelf). The technical success rate is high with acceptable short-term outcomes and moderate re-intervention rates comparable to existing platforms. Further follow-up will evaluate long-term outcomes.

KEYWORDS

complex endovascular aortic repair, inner branches, thoracoabdominal aneurysm repair, off-the-shelf, aortic stent graft

Introduction

Thoracoabdominal aortic aneurysms (TAAAs) are among the most challenging cases for vascular surgeons and remain considerable even since the implementation of complex endovascular treatment perioperative morbidity and mortality (1). Fenestrated and branched endografts (f/bEVAR) have reduced perioperative mortality and morbidity considerably, yet the ideal endovascular solution regarding specific complications, such as

endoleaks, bridging stent occlusion, and migration remains controversial (2, 3). So far, patient-specific, custom-made endografts with fenestrations or outer branches have been implemented widely for the elective and acute setting with technical success rates of approximately 100%. Yet, the complication rates of 6%–10% spinal cord ischemia (SCI), 15% renal deterioration, and re-intervention rates up to 25% during the first 12 months have to be noticed and should be discussed with the patients (4–10).

While branched technology has demonstrated better long-term results regarding patency and prosthesis integrity, typically a narrow visceral aortic segment is still an indication for fenestrated grafts (6, 7, 10–15). Here, the latest configuration available, the inner-branched EVAR (iBEVAR), aimed to overcome these potential limitations (**Figure 1**). Advantages include increased anatomical suitability in narrow aortas while providing enhanced sealing between the main body and the bridging stents (11, 13).

Recently, a pre-cannulated "off-the-shelf" endograft with four inner branches (E-nside; Artivion, Germany) has become available and enabling iBEVAR solution even for urgent and emergency cases (16, 17). Up to now, only 84 cases of iBEVAR procedures ≥4 inner branches have been reported in three small cohort studies (11, 13, 14).

Thus, this study aims to evaluate the initial experience with the custom-made and off-the-shelf inner-branched devices in complex aortic aneurysm repair in a mixed cohort from a high-volume center.

Methods

Data collection and study population

All consecutive patients treated with inner-branch custom-made and off-the-shelf aortic stent grafts with at least four branches by manufacturer Artivion® (Hechingen, Germany) between 01/2019 and 12/2022 were prospectively recorded in the Department of Visceral, Thoracic and Vascular Surgery at the Carl Gustav Carus University Hospital, Dresden. The data for each case was analyzed retrospectively based on electronic patient records and imaging. Demographics, comorbidities, radiologic data (anatomic features of the aneurysms, and target vessels), treatment modalities, complications, length of hospital stay, and follow-up examinations were collected. Exclusion criteria were patients with confirmed rupture and devices with less than four inner branches.

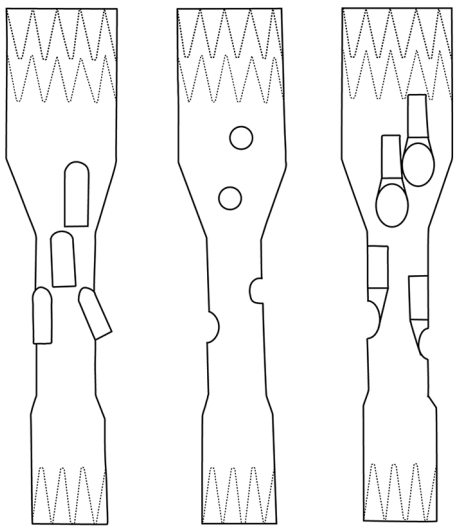

FIGURE 1
Sketches of FEVAR, BEVAR, and iBEVAR. Left: BEVAR (outer branches). Middle: FEVAR (fenestrations). Right: iBEVAR (inner branches).

Ethics approval

All procedures in studies involving human participants complied with the ethical standards of the institutional research committee.

Under the guidelines for research on human subjects, the local ethics committee at the Technische Universität Dresden approved the study (decision number BO-EK-87022023). The ethics committee was registered as an institutional review board (IRB) at the Office for Human Research Protections (OHRP) (registration number (IRB00001473 and IORG0001076).

Treatment selection and procedure planning

The iBEVAR repair was offered to patients considered appropriate by the head of the department and the company and after careful assessment for open/endo repair possibilities. This decision was reviewed in all cases after a multidisciplinary vascular board and anesthesiologic assessment. Preoperative work-up included echocardiography and pulmonary function. In the last years, iBEVAR was increasingly favored over FEVAR or BEVAR due to one or more of the following indications:

1. Unfavorable target vessel angulation for FEVAR.
2. Narrow aortic lumen (<28 mm) at the visceral segment.
3. Missing circumferential contact with the aortic wall at the level of the fenestrations/branches.
4. Type Ia endoleak after failed endovascular aortic repair (EVAR) with a short or severely angulated neck (BEVAR in EVAR).

Endograft procedures were planned according to patient-specific anatomy using thin-slice computed tomography angiography (CTA) and multiplanar reconstructions. All CTA scan measurements were analyzed by an expert operator and compared with the ones obtained by the Artivion engineering team before final approval. All decisions were finally discussed with the patients, and ideally their relatives and alternative treatment options (i.e., open repair) were offered when suitable. Informed consent for the operation was obtained from all patients.

Stent grafts design

The used endografts include inner-branch endografts, i.e., custom-made E-xtra Design and off-the-shelf E-nside stent grafts (Artivion, Hechingen, Germany). The inner branches were preferentially designed in an antegrade configuration with diameters of 8 and 6 mm for the coeliac trunk (CA) and superior mesenteric artery (SMA) and for the renal arteries, respectively. All branches have an enlarged and oval-shaped outlet to allow variability of the bridging stents. The augmentation of the branch outlets should allow the orientation of the bridging stent graft in many axial and sagittal directions, thus enabling the evolution from custom-made application to an off-the-shelf device, which has now been accomplished for the E-nside prosthesis (17). The endografts were loaded on a 24F delivery system. The rotational orientation of the endograft is based on appropriate visualization of the "E" markers of the device. A ring-shaped radiopaque marker is positioned at the inlet of each inner branch and three dot markers at their outlets, allowing orientation under fluoroscopy (**Figure 2**).

In the case of E-nside, the stent graft is available in four different versions with proximal diameters of 38 and 33 mm and distal diameters of 30 and 26 mm. All four inner branches are pre-canulated. Further specifications can be found in the Instructions for Use (IFU) (17).

Procedure technique

All procedures were performed in a hybrid operating room under general anesthesia. Patients were administered systemic heparin to maintain activated clotting times (ACT) equaled to 250 s (checked in 30-min intervals). Lumbar drain for prevention of spinal cord ischemia was placed in selected cases at the discretion of the surgeon, generally in patients requiring long segment repair.

Ultrasound-guided percutaneous femoral access was obtained on both sides including closure devices. Additional open left axillary access was obtained where necessary. The endograft was deployed under fluoroscopy guidance with the markers of the inner-branch exit positioned 5 to 10 mm above the target vessel ostium. The rotational orientation of the endograft was based on the appropriate adjustment of the "E" markers.

Over time, a total femoral approach using a steerable sheath (Oscor, Florida, United States) was established whenever possible (**Figure 2**). Balloon-expandable stent grafts [primarily VBX stent graft (W.L. Gore & Associates, Flagstaff, AZ, United States), Advanta V12 (Maquet-Atrium Medical Inc., Hudson, NH, United States), or iCover (iVascular, Sant Vicenç dels Horts, Barcelona)] were used based on surgeon's choice and availability.

Postoperative course

For spinal perfusion protection, a mean arterial pressure of >80 mm Hg was aimed in accordance with the current European Society for Vascular Surgery (ESVS) guidelines (18). The duration of lumbar drainage was 24–36 h. If no neurologic deficit occurred, the drain was clamped for an additional 6–8 h before removal.

Patients subsequently received ASA 100 mg and clopidogrel 75 mg for 6 months without loading doses. Thereafter, only aspirin was continued.

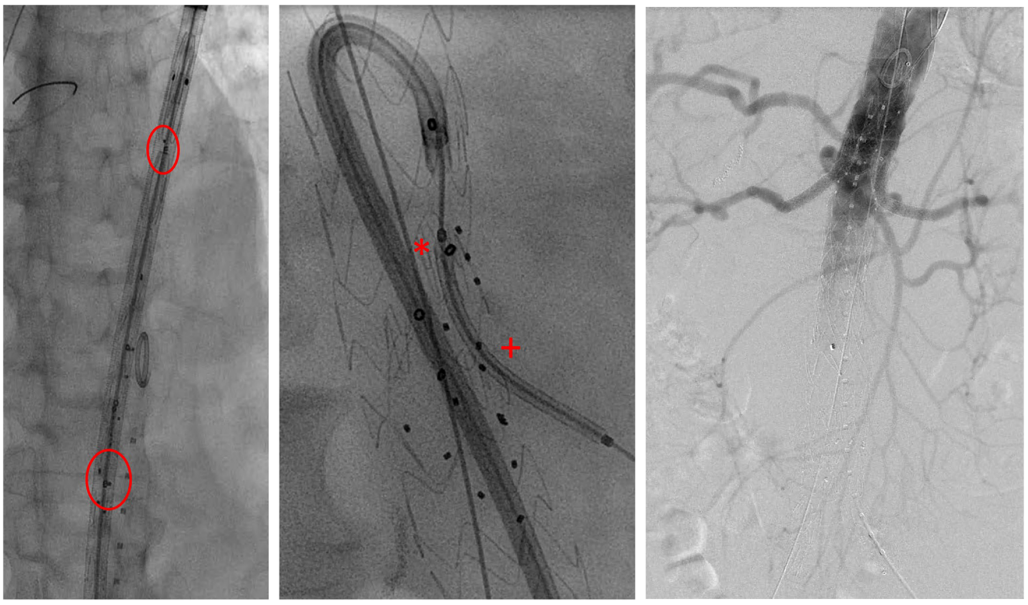

FIGURE 2
Intraoperative imaging. Left: stent graft depicted before deployment in fluoroscopy (circle: E-markers for orientation). Middle: cannulation of AMS-branch using a steerable sheath with bridging stent in position (*branch inlet marker; $^{+}$branch outlet marker). Right: final angiography.

CTA was performed on the first or second postoperative day (**Figure 3**). Routine follow-up consisted of clinical examination, duplex sonography, and CTA every 3–6 months during the first year and at least annually after that. All follow-up CTA studies were reviewed by a radiologist and analyzed within a vascular multidisciplinary board.

Outcome parameters and definitions

The primary endpoint of this study was the technical and clinical success with morbidity and mortality rates in the perioperative period. According to the reporting standards for complex aortic repair by Oderich et al., clinical success was defined as successful deployment and implantation of the aortic modular components and side branches in addition to the absence of important disabling permanent clinical sequelae (e.g., death, aneurysm rupture, graft infection, conversion, paraplegia, and other major complications) (19). Secondary outcome parameters were overall survival, patency, and re-intervention rates during follow-up. Target vessel success was defined as successful cannulation and stent implantation in the target vessel without evidence of peripheral embolism or dissection and proper branch perfusion. The perioperative period was defined as the first 30 days after treatment or during a hospital stay if the length was more than 30 days. The maximum aortic diameter was assessed by computed tomography as the axial outer–outer diameter. The aortic diameter in the reno-visceral segment (IV) was measured at the level of the superior mesenteric artery. The target vessel diameter was determined in the first centimeters after vessel takeoff. All measurements were made after axial alignment in multiplanar reconstruction.

Complications were categorized according to the Society for Vascular Surgery (SVS) reporting standards for endovascular aortic repair and the Clavien–Dindo classification (19, 20). Technical success was defined as the correct placement of the main body and bridging stents and exclusion of the target pathology without evidence of type I or III endoleaks in accordance with the reporting standards for endovascular aortic aneurysm repair (9). Assisted primary success was defined if

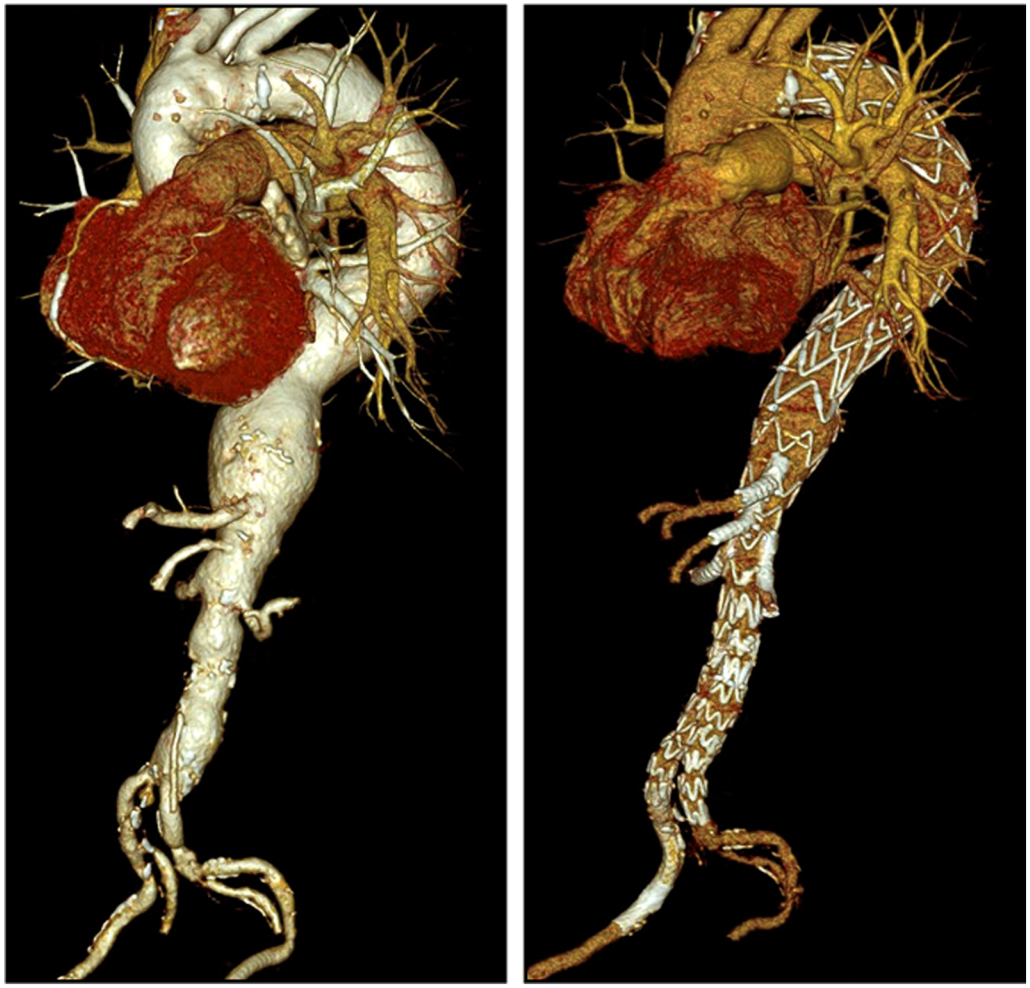

FIGURE 3
Pre- and postoperative CTA in 3D volume rendering technique. Left: preoperative TAAA type II. Right: postoperative after iBEVAR. CTA, computed tomography angiography; TAAA, thoracoabdominal aortic aneurysm.

further unplanned treatment procedures (e.g., due to a type Ia endoleak) were necessary during the primary procedure for the exclusion of the target pathology. The follow-up period was the period from hospital discharge until the last available clinical examination.

Statistical analysis

Statistical analysis was performed using IBM SPSS for Windows, Version 21.0 (IBM Corp., Armonk, NY, United States). All clinical characteristics were grouped to build categorical or nominal variables. Dichotomous variables were recorded as absolute frequencies (number of cases) and relative frequencies (percentages). Continuous data are presented as mean and SD, non-symmetrical with median, and interquartile range (IQR). Pearson's chi-squared or Fisher's exact test was used to analyze categorical variables. Differences between means were tested with a *t*-test or Mann–Whitney *U*-test. Survival and patency data were analyzed using Kaplan–Meier estimates, and differences were appointed by the log-rank test. A two-sided *P*-value <0.05 was considered statistically significant.

Results

Study population and patient characteristics

The study included 44 patients (81.8% male, age 76.57 ± 6.58 years). Since 2017, there has been a steady increase in the number of patients treated with iBEVAR. A total of 34 patients and 10 patients (22.7%) received a custom-made and an off-the-shelf prosthesis with four (90.9%; $n = 40$) or five inner branches (9.1%; $n = 4$), respectively, all downward facing. An endograft body with integrated iliac limbs was used in 11 patients, and completion EVAR (plus iliac branch device) followed in 19 (two) patients, respectively. Comorbidities and risk factors are shown in Table 1.

TABLE 1 Demographic and clinical data.

Variable[a]	$n = 44$ (%)
Demographic data	
Age (years)	76.57 ± 6.48
Sex (male/female)	36/8 (81.8/18.2)
Risk factors and comorbidities	
Chronic kidney disease[b]	11 (25)
Heart failure (>NYHA II)	10 (22.7)
Atrial fibrillation	8 (18.2)
Hypertension	44 (100)
CHD	14 (31.8)
Peripheral artery disease	12 (27.3)
Myocardial infarction	13 (9)
Diabetes mellitus	15 (34.1)
COPD	7 (15.9)
Nicotine abuse	19 (43.2)
Coincident aortic pathologies[c]	
Dissection	1 (2.3)
PAU	3 (6.8)
IMH	2 (4.5)
Aneurysm	12 (27.3)

CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; IMH, intramural hematoma; PAU, penetrating aortic ulcer.
[a]Continuous data presented as mean ± SD.
[b]GFR < 30 ml/min/1.73 m^2.
[c]Independent of the indication pathology.

TABLE 2 Indications.

Variables[a]	$n = 44$ (%)
TAAA[b]	16 (36.4)
Type 2	5 (31.3)
Type 3	2 (12.5)
Type 4	8 (50)
Type 5	1 (6.3)
Distal descending/visceral aortic pathologies	7 (15.9)
PAU	3 (6.8)
IMH	1 (2.3)
Secondary expanding type B dissection	3 (6.8)
Complex AAA (para-/suprarenal)	11 (25)
Endoleak type IA from previous EVAR	10 (22.7)
Aortic diameters	
Minimum diameter segment IV (mm)	25.5 ± 4.3
Maximum diameter (mm)	63.9 ± 13.6

TAAA, thoracoabdominal aortic aneurysm IMH, intramural hematoma; PAU, penetrating aortic ulcer; AAA, abdominal aortic aneurysm.
[a]Continuous data presented as mean ± SD.
[b]According to the Crawford classification (19).

Indications

Treatment indications were TAAAs in 23, complex abdominal aneurysms in 11, and type Ia endoleaks (iBEVAR in EVAR) in 10 patients (Table 2). Thoracoabdominal pathologies included aneurysms (36.4%; $n = 16$), secondary expanded aortic dissections (6.8%; $n = 3$), and penetrating aortic ulcers ($n = 3$) and intramural hematoma ($n = 1$). The mean maximum aortic diameter was 63.9 ± 13.6 mm, and the mean aortic diameter in the reno-visceral segment (IV) was 25.5 ± 4.2 mm. Of note, despite rupture being an exclusion criterion, no iBEVAR for rupture was performed during the study period.

Technical results

Lumbar drain was established in 12 patients pre-operatively (42% TAAA; 34% type 1a endoleak repair). An entirely percutaneous implantation was possible in 75% ($n = 33$) of the patients, and access *via* an iliac conduit was necessary in four patients (9.1%). Primary technical success after complete implantation was 95% (42/44). Two unexpected immediate-type Ia endoleaks were treated by proximal extension during the

TABLE 3 Bridging stent grafts and target vessels in $n = 44$ patients.

		Celiac trunk	Superior mesenteric artery	Right renal artery	Left renal artery	Σ
Stent type (%)	Viabahn VBX	11 (25)	12 (27)	15 (34)	11 (25)	49 (28)
	Advanta V12	24 (55)	24 (55)	19 (43)	23 (52)	90 (51)
	iCover	8 (18)	8 (18)	6 (14)	6 (14)	28 (16)
	Other	1 (2)	—	4 (9)	2 (5)	7 (4)
Additional lining (uncovered) (%)		3 (7)	1 (2)	5 (11)	4 (9)	13 (7)
Bridging stent extension (%)[b]		16 (36)	8 (18)	8 (18)	8 (18)	40 (23)
Target success (%)		44 (100)	44 (100)	44 (100)	42 (96)	178 (99)
Vessel angulation[a] (°)		44.1 ± 20.7	41.7 ± 14.2	64.6 ± 23.5	67.3 ± 17.8	—
Vessel diameter[a] (mm)		6.9 ± 1.4	8.2 ± 1.7	5.9 ± 0.9	5.9 ± 1.1	—

[a]Continuous data presented as mean ± standard deviation.
[b]Additional stent implantation necessary.

same session (primary assisted technical success 100%). The target vessel success was 99% (178/180) (Table 3). One dissection of the renal artery with consecutive occlusion with the subsequent need for nephrectomy was seen. In another patient, cannulation of the left renal artery proved to be frustrated despite all efforts. In both cases, the inner branch was successfully occluded with a vascular plug. The median contrast volume used was 200 ml (range, 85–350 ml) with a median fluoroscopy time of 85 min (range, 44–136 min). There were eight (18%) unplanned procedure extensions due to access complications (Table 4).

Early results (perioperative)

There was no in-hospital mortality. Complete permanent SCI developed in 6.8% ($n = 3$) of patients immediately after the procedure. All these patients were treated due to a thoracoabdominal aneurysm ($n = 2$ type II, $n = 1$ type IV). No transient or late SCI was observed. One of these patients had already received a preoperative lumbar drain, the two other affected patients immediately after symptom onset. In addition, immediate postoperative lumbar drainage showed no symptom improvement in the two affected patients. Further neurological complications included one minor stroke on postoperative day 5. The combined morbidity was 45% according to the Clavien–Dindo classification (Tables 4, 5). In detail, access site complications occurred in seven (15.9%) patients (4× false aneurysm; 3× surgical site infection). Two (4.5%) and 10 (22.7%) patients developed relevant cardiac and pulmonary complications (2.3% re-intubation), respectively. Temporary dialysis was necessary for three (6.8%) patients. All patients were dismissed without dialysis.

Routine postoperative CTA revealed a type III endoleak in three patients (8.6%). These patients received a direct re-intervention with balloon dilatation/stent deployment at sealing zones. Furthermore, one patient showed an asymptomatic retrograde type B dissection, which was treated endovascularly 3 weeks later to allow possible spinal cord blood supply conditioning. No relevant stent migration or branch stenoses were observed. The mean hospital length of stay was 16 ± 19 days and 4 ± 11 days in ICU.

Short- and midterm results (follow-up)

The median follow-up was 12 months (range 0–52). Estimated Kaplan–Meier 1-year survival manifested at 95% and branch patency at 98% (177/180) (Figure 4). One branch occlusion of the celiac trunk (asymptomatic, at 9 months) was seen. During

TABLE 4 Perioperative course and complications[a] according to SVS reporting standards for endovascular aortic aneurysm repair (19).

Variables	$n = 44$ (%)
Intraoperative mortality	—
Primary technical success	42 (95.5)
Type Ia endoleak	2 (4.5)
Primary assisted technical success	44 (100)
Aortic dissection (within 30 days of AAA repair)	1 (2.3)
Grade 1: incidentally noted, asymptomatic	—
Grade 2: resolved with endovascular repair	1 (2.3)
Grade 3: open repair or fatal	—
Arterial perforation or rupture	2 (4.5)
Grade 1: spontaneous closure	—
Grade 2: stent graft or limited retroperitoneal iliac repair	1 (2.3)
Grade 3: laparotomy/thoracotomy	1 (2.3)
Access artery dissection or thrombosis	3 (6.8)
Grade 1: non-flow limiting dissection, local repair	2 (4.5)
Grade 2: stent, limited retroperitoneal bypass	1 (2.3)
Grade 3: conversion to open AAA repair	—
Access site false aneurysm	4 (9.1)
Grade 1: resolved spontaneously, compression/thrombin	2 (4.5)
Grade 2: surgical repair	2 (4.5)
Grade 3: ruptured	
Access site infection	3 (6.8)
Grade 1: resolved with oral antibiotics	—
Grade 2: operative drainage, intravenous antibiotics	2 (4.5)
Grade 3: major debridement, artery repair	1 (2.3)
Insufficiency closure system	4 (9.1)
Reno-visceral ischemia	2 (4.5)
Bowel resection	1 (2.3)
Nephrectomy	1 (2.3)
Acute limb ischemia	4 (9.1)
Balloon catheter thrombectomy/embolectomy	1 (2.3)
Thrombectomy/endarterectomy	2 (4.5)
Bypass graft	1 (2.3)

AAA, abdominal aortic aneurysm.
[a]According to SVS reporting standards for endovascular aortic aneurysm repair (19, 33).

TABLE 5 Systemic complications[a] and grading[b] according to Clavien–Dindo classification (20).

Variables	$n = 44$ (%)
Cardiac	
Grade 1: little or no hemodynamic consequence	3 (6.8)
Grade 2: symptomatic necessitating intravenous medication or PTCA	2 (4.5)
Grade 3: cardiac arrest, resuscitation	—
Pulmonary	
Grade 1: recovery with medical treatment	—
Grade 2: prolonged hospitalization/intravenous antibiotics	9 (20.5)
Grade 3: intubation, tracheostomy, deterioration in pulmonary function	1 (2.3)
Renal insufficiency	
Grade 1: no dialysis	4 (9.1)
Grade 2: temporary dialysis, prolonged hospitalization, permanently reduced renal function	3 (6.8)
Grade 3: permanent dialysis	—
Cerebrovascular	
Grade 1: temporary deficit with recovery within 24 h	3 (6.8)
Grade 2: delayed recovery, infarct on CT or magnetic resonance, permanent deficit with mild impairment	1 (2.3)
Grade 3: severe impairment or fatal outcome	—
Bowel ischemia	
Grade 1: recovered without intervention	—
Grade 2: recovered with intravenous antibiotics	—
Grade 3: bowel resection	2 (4.5)
Spinal cord ischemia	
Grade 1: resolution within 24 h	—
Grade 2: resolution within 1 month or minor permanent deficit, able to walk without support	—
Grade 3: major permanent deficit	3 (6.8)
Septic disease pattern	4 (9.1)
Clavien–Dindo grading complications[b]	20 (45.5)
IIIa	10 (22.7)
IIIb	7 (15.9)
IVa	3 (6.8)
IVb	—
In-hospital mortality	0 (0)

PTCA, percutaneous transluminal coronary angioplasty.
[a]According to SVS reporting standards for endovascular aortic aneurysm repair (19).
[b]According to the Clavien–Dindo classification (20).

follow-up, two relevant type 2 endoleaks were treated successfully in two patients [$n = 1$ coiling inferior mesenteric artery (20 mm progress in 18 months) and $n = 1$ polymer embolization of the aneurysm sac (9 mm progress in 9 months)]. Overall, re-intervention (due to aneurysm sac enlargement) was necessary for six patients including the three endoleaks treated during the same hospitalization ($n = 5$ endoleaks, $n = 1$ retrograde type B dissection) (**Figure 5**). Of three late deaths, one was aortic-related due to a stent graft infection.

Discussion

This study demonstrates high technical success and comparable in-hospital, midterm, and long-term survival and re-intervention rates to classical fenestrated or outer-branched endografts for a mixed cohort of 44 patients treated with custom-made and off-the-shelf iBEVAR aortic prosthesis (11, 13, 15, 21, 22). This is currently one of the largest series on this relevant topic.

Although fenestrated and outer-branch aortic endografts have evolved to be applicable options for the treatment of thoracoabdominal aortic pathologies and complex AAAs, there are some specific limitations of the existing technology (11, 13, 21). So far, fenestrated endografts are preferred when aortic wall apposition is given at the origin of the visceral vessels. The fenestrations can be accessed through the femoral arteries, avoiding the need for an upper limb (brachial artery) access. But the sealing between the bridging stent and the main body relies only on the reinforced fenestration ring, comprising the risk for stent migration or fracture (14, 23, 24). In contrast, outer branches offer a stable overlap between the main body and the bridging stent. However, a wider aortic lumen is required (14). This was a relevant restriction, given the diameters seen in our cohort (**Table 2**).

Here, iBEVAR is a valid alternative (25–27). Historically, Abisi et al. reported that up to 16% of their patients were considered to be more suited for an iBEVAR due to severe angulation and narrow working lumen (11). Also, we were able to demonstrate a wide applicability for various aortic pathologies (**Table 2**).

Previous numerous reports on the outcome of F/BEVAR procedures showed high technical success with low perioperative mortality and morbidity but high re-intervention rates (8, 9, 22, 28). In a prospective multicenter study for fenestrated endovascular treatment of juxtarenal abdominal aortic aneurysms, Oderich et al. reported 100% technical success with no perioperative mortality and 22% secondary interventions (22). Doonan et al. observed a 30-day mortality of 6.3% and 5.7% of SCI, as well as 13.5% re-interventions in 141 patients with thoracoabdominal pathologies (28). A systematic review and meta-analysis for the t-Branch off-the-shelf endograft (197 patients, 19% urgent) determined a pooled technical success of 92.8%, 5.8% early mortality, and 12.2% spinal cord ischemia (8).

To date, there are only a few studies that reported results on inner-branch endografts for the visceral segment, and most of them are confounded by various endograft configurations with fenestrations and outer branches (10–12, 29, 30). Silverberg et al. reported on 27 patients treated with inner-branch custom-made device (CMD) (90 inner branches) with high technical success (96%) and low complication rates (3.7% ($n = 1$) in-hospital mortality and spinal cord ischemia, respectively) (13). Abisi et al. observed no major complication or 30-day mortality in 18 patients provided with CMD inner branch (11). So far, the largest multicenter study from Italy by Simonte et al. reports on 45 patients treated with a CMD inner-branch graft with reasonable technical success (93.3%), no in-hospital mortality, and 6.7% ($n = 3$) persistent spinal cord ischemia. They publicized internal data provided by Artivion, that the request for inner branches increased up to 10-fold, and described inner branches as their preferred treatment device (14).

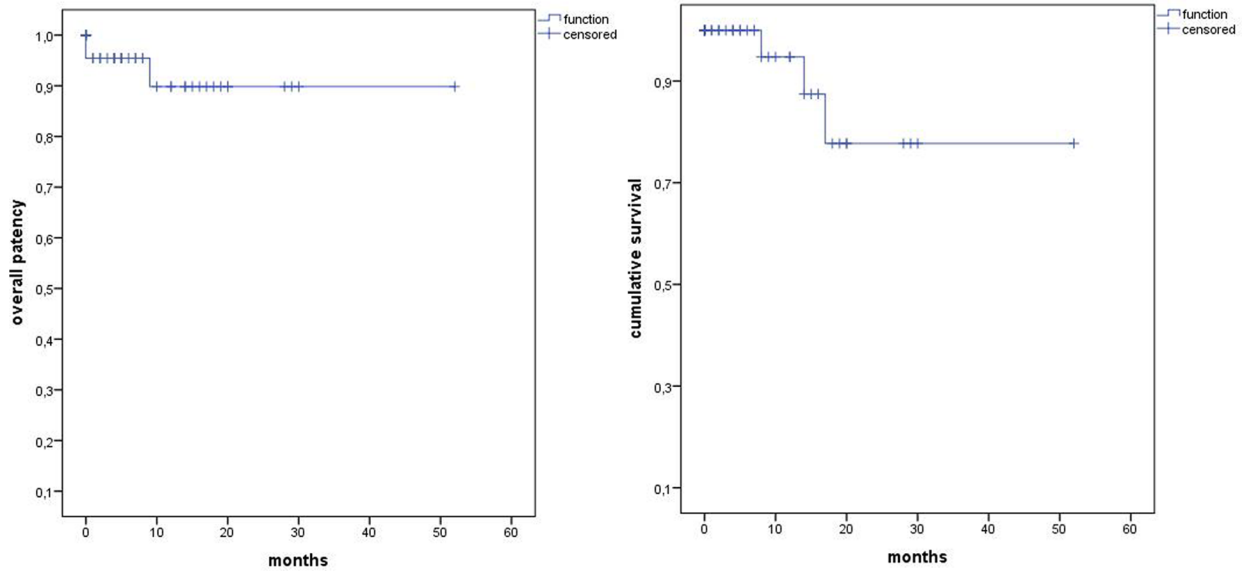

FIGURE 4
Kaplan–Meier estimates of overall survival and overall patency.

In contrast to this, Katsargyris et al. described the catheterization of inner branches as a difficult procedure in visualizing and orientating to identify the inlet of the branch (12). Based on our experience and with a corresponding learning curve, we were recently able to perform 75% of the procedures exclusively percutaneously from transfemoral *via* a steerable sheath enabling the reduction of procedural steps and upper limb access complications (11, 31). In our experience, the working space in the main body was sufficient for cannulation (11). In comparison, our fluoroscopy time and amount of contrast volume were quite similar to previous publications (13, 14).

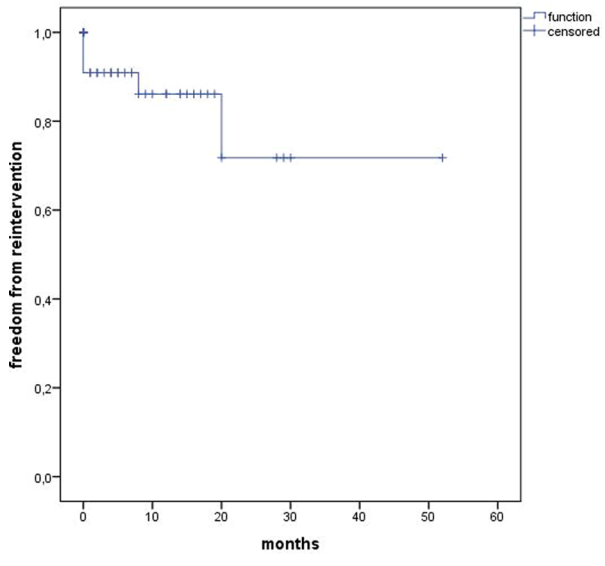

FIGURE 5
Kaplan–Meier estimates for freedom from re-intervention.

Considerable re-intervention rates are the Achilles heel of endovascular repair, increasing with the procedural complexity (7, 13–15, 23, 32). We observed an overall re-intervention rate due to endoleaks of 11.3% ($n = 3$), comparable with the previous literature (7, 10, 13, 14). It should be noted that the follow-up is still limited (mean follow-up of 12 months in this study) because the new implementation of this technology and long-term results are still pending. However, a direct comparison of re-intervention rates between FEVAR and outer-branch BEVAR is not appropriate, as most publications have used both technologies together without further distinction. Regardless, a recent study evaluated that branch endoleaks have a high rate (up to two-thirds) of spontaneous resolution and might resolve more often spontaneously compared with fenestration endoleaks. Further, they concluded that small target vessel endoleaks in pre-dismissal imaging may be initially observed and persistent or late endoleaks can be successfully treated by endovascular re-intervention (7).

By now, the E-nside grafts allow treatment with the advantages of inner branches in an off-the-shelf device. Demonstrated in a meta-analysis on the t-Branch, representing a widely accepted off-the-shelf solution for urgent/emergency treatments, acceptable clinical results with a mortality of 5.8% and 12.2% rate of spinal cord ischemia (1.2% permanent paraplegia) in elective and urgent cases can be reached (8).

There are several reports of access complications, which also appeared in our procedures (**Table 4**) (10, 13). Hence, careful case planning of the access is crucial to reduce complications.

This study has some limitations. First, it is limited by the small number of cases and to the retrospective non-randomized single-

center study design, generating bias linked to a retrospective data collection and device selection. Furthermore, during the study period of 5 years, there has been a learning progress and gain in expertise with this endovascular technique that may have affected treatment procedures. Lastly, for teaching purposes, procedures might not be directly comparable due to confounding bias between operators.

Conclusion

This retrospective study demonstrates that inner-branch endografts for complex aortic repair are a viable option, especially for narrow aortic visceral segment pathologies. Our results show excellent technical results and early outcomes with comparable and acceptable re-intervention and spinal cord ischemia rates. These encouraging results in a mixed cohort and elective and urgent setting may suggest iBEVAR as a future primary treatment for complex aortic pathologies warranting long-term results.

Data availability statement

The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the local ethics committee of the Technische Universität Dresden approved this study (decision number BO-EK-87022023). The ethics committee is registered as an institutional review board (IRB) at the Office for Human Research Protections (OHRP) (registration numbers (IRB00001473 and IORG0001076).

Author contributions

MK and AB designed the study, collected and analyzed the data, and drafted the manuscript. SW and BL drafted the manuscript. HN created the volume renderings and worked on the final manuscript. CR analyzed the data and worked on the final manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Retrograde type A aortic dissection during or after thoracic endovascular aortic repair: a single center 16-year experience

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Objective: This article aims to investigate the incidence rate of retrograde type A aortic dissection (RTAD) and the risk factors of RTAD in relation to thoracic endovascular aortic repair (TEVAR).
Methods: Patients with thoracic aortic disease who underwent TEVAR at Henan Provincial People's Hospital from January 2004 to December 2019 were enrolled in the present research. The risk factors associated with RTAD following TEVAR using univariate and multiple logistic regression analyses.
Results: During the study period, A total of 1,688 TEVAR patients were included in this study, and of these, 1,592 cases were included in the type B aortic dissection (TBAD) group, and 96 cases were included in the non-TBAD group. There were 1,230 cases of aortic dissection and 362 cases of aortic intramural hematoma and/or penetrating ulcer in the TBAD group. The non-TBAD group included 68 cases of thoracic aortic aneurysm, 21 cases of thoracic aortic pseudoaneurysm, and seven cases of congenital aortic coarctation. The overall incidence rate of RTAD was 1.1% (18/1,688) in patients, all of which occurred in the TBAD group. The cohort comprised 18 RTAD patients with an average age of 56.78, consisting of 13 males and 5 females. Among them, 13 individuals exhibited hypertension. Ten instances happened within the TEVAR perioperative period, including two cases during the surgery, six cases occurred within three months, two cases occurred after one year, and the longest interval was 72 months following TEVAR. TEVAR was successfully implemented in 17 patients, while the operation technique was temporarily altered in one case. The new entry position for RTAD was identified as the proximal region of the stent graft (SG) in 13 patients, while in five cases, the entry site was more than 2 cm away from the proximal region of the SG. 17 cases were at the greater curvature of the aorta, and one case was at the lesser curvature. Multivariate logistic regression analysis revealed that the SG oversizing ratio is a relevant risk factor for RTAD. However, ascending aortic diameter, aortic arch type, SG type, and anchored region were not directly related to the occurrence of RTAD.
Conclusion: RTAD is a rare yet catastrophic complication. It could occur both during the procedure, early and late postoperative periods. Maintaining an appropriate SG oversizing ratio is crucial to minimize the risk of RTAD.

KEYWORDS

aortic dissection, endovascular repair with stent graft, retrograde type A dissection, oversizing ratio, risk factors

Introduction

The development of thoracic endovascular aortic repair (TEVAR) represents a cornerstone in the current treatment of thoracic aortic diseases due to the established features of minimal invasiveness and promising therapeutic effects (1). Continual advancements in surgical techniques, coupled with the evolution of stent graft devices, have significantly contributed to improved clinical outcomes and expanded the range of clinical indications (2). In particular, the TEVAR has demonstrated favorable medium and long-term results and was reported as a class I recommendation for complicated type B aortic dissection (TBAD) in the European Society of Cardiology guidelines and Vascular Societies guidelines (3). Remarkably, although TEVAR boasts high success rates, retrograde type A aortic dissection (RTAD) remains a critical vulnerability and a significant challenge in the field (4, 5). As reported in previous literature, the prevalence of RTAD varies from 2% to 12%, with mortality rates exceeding 40% (2, 6–8). RTAD could occur immediately, intraoperatively, perioperatively, or during follow-up. Given its catastrophic consequence, early detection and prevention of risk factors of RTAD are of paramount importance. RTAD may be linked to the lesions of the aortic wall, such as heritable connective tissue disorders, wall edema in the acute stage, radial force, and device oversizing (9). Moreover, both the natural progression of the disease and potential iatrogenic injuries resulting from endovascular manipulation of the arch could contribute equally to the occurrence of RTAD (7). The specific risk factors associated with RTAD continue to be a subject of debate, as previous studies have yielded conflicting findings. Some researchers have hypothesized that the use of a proximal bare stent, aimed at enhancing stent graft fixation within the aortic arch, could potentially elevate the risk of RTAD (10–12). Nevertheless, recent studies have concluded the conflicting findings (9, 13). In the present study, we present our experience with RTAD following TEVAR in patients with TBAD and other thoracic aortic disorders, intending to identify the risk variables for RTAD that will allow the clinician to reduce this fatal complication. Furthermore, these findings will improve our capacity to counsel patients undergoing TEVAR for thoracic aortic disorders about surgical risk and long-term outcomes.

Methods

Cohort

In the present retrospective study, patients with thoracic aortic disease including dissections, intramural hematomas, penetrating ulcers, aneurysms and coarctations were enrolled at the Department of Vascular Surgery, Zhengzhou University People's Hospital, Henan Provincial People's Hospital from January 1, 2004 to December 31, 2019. The study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Henan Provincial People's Hospital, People's Hospital of Zhengzhou University. Inclusion criteria: (I) All patients who underwent TEVAR for any indication; (II) The participants with complete clinical data. Exclusion criteria: (I) Patients with incomplete imaging data and definitive diagnosis; (II) Patients accepted conservative treatment without TEVAR.

Surgical techniques

The surgical techniques were established based on preoperative computed tomography angiography (CTA). All TEVAR procedures adhered to standardized protocols for TEVAR (14, 15). The stage of TBAD and timing of surgery was defined as an acute stage if it was detected within 14 days of symptom onset, subacute stage 14–90 days, and chronic stage after 90 days. If the proximal landing zone measured less than 15 mm from the origin of the left subclavian artery, one of the following procedures was employed to construct an additional proximal landing zone: (I) chimney technique; (II) fenestration techniques; (III) branch stent repair techniques; (IV) coverage of the left subclavian artery (LSA) on purpose, if the right vertebral artery was patent and the left one was not dominant; (V) the left common carotid artery (LCCA) and LSA bypass; (VI) right common carotid artery, LCCA and LSA bypass; (VII) ascending aorta, iliac artery/LCCA bypass. The stent graft is anchored to the healthy vessel wall using the procedures described above. Four models of stent graft device were used: (I) proximal bare stent: Talent and Valiant (Medtronic Vascular, Santa Rosa, Calif), Hercules (Microport, Shanghai, China), Ankura (Lifetech, Shenzhen, China); (II) proximal barbs: Zenith TX2 (Cook Medical, Bloomington, Ind); (III) proximal flared scallops or partially uncovered stents: Gore TAG/C-TAG (W. L. Gore & Associates, Flagstaff, Ariz); (IV) fully covered stent grafts: Castor (Microport, Shanghai, China).

Follow up

In this study, patients were followed up in the form of telephone interviews, outpatient CTA re-examination, and medical record inquiries until the patient's death or the end of this study. Patients will be followed up at 1, 3, 6, and 12 months after the surgery, with subsequent annual follow-ups until loss to follow-up or mortality occurs.

Statistical analysis

Statistical analyses were performed with EmpowerStats based on R software (R version 4.2.0). Measurement data were expressed as mean ± standard deviation (SD), and comparison between groups was performed by Student's t-test or one-way analysis of variance (ANOVA). Qualitative data were presented by rate (%), and the intergroup comparison was performed by the Chi-square test. Univariate logistic analysis was used to identify the risk factors associated with RTAD. Logistic multivariate regression analysis to adjust the different potential

confounders was performed to determine the effects of oversize ratio and aortic diameter on RTAD.

Results

Baseline characteristics

A total of 1,688 TEVAR patients were included in this study, and of these, 1,592 cases were included in the TBAD group, and 96 cases were included in the non-TBAD group. The specific flow chart is shown in Figure 1. There were 1,230 cases of aortic dissection and 362 cases of aortic intramural hematoma and/or penetrating ulcer in the TBAD group. The non-TBAD group included 68 cases of thoracic aortic aneurysm, 21 cases of thoracic aortic pseudoaneurysm, and seven cases of congenital aortic coarctation. A total of 37 patients diagnosed with Marfan syndrome were included in the study, with one case in the RTAD group and 36 cases in the non-RTAD group. The overall incidence rate of RTAD was 1.1% (18/1,688) in patients, all of which occurred in the TBAD group. TEVAR-related complications such as endoleak (8.1%), paraplegia (1.2%), stent graft infection (1.1%) and access injuries (1.0%) were also recorded in the presented research. The basic details of the patients in the RTAD and non-RTAD groups are presented in Table 1.

The basic information for RTAD patients

Among the 18 patients (13 males, five females; mean age, 56.78 years [range, 38–79 years]; Table 2). RTAD occurrences were observed at different time points. Specifically, ten patients with RTAD happened within the TEVAR perioperative period, with two cases during the surgery, six cases occurred within three months, two cases occurred after one year, and the longest interval being 72 months following TEVAR. The longest follow-up period was 130 months, and the shortest was only one day in RTAD group. Four patients were lost to the follow-up. Seven patients died during the follow-up period. TEVAR was initially implemented in 17 cases, while the operation procedure was temporarily altered in one case. The SG utilized comprised ten cases of Medtronic Vialiant, three cases of Cook Zenith, three cases of Gore TAG, and one case of Shanghai MicroPort Castor integrated branching stent. The position of the new entry in 13 RTAD patients was at the proximal region of the SG, and five instances were more than 2 cm distant from the proximal region of the SG. Besides, 17 cases were at the greater curvature of the aorta, and 1 case was at the lesser curvature. It is noteworthy that two cases developed RTAD during the operation. Although the initial surgical plan for case six was to perform a thoracotomy with ascending aorta IA/LCCA bypass and TEVAR, an interim and urgent change was made to perform ascending aortic replacement, total arch replacement with frozen elephant trunk. This decision was prompted by the presence of a dissection observed during the clamping of the ascending aortic wall while reconstructing the branches of the arch. This patient was discharged from the hospital following a satisfactory recovery and was lost to follow-up. In another case with intramural hematoma of TBAD, dilation of a narrow TAG stent with a GORE trilobate balloon resulted in a new entry at the greater curvature of the proximal region of the SG. As a remedial measure, the patient underwent rescue implantation of the second TAG stent after an emergency LCCA-LSA bypass. The patient showed good recovery and remained in a stable condition during the last follow-up. Six of the remaining 16 RTAD patients underwent successful surgical repairs. Case 2 with a favorable outcome and a follow-up of 130 months, was the only one that respectively had ascending aortic replacement, hemi-arch replacement with frozen elephant trunk and ascending aortic replacement, total arch replacement with frozen elephant trunk due to the pain in the chest and back at postoperative five weeks and 90 months (Figure 2). In 10 RTAD patients treated conservatively, seven deaths occurred, and three patients were lost to follow-up. Case one with ascending aorta hematoma formation but no clear entry tear developed RTAD in the perioperative period. At six months of follow-up, the ascending aortic entry tear was visible and located at the proximal portion

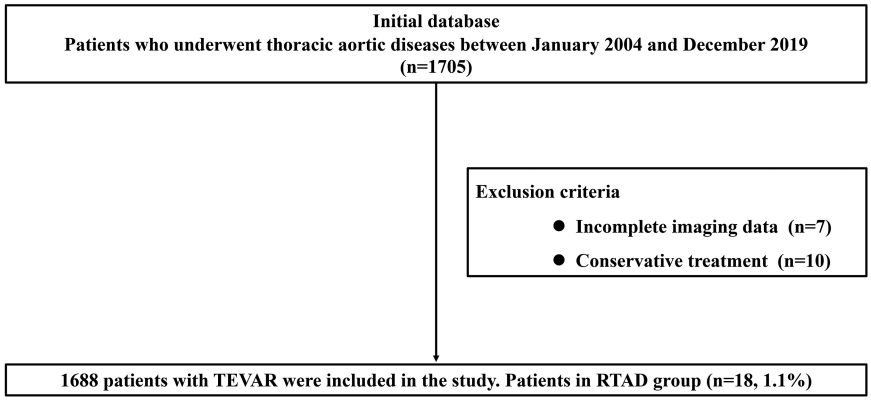

FIGURE 1
Flow chart of the specific content.

TABLE 1 Baseline characteristics of TBAD patients who underwent TEVAR.

Variables	Non-RTAD (n = 1,670)	RTAD (n = 18)
Age	52.48 ± 12.70	56.78 ± 13.36
Gender		
Female	255 (15.27%)	5 (27.78%)
Male	1,415 (84.73%)	13 (72.22%)
Trauma		
No	1,613 (96.59%)	18 (100.00%)
Yes	57 (3.41%)	0 (0.00%)
Connective tissue disease		
No	1,632 (97.72%)	17 (94.44%)
Yes	38 (2.28%)	1 (5.56%)
Hypertension		
No	417 (24.97%)	5 (27.78%)
Yes	1,253 (75.03%)	13 (72.22%)
Diabetes		
No	1,652 (98.92%)	18 (100.00%)
Yes	18 (1.08%)	0 (0.00%)
Cardiovascular and cerebrovascular diseases		
No	1,456 (87.19%)	13 (72.22%)
Yes	214 (12.81%)	5 (27.78%)
Renal insufficiency		
No	1,620 (97.01%)	18 (100.00%)
Yes	50 (2.99%)	0 (0.00%)
Smoking		
No	1,084 (64.91%)	9 (50.00%)
Yes	586 (35.09%)	9 (50.00%)
Pathological type		
TBAD	1,574 (94.25%)	18 (100.00%)
Non-TBAD	96 (5.75%)	0 (0.00%)
Pathological stage		
Acute	1,417 (84.85%)	16 (88.89%)
Chronic	253 (15.15%)	2 (11.11%)
Onset dime (day)	5.00 (3.00–10.00)	3.00 (2.00–6.75)
Surgical producers		
TEVAR	1,301 (77.90%)	11 (61.11%)
(Non-thoracotomy) Hybrid	147 (8.80%)	2 (11.11%)
(Thoracotomy) Hybrid	71 (4.25%)	2 (11.11%)
TEVAR (Fenestration Technique)	53 (3.17%)	1 (5.56%)
TEVAR (Branch Stent Repair Techniques)	47 (2.81%)	1 (5.56%)
TEVAR (Chimney Technique)	51 (3.05%)	1 (5.56%)
Timing of surgical intervention		
Chronic phase	135 (8.08%)	2 (11.11%)
Subacute phase	156 (9.34%)	0 (0.00%)
Acute phase	1,379 (82.57%)	16 (88.89%)
Different types of stents		
Poximal barbs	164 (9.82%)	3 (17.65%)
Fully covered SG	47 (2.81%)	1 (5.88%)
Proximal flared scallops or partially uncovered sStents	465 (27.84%)	3 (17.65%)
Proximal bare stent	994 (59.52%)	10 (58.82%)
Oversizing ratio	11.18 ± 4.77	7.53 ± 3.54
≤10%	860 (51.50%)	14 (82.35%)
11%–20%	750 (44.91%)	3 (17.65%)
>20%	60 (3.59%)	0 (0.00%)
Proximal landing zone*		
Zone 0	199 (11.92%)	4 (23.53%)
Zone 1	431 (25.81%)	5 (29.41%)
Zone 2	944 (56.53%)	8 (47.06%)
Zone 3	96 (5.75%)	0 (0.00%)
Arch type**		
Type Ⅰ	632 (37.84%)	7 (38.89%)
Type Ⅱ	844 (50.54%)	8 (44.44%)
Type Ⅲ	194 (11.62%)	3 (16.67%)
Diameter of ascending aorta	38.06 ± 4.93	40.56 ± 6.78
<40 mm	1,054 (63.11%)	6 (33.33%)
≥40 mm	616 (36.89%)	12 (66.67%)

TEVAR, Thoracic Endovascular Aortic Repair; SG, Stent Graft; TBAD, Stanford type B aortic dissection.

*Refer to the Ishimaru aortic arch type.

**Refer to the Myla aortic arch type.

of the SG. At 33 months of follow-up, stent induced new entry (SINE) occurred at the distal part of SG. At 46 months of follow-up, both proximal RTAD and distal SINE advanced. He died at 56 months due to acute left heart failure combined with mitral valve prolapse (**Figure 3**). The characteristics of 18 patients complicated with RTAD during or after TEVAR were presented in **Table 2**.

Univariate logistic regression analysis affecting the incidence of RTAD

There was a statistically significant association between the SG oversizing ratio (OR = 0.82, 95%CI = 0.73–0.93, P = 0.0011) and diameters of ascending aorta (OR = 1.09, 95%CI = 1.01–1.18, P = 0.0316) to the occurrence rate of RTAD. There was no statistically significant between the operation timing, the type of SG, medical history data, and operation mode were to the incidence of RTAD (P > 0.05). Full details are shown in **Table 3**.

Multivariate logistic regression analysis affecting the incidence of RTAD

The results of multivariate logistic regression analysis following the adjustment for confounding factors showed that the oversizing ratio influenced the incidence of RTAD (P < 0.05). The diameter of the ascending aorta, on the other hand was not associated with RTAD (P > 0.05). Details are supplied in **Table 4**.

Discussion

The occurrence of RTAD during or following TEVAR is rare but carries severe consequences (16–18). Wang et al. (8) noted in a meta-analysis that the overall incidence of RTAD was 2.2%. Eggebrecht et al. (2) reported an overall incidence of RTAD of 1.3% and a mortality rate of 42% in a multicenter retrospective study. Analyzing the statistical data of 1,688

TABLE 2 Characteristics of 18 patients complicated with RTAD during or after TEVAR.

Cases	Age	Gender	Coexisting conditions	Stent graft	Oversizing ratio	Onset time	Location of new tear	Cause of RTAD	Treatment	Follow-up and outcome
1	58Y	M	Hypertension	MEDTRONIC VALIANT	10	12D	TSG	SG	Medical	56M(died)
2	38Y	M	Hypertension	MEDTRONIC VALIANT	10	5W	TSG	SG	Surgery	130M
3	48Y	F	Marfan	COOK Zenith	13	3M	TSG	SG	Medical	3M(lost)
4	43Y	M	–	MEDTRONIC VALIANT	6	72M	≥2 cm (TSG)	Progress	Surgery	111M
5	72Y	M	Hypertension	MEDTRONIC VALIANT	5	16D	≥2 cm (TSG)	Clamp	Medical	97M(died)
6	44Y	M	Hypertension	–	–	Intraoperative	Ascending Aorta	Clamp	Surgery	1M(lost)
7	66Y	M	Hypertension	COOK Zenith	10	3M	TSG	SG	Medical	3M(lost)
8	43Y	M	Hypertension	COOK Zenith	9	3M	≥2 cm (TSG)	Progress	Surgery	96M
9	79Y	F	Hypertension	GORE TAG	6	9D	TSG	SG	Medical	24M(died)
10	78Y	M	–	GORE TAG	11	1W	TSG	SG	Medical	6M(died)
11	43Y	M	–	GORE TAG	11	Intraoperative	TSG	Dilation	Surgery	46M
12	60Y	M	Hypertension	MEDTRONIC VALIANT	9	1W	TSG	SG	Medical	2D(died)
13	55Y	F	Hypertension	MEDTRONIC VALIANT	8	3M	TSG	SG	Surgery	37M
14	43Y	M	Hypertension	MEDTRONIC VALIANT	0	4W	TSG	SG	Surgery	36M
15	59Y	M	–	MEDTRONIC VALIANT	6	4D	TSG	SG	Medical	6D(lost)
16	62Y	F	Hypertension	MEDTRONIC VALIANT	2	9D	TSG	SG	Medical	2D(died)
17	55Y	M	Hypertension	MEDTRONIC VALIANT	3	11D	TSG	Dilation	Surgery	26M
18	76Y	F	Hypertension	Microport Castor	9	6W	≥2 cm (TSG)	Progress	Medical	1D(died)

M, Male; F, Female; Y, Year; M, Month; W, Week; D, Day; TSG, tip of stent graft; SG, Stent graft; RTAD, Retrograde type A aortic dissection; TEVAR, thoracic endovascular aortic repair.

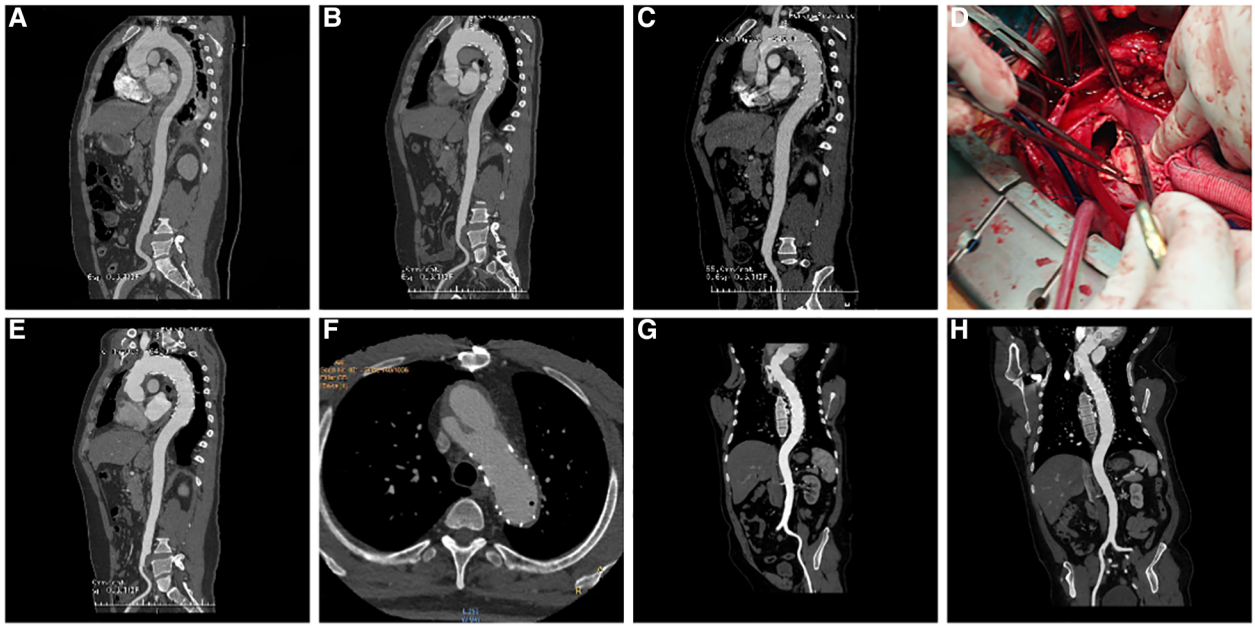

FIGURE 2
(A) three-dimensional (3D) reconstruction of preoperative surgery CTA showed intramural hematoma of descending aorta; (B) CTA demonstrated that the intramural hematoma was thinner than that before ten days following TEVAR; (C) five weeks following TEVAR, 3D reconstruction of CTA showed RTAD; (D) "ascending aortic replacement, hemi-arch replacement, and stented elephant trunk" was implemented in the emergency, and the entry tear was at the proximal stent; (E) CTA two weeks following the surgery showed changes in the ascending aorta and the arch after replacement; (F) At 90 months after the first surgery, local dissecting aneurysms at the arch were observed; (G) "ascending aortic replacement, total arch replacement, and stented elephant trunk" were performed during the second surgery; (H) CT re-examination on the nine months after second surgery. CTA, CT angiography; TEVAR, Thoracic Endovascular Aortic Repair; RTAD, Retrograde Type A Aortic Dissection; 3D, three dimension.

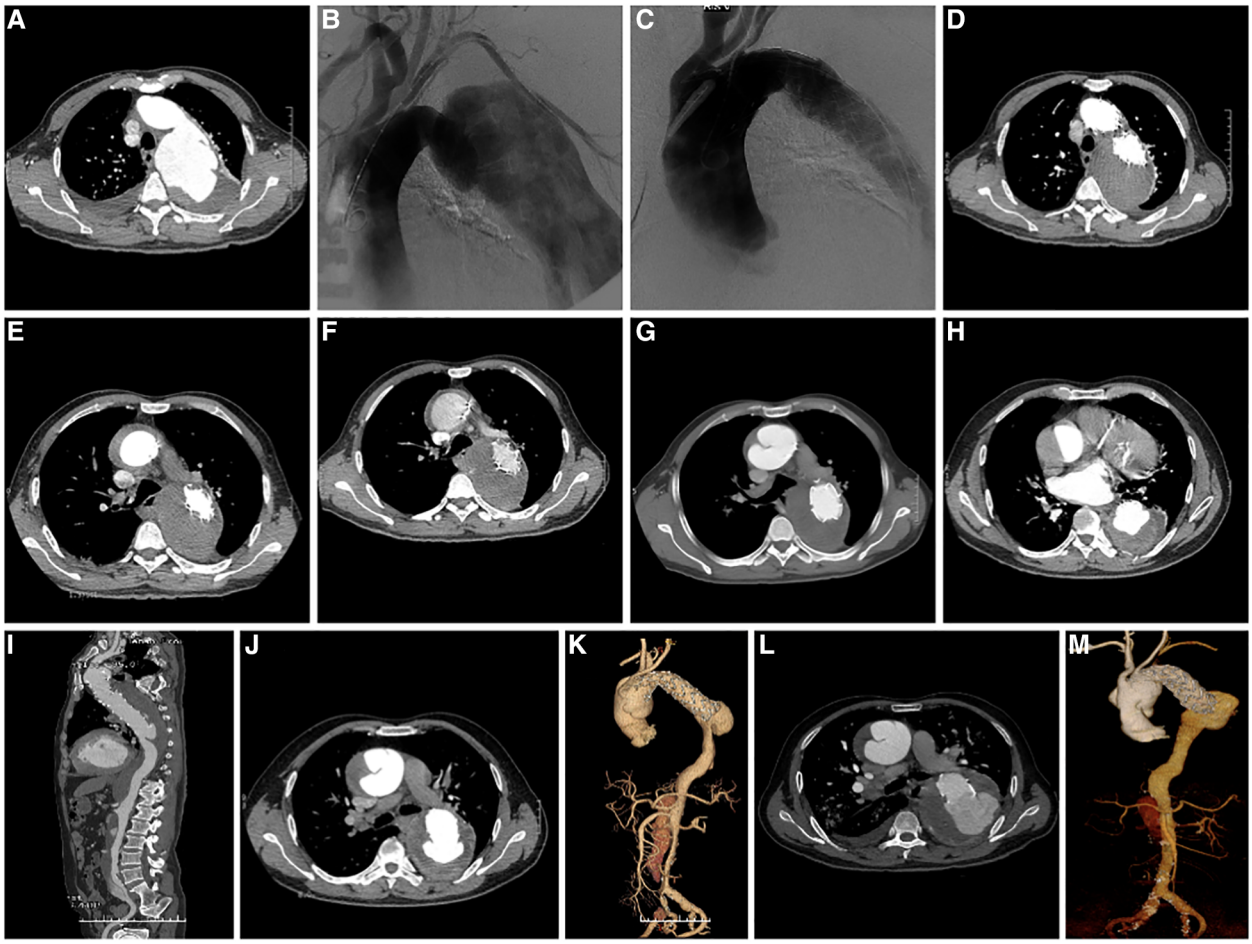

FIGURE 3
(A) preoperative CTA axial image of TEVAR showed TBAD; (B) Pre-stenting DSA shows a large false lumen with significant compression of the true cavity, and the entry located distal to the LSA; (C) DSA after stenting showed complete occlusion of the entry, widening of the true lumen, and improved blood flow; (D) CTA axial image ten days following TEVAR showed complete occlusion of the entry, thrombosis of the false lumen, and good visualization of the true lumen; (E) CTA at 13 days after TEVAR showed intermural hematoma formation in the ascending aorta; (F) CTA at three weeks after TEVAR showed intermural hematoma formation in the ascending aorta, with no significant change compared to the previous CTA; (G) CTA at 20 weeks after TEVAR showed progression of ascending aortic coarctation; (H) axial image of CTA at 32 months after TEVAR showed proximal RTAD and distal SINE; (I) 3D reconstruction of CTA at 32 months after TEVAR showed proximal RTAD and distal SINE; (J) axial image of CTA at 46 months after TEVAR showed progression of proximal RTAD and distal SINE. (K) 3D reconstruction of CTA at 46 months after TEVAR showed progression of both proximal RTAD and distal SINE; (L) Axial images of CTA at 56 months after TEVAR showed progression of both proximal RTAD and distal SINE; (M) 3D reconstruction of CTA at 56 months after TEVAR showed progression of both proximal RTAD and distal SINE. CTA, CT angiography; TEVAR, Thoracic Endovascular Aortic Repair; RTAD, Retrograde Type A Aortic Dissection; 3D, three dimension; SINE, Stent Induced New Entry.

TABLE 3 Univariate analysis of the variables for RTAD occurrence.

Variables	Value	RTAD occurrence	
		OR (95%CI)	*P*-value
Age	52.52 ± 12.71	1.03 (0.99, 1.06)	0.1553
Gender			
Female	260 (15.40%)	1.0	
Male	1,428 (84.60%)	0.47 (0.17, 1.33)	0.1531
Trauma			
No	1,631 (96.62%)	1.0	
Yes	57 (3.38%)	0.00 (0.00, Inf)	0.9870
Connective tissue disease			
No	1,649 (97.69%)	1.0	
Yes	39 (2.31%)	2.53 (0.33, 19.47)	0.3738
Hypertension			
No	422 (25.00%)	1.0	
Yes	1,266 (75.00%)	0.87 (0.31, 2.44)	0.7845

(*Continued*)

TABLE 3 Continued

Variables	Value	RTAD occurrence	
		OR (95%CI)	*P*-value
Diabetes			
No	1,670 (98.93%)	1.0	
Yes	18 (1.07%)	0.00 (0.00, Inf)	0.9888
Cardiovascular and cerebrovascular diseases			
No	1,469 (87.03%)	1.0	
Yes	219 (12.97%)	2.62 (0.92, 7.41)	0.0702
Renal insufficiency			
No	1,638 (97.04%)	1.0	
Yes	50 (2.96%)	0.00 (0.00, Inf)	0.9878
Smoking			
No	1,093 (64.75%)	1.0	
Yes	595 (35.25%)	1.85 (0.73, 4.69)	0.1946
Other complications			
No	1,396 (82.70%)	1.0	
Yes	292 (17.30%)	2.42 (0.90, 6.50)	0.0797
Pathological type			
TBAD	1,592 (94.31%)	1.0	
Non-TBAD	96 (5.69%)	0.00 (0.00, Inf)	0.9890
Pathological stage			
Acute	1,433 (84.89%)	1.0	
Chronic	255 (15.11%)	0.70 (0.16, 3.06)	0.6359
Surgical producers			
TEVAR	1,312 (77.73%)	1.0	
(Non-thoracotomy) Hybrid	149 (8.83%)	1.36 (0.30, 6.08)	0.6879
(Thoracotomy) Hybrid	73 (4.32%)	2.81 (0.62, 12.71)	0.1,785
TEVAR (Fenestration Technique)	52 (3.08%)	1.96 (0.25, 15.27)	0.5208
TEVAR (Branch Stent Repair Techniques)	102 (6.04%)	0.00 (0.00, Inf)	0.9888
Timing of surgical intervention			
Chronic phase	137 (8.12%)	1.0	
Subacute phase	156 (9.24%)	0.00 (0.00, Inf)	0.9858
Acute phase	1,395 (82.64%)	0.78 (0.18, 3.44)	0.7463
Mean time from disease onset to surgery	89.14 ± 470.25	1.00 (1.00, 1.00)	0.6847
Different stent design			
Poximal barbs		Ref	
Fully covered SG		2.2 (0.2, 21.9)	0.505
Proximal flared scallops or partially uncovered stents		0.4 (0.1, 1.8)	0.205
Proximal bare stent		0.5 (0.1, 2.0)	0.368
Oversizing ratio (%)	11.15 ± 4.77	0.82 (0.73, 0.93)	0.0011
Proximal landing zone			
Z0	203 (12.03%)	1.0	
Z1	436 (25.84%)	0.58 (0.15, 2.17)	0.4163
Z2	952 (56.43%)	0.42 (0.13, 1.41)	0.1618
Z3	96 (5.69%)	0.00 (0.00, Inf)	0.9886
Arch type**			
Type Ⅰ	639 (37.86%)	1	
Type Ⅱ	852 (50.47%)	0.86 (0.31, 2.37)	0.7647
Type Ⅲ	197 (11.67%)	1.40 (0.36, 5.45)	0.6311
Retrograde tear conditions			
No obvious retrograde tear	956 (56.64%)	1	
Retrograde tear to aortic arch	538 (31.87%)	1.79 (0.71, 4.54)	0.2198
Retrograde tear to ascending aorta	194 (11.49%)	0.00 (0.00, Inf)	0.9900
Diameter of ascending aorta (mm)	38.08 ± 4.96	1.09 (1.01, 1.18)	0.0316

SG, Stent graft; RTAD, retrograde type A aortic dissection; OR, odds ratio; CI, confidence interval.
**The classification of the aortic arch follows the methodology proposed by Myla.

TABLE 4 Multivariate logistic regression analysis of stent graft oversizing ratio, ascending aortic diameter and incidence of RTAD.

Variables	RTAD			
	Non-adjusted OR (95%CI)	*P*-value	adjusted OR (95%CI)	*P*-value
SG oversizing ratio	0.83 (0.74, 0.94)	0.0026	0.83 (0.73, 0.94)	0.0028
Ascending aorta diameter	1.06 (0.97, 1.15)	0.1818	1.06 (0.96, 1.17)	0.2373

SG, Stent graft; RTAD, retrograde type A aortic dissection; OR, odds ratio; CI, confidence interval.

TEVAR patients at our facility over the past 16 years, we found an overall incidence of RTAD at 1.1%, accompanied by a 39% all-cause mortality rate.

Is the design of the SG connected to the occurrence of RTAD? Dong et al. (7) reported 11 cases of proximal bare SG, nine cases of a new entry at the proximal region of the bare stent, and one case inside the anchoring area of the bare stent. Therefore, the authors concluded that the proximal bare stents were closely associated with the occurrence of RTAD. However, there is no consensus on this point of view. Ma et al. (13) hold the point that the radial force strength and the leverage effect of the SG rather than proximal bare SG were associated with RTAD. Ten patients in the current series had SG incorporated proximal bare metal stent, while the remaining seven had no proximal bare SG implanted, including three proximal barbs devices, three proximal flared scallop devices, and a covered debranching stent. The RTAD group consisted of patients who had a wide range of SG implanted and our statistical analysis indicated that the occurrence of RTAD was not directly linked to the stent design. It is worth noting that among the RTAD patients, three had Gore TAG stents with flared scallops, which were observed to have a significant abduction force when examined *in vitro*. To address this issue, a second-generation device called the Gore C-TAG (Comfortable TAG) was developed, where the proximal flared scallops of the SG were replaced with partially uncovered stents measuring 4–5 mm in length. This modification effectively reduced the abduction force of the proximal stent. Furthermore, the utilization of the Gore C-TAG in our department has significantly surpassed the usage of its previous generation counterparts. Notably, no cases of RTAD have been observed in patients treated with the C-TAG stent, which may be attributed to its improved compliance and reduced radial force. The compliance of a stent plays a crucial role in determining the risk of RTAD, as supported by several literatures (19–22).

Is there a link between the pathological nature of the disease and the development of RTAD? Dong et al. (7) have highlighted that Marfan syndrome is an important risk factor for the occurrence of RTAD. The pulsatile movement of the stent against the aortic wall during the cardiac cycle could cause damage to the aortic wall, leading to RTAD, particularly in patients with aortic dissection and connective tissue disorders such as Marfan syndrome. In our cohort, all 18 RTAD patients had aortic dissection, and one patient had Marfan syndrome. However, further evidence was needed to support the notion that aortic dissection was associated with RTAD than other thoracic aortic conditions.

Previous literature believed that a greater oversizing ratio was related to a higher RTAD. Kpodonu et al. (23) conducted a series of investigations involving seven cases with RTAD. Among these cases, two had a SG oversizing ratio close to 20%, and three had an oversizing ratio exceeding 20%. The study concluded that when the SG oversizing ratio surpasses 20%, the excessive radial force exerted on the intima may lead to intimal damage, potentially causing RTAD. Similarly, academics considered that 10%–15% of the SG oversizing ratio is sufficient and that excessive SG oversizing ratio should be avoided to prevent RTAD (7). However, Holger et al. (2) put forward different viewpoints and reported a multicenter study of 48 cases of RTAD with an average SG oversizing ratio of 6%. Among the 18 RTAD patients, the average oversizing rate was 7.5%. Notably, 82% of these cases fell within the range of 10% oversizing, with only three cases (18%) exceeding this threshold. The statistical analysis demonstrated a significantly higher incidence of RTAD in TEVAR patients with stent oversizing less than 10% compared to those with stent oversizing greater than 10%. This finding suggests that the presence of a certain gap, commonly referred to as a "bird beak" between the stent and the vessel wall may contribute to the up and down movement of the stent with each cardiac cycle, directly leading to RTAD. In our experience, appropriately increasing the SG oversizing ratio, especially for the Gore stent, could indeed reduce the "bird beak" phenomenon. It is worth drawing attention to that RTAD was not detected in 60 patients with SG oversizing greater than 20%. However, the sample size might have been too small to depict reality.

According to Canaud et al. (24), the proximal sealing zone in the aortic arch is one of the risk factors for the occurrence of RTAD. In our study, 96.8% RTAD patients had involvement in the Z0–2 region, but there was no significant difference in the incidence of RTAD between the Z0–2 and Z3–4 regions. With the extensive application of fenestration and debranching techniques in clinical practice, manipulation of the arch undoubtedly raises the frequency of RTAD (22, 25–27).

The diameter of the ascending aorta is also linked to the presence of RTAD. Williams et al. (10) proposed that the ascending aorta diameter exceeding 40 mm is a risk factor for the occurrence of RTAD, which contradicts our findings. Notably, two patients with ascending aorta diameters greater than 40 mm in the RTAD group were caused by iatrogenic factors. Therefore, caution should be taken when undertaking hybridization to avoid RTAD (6, 28, 29).

It is reported that surgical procedures were accountable for approximately 5% of aortic dissections (30, 31). Although the results of the present study showed that different surgical timing and methods did not directly affect the occurrence of RTAD, RTAD may be induced in certain specific surgical procedures such as balloon dilation. Two RTAD patients with aortic dissection in this research were associated with balloon dilation, and one of them with new dissection formation when an inadequately deployed stent in descending aortic arch was dilated

by balloon. In another patients, chimney stent implantation of the LCCA and balloon dilation were performed urgently due to accidental stent displacement that covered the LCCA. Although no abnormalities were detected during the TEVAR procedure, a significant bouncing movement of the bare stent was observed during balloon expansion of the chimney stent when reviewing intraoperative angiography. This vigorous movement of the stent has the potential to damage the vascular wall and contribute to the occurrence of RTAD. Impressively, individuals with thoracic aortic aneurysm and aortic coarctation did not experience RTAD after balloon dilation in the current study. Therefore, balloon dilation should be avoided in patients with aortic dissection.

Gender, age, comorbidities, and arch type were not shown to be directly connected to the occurrence of RTAD in this research. It is worth noting that 94% of patients in this research have an aortic dissection, and the average age is 52 years old, which is 10–15 years younger than the average age reported in Europe and the United States. Additionally, these patients had fewer underlying diseases, which could be one of the reasons for the relatively low overall incidence of RTAD (32, 33).

So, how could RTAD be effectively avoided? (I) If TEVAR is selected for aortic dissection patients with connective tissue disease, emphasis should be made on operational issues such as avoiding unnecessary operations in the arch and selecting stent grafts with higher flexibility; (II) The right SG oversizing might assist the stent in conforming better with the aortic wall; (III) When the diameter of the ascending aorta exceeds 40 mm, especially in the presence of calcification and other abnormalities, it is advisable to avoid surgical intervention in the ascending aorta. If circumstances permit, simultaneous replacement of the ascending aorta is a preferred alternative; (IV) Balloon dilation was not recommended for patients with aortic dissection during TEVAR. This study offered objective data on the rate of RTAD utilizing a large sample size from a single center. However, it has to be mentioned that the primary limitation of this study is its retrospective characteristic.

Conclusion

RTAD is a rare yet catastrophic complication. It could occur both during the procedure, early and late postoperative periods. Maintaining an appropriate SG oversizing ratio is crucial to minimize the risk of RTAD.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by The study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Henan Provincial People's Hospital, People's Hospital of Zhengzhou University. The patients/participants provided their written informed consent to participate in this study.

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

GQW: conception and design, collection and assembly of data, data analysis and interpretation, manuscript writing; YFQ and SST: collection and assembly of data, data analysis and interpretation, manuscript writing; KWZ and STZ: collection of data, data analysis and interpretation; TXL: conception and design, financial support, administrative support, manuscript writing, final approval of the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Patent iliolumbar artery increase no risk of type II endoleaks after endovascular abdominal aortic aneurysm: a case-control study

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Objective: The aims of the present study were to explore the risk factors for type 2 endoleaks (T2ELs) after endovascular aneurysm repair (EVAR) and the association between T2ELs and the iliolumbar artery.

Materials and methods: A single-center, retrospective case–control study in West China Hospital was conducted among patients with infrarenal abdominal aortic aneurysm (AAA) who underwent EVAR between June 2010 and June 2019. The associations of patient characteristics, anatomical factors, internal iliac artery embolization, and ILA with the primary outcome were analyzed. The secondary objective was to analyze survival and reintervention between the T2EL group and the non-T2EL group. Kaplan–Meier survival, propensity matching analysis and multivariate logistic regression analysis were used.

Results: A total of 603 patients were included. The median follow-up was 51 months (range 5.0–106.0). There was a significant difference in the diameter of the lumbar artery (LA), middle sacral artery (MSA) and inferior mesentery artery (IMA), proportion of thrombus and LA numbers. The univariate analysis showed that T2ELs were more likely to develop more thrombus in aneurysm cavity (OR = 0.294, $p = 0.012$), larger MSA (OR = 1.284, $p = 0.04$), LA (OR = 1.520, $p = 0.015$), IMA (OR = 1.056, $p < 0.001$) and more LAs (OR = 1.390, $p = 0.019$). The multivariate analysis showed that the number of LAs (HR: 1.349, 95% CI: 1.140–1.595, $p < .001$) and the diameter of the IMA (HR: 1.328, 95% CI: 1.078–1.636, $p = 0.008$) were significantly associated with T2ELs. There were no new findings from the propensity score matching. The reintervention-free survival rates were significantly different between the two groups ($p = 0.048$). Overall survival and AAA-related death rates were not different between the two group. This was consistent with the PSM analysis.

Conclusion: The iliolumbar artery and the different internal iliac artery interventions may not increase the incidence of T2ELs. But the numbers of LAs and IMA diameter were independent risk factors for T2Els. T2ELs was associated with the reintervention but did not affect long-term survival or increase aneurysm-related mortality after EVAR.

KEYWORDS

abdominal aortic aneurysm, endovascular aortic repair, type 2 endoleaks, iliolumbar artery, risk factors

Introduction

Abdominal aortic aneurysm (AAA) is defined as a disease with an abdominal aortic diameter of more than 3 cm or 50% greater than the normal aortic diameter (1, 2). Although endovascular aortic aneurysm repair (EVAR) has become the first choice of treatment because of its advantages of less trauma, faster recovery and lower perioperative mortality, several studies have shown that the reintervention rate of EVAR is higher than that of OSR (3–5). Endoleaks, an important cause of reintervention, is a common and unique complication of EVAR and occurs in approximately 1/3 of postoperative patients (6). Type II endoleaks (T2ELs) are caused by retrograde blood flow from the side branches of the abdominal aorta entering the aneurysm sac after excluding the aneurysm, and they are the most common type of endoleaks, with an incidence rate between 8% and 44% (7–9).

The treatment methods for T2ELs include trans-lumbar direct embolization of the aneurysm sac, embolization of the aortic branches through the superior mesenteric artery or lumbar arteries, trans-cavity embolization, and open or laparoscopic clipping of side branches (10). Postoperative reintervention of the T2EL is challenging, while intervening in the anatomical risk factors seems to be more advantageous intraoperatively. Abdominal aortic collateral artery embolization can reduce the incidence of T2ELs and the reintervention rate (11–18) and promote the reduction of aneurysms after EVAR (12, 13, 16–18), with a lower incidence of complications (12). The high anatomical risk factors for T2ELs include patent IMA and LA (16, 19, 20). In addition, the incidence of T2ELs was also associated with the internal iliac artery ranging from 0 to 3.8% (21), and some investigators believe it was related to the iliolumbar artery (21, 22). The iliolumbar artery and lumbar artery are connected through collateral circulation and can communicate with the fourth lumbar artery (23–25). However, no studies have investigated the association between the iliolumbar artery and T2ELs after EVAR. The purpose of this study was to investigate the relationship between the iliolumbar artery and T2ELs after EVAR.

Method

Study design

This was a single-center, retrospective case–control study. The primary objective of this study was to investigate the relationship between the iliolumbar artery and T2ELs. The secondary objective was to investigate the effect of postoperative T2ELs on long-term mortality and reintervention rates. The patients with T2ELs were screened by a color Doppler ultrasound system and PACS system. The diameter of the ilio-lumbar artery was measured within approximately 1.5 cm of its origin, and the location of its origin was recorded.

Study population/participants

Patients with AAA who underwent EVAR in the Department of Vascular Surgery, West China Hospital, Sichuan University from June 2010 to June 2019 were enrolled. The exclusion criteria of this study were formulated as follows: (1) thoracoabdominal aortic aneurysm, para-renal abdominal aortic aneurysm, or suprarenal abdominal aortic aneurysm. (2) Patients undergoing hybrid abdominal aortic aneurysm surgery. (3) Abdominal aortic dissection aneurysm or pseudoaneurysm or perforating ulcer. (4) Ruptured abdominal aortic aneurysm or EVAR conversion to open surgery. (5) Patients who had no abdominal aortic CT before the operation and no follow-up records. (6) Patients with type I and III endoleaks.

Data collection

The standardized electronic data system of West China Hospital, HIS system of medical records and PACS system of imaging data were used to obtain the data of the research subjects. Data were collected from patient medical records and included the following baseline and anatomical variables and operation information: age, sex, preoperative AAA diameter, neck length, maximum iliac artery diameters, anatomical characteristics of the internal iliac artery and iliolumbar artery, anesthesia method, etc. To ensure the accuracy of the data, 20% of the data were randomly checked by senior physicians in vascular surgery. If the measurement deviation was more than 10%, the senior physicians remeasured and corrected the data. Patients were divided into two groups: with or without T2ELs (The case group was T2ELs and the control group was non-T2ELs).

Surveillance protocol

Ethics

This study was approved by the Ethics Committee of West China Hospital, Sichuan University. All the study participants provided written informed consent stating that the clinical data could be used in clinical research.

Analysis method

All statistical analyses were performed using SPSS version 25 (IBM Corporation, Armonk, NY). The data are presented as the mean ± standard deviation for continuous variables and as the frequency (percentage) for categorical variables, which were compared using the two-sample t-test, Fisher's exact test, and Pearson's χ^2 test where appropriate. Overall survival and AAA-related mortality were generated using the Kaplan–Meier method, and the log-rank test was used to compare the differences. Differences with a p value <.05 were significant. The propensity matching score was used to calibrate the baseline.

Result

Baseline

A total of 603 patients were included (T2EL, 505. N-T2EL, 98, Supplementary Figure S4). Baseline characteristics are depicted in Table 1. The mean patient age was 72.0 ± 8.3 years, and males comprised 83.9% of patients. No endoleaks were identified in 505 patients (83.7%), and T2ELs were found in 98 patients (16.3%). Except for CKD, there was no significant difference between the two groups in preoperative comorbidities. T2EL patients had a lower prevalence of CKD (2.8%) than N-T2EL patients (7.1%, $p = 0.031$). Oral beta-blockers were more common in the N-T2EL group than in the T2EL group ($p = 0.01$). The median follow-up duration was 49.0 months (IQR: 42; range 1.0–136.0) in the N-T2EL group and 54.2 months (IQR: 35.5; 1.0–138.0) in the T2EL group.

TABLE 1 Baseline characteristics of patients with or without T2ELs after EVAR.

	N-T2EL ($N = 505$)	T2EL ($N = 98$)	p
Age	72.1 ± 8.3	72.4 ± 8.0	0.43
Male gender	426 (84.4%)	80 (81.6%)	0.502
Smoking history	309 (61.2%)	59 (60.2%)	0.855
Hypertension	342 (67.7%)	64 (65.3%)	0.641
Diabetes	66 (13.1%)	12 (12.2%)	0.824
COPD	104 (20.6%)	24 (24.5%)	0.388
Dyslipidemia	27 (27%)	7 (7.1%)	0.483
Coronary artery disease	92 (18.2%)	22 (22.4%)	0.328
Chronic kidney disease	14 (2.8%)	7 (7.1%)	0.031
Anesthesia method			0.377
Local anesthesia	370 (73.3%)	76 (77.6%)	
General anesthesia	135 (26.7%)	22 (22.4%)	
Medication			
Statin	90 (17.8%)	20 (20.4%)	0.544
Antiplatelet	413 (81.8%)	84(85.7%)	0.272

Data are presented as n (%) or mean ± standard deviation.
COPD, chronic obstructive pulmonary disease; ACEI, angiotensin-converting enzyme inhibitor.

The vascular morphologic characteristics are shown in Table 2. Our results showed that the proportion of thrombus in the aneurysm cavity ($p = 0.011$), the diameter of the median sacral artery ($p = 0.04$), lumbar artery ($p = 0.015$), inferior mesenteric artery ($p < 0.001$) and the number of lumbar arteries ($p = 0.019$) were significantly different between the two groups. The diameter of the ILA in the N-T2EL group was 2.3 ± 0.7 mm, and in the T2EL group, the right ILA was 2.4 ± 0.6 mm, and the left ILA was 2.5 ± 1.4 mm (Table 3).

In Table 4, patient characteristics were compared based on the type of IIA embolization performed and primary IIA occlusion. A total of 443 individuals did not undergo any preoperative IIA intervention (T2EL, 72.4%. N-T2EL, 73.7%). In addition, 160 patients (26.5%) received the intervention. Sixty patients (T2EL, 10.7%. N-T2EL, 6.1%) accepted unilateral stent-covered IIA without embolization, and 10 patients (T2EL, 1.8%. N-T2EL, 1.0%) bilateral stent coverage without embolization. Unilateral stent coverage with embolization was performed in 59 patients (T2EL, 9.5%. N-T2EL, 11.2%), and bilateral stent coverage with embolization was completed in 31 patients (T2EL, 4.4%). N-T2EL, 9.2%). Our analysis showed no significant difference between the two groups in the intervention mode of IIA ($p = 0.224$). There was also no difference in primary iliac artery occlusion between the two groups ($p = 0.723$). No variable was significantly different in the anatomic origin of ILA between the two groups.

In the univariate analysis (Table 2), our results showed that T2ELs may have larger MSA (OR = 1.284, $p = 0.04$), LAs (OR = 1.520, $p = 0.015$), and IMA (OR = 1.056, $p < 0.001$) and more LAs (OR = 1.390, $p = 0.019$). And the patients with T2EL may have smaller proportion of thrombus in the aneurysm cavity (OR = 0.294, $p = 0.012$).

The factors with $p < 0.1$ in the univariate analysis in Tables 1, 2 were subjected to a subsequent multivariate analysis to evaluate the

TABLE 2 Univariable analysis of patients with or without T2ELs after EVAR.

	OR (95% CI)	p	OR (95% CI)	p
Age	0.990 (0.964–1.016)	0.429	0.993 (0.967–1.020)	0.616
Max-diameter of AAA (mm)	1.009 (0.993–1.025)	0.263	1.004 (0.988–1.021)	0.606
diameter of AAA neck (mm)	1.048 (0.969–1.133)	0.244	1.035 (0.95–1.128)	0.427
Length of AAA neck (mm)	1.000 (0.983–1.017)	0.965	0.998 (0.980–1.016)	0.804
Proportion of thrombus	0.294 (0.113–0.763)	0.012	0.72 (0.262–1.977)	0.523
α angle	1.003 (0.996–1.011)	0.409	1.00 (0.992–1.009)	0.908
β angle	1.002 (0.994–1.009)	0.671	1.00 (0.992–1.008)	0.994
Diameter of right CIA	1.007 (0.985–1.030)	0.515	1.008 (0.985–1.032)	0.513
Diameter of left CIA	1.015 (0.990–1.040)	0.244	1.020 (0.999–1.042)	0.068
Diameter of right IIA	1.017 (0.983–1.052)	0.324	1.016 (0.981–1.053)	0.374
Diameter of left IIA	1.020 (0.993–1.048)	0.148	1.021 (0.991–1.052)	0.168
Diameter of MSA	1.284 (1.011–1.631)	0.040	0.962 (0.746–1.242)	0.767
Diameter of LA	1.520 (1.067–2.164)	0.02	1.161 (0.775–1.740)	0.468
Diameter of IMA	1.056 (1.241–1.829)	<0.001	1.137 (0.919–1.407)	0.236
Numbers of patent LA	1.390 (1.195–1.618)	<0.001	1.100 (0.927–1.306)	0.273
Diameter of right ILA	1.394 (0.996–1.951)	0.053	1.164 (0.810–1.673)	0.412
Diameter of left ILA	1.221 (0.960–1.553)	0.103	1.101 (0.865–1.401)	0.433

HR, odds ratio; CIA, celiac internal artery; MSA, median sacral artery. IMA, inferior mesentery artery; IIA, internal iliac artery; LA, lumbar artery; ILA, ilioiliac lumbar artery.

TABLE 3 Anatomic characteristics of patients.

	T2EL (−)	N-T2EL (+)	*p*
Max-diameter of AAA (mm)	53.7 ± 13.4	55.3 ± 13.8	0.263
Diameter of neck	21.3 ± 2.6	21.6 ± 2.9	0.244
Length of neck	28.1 ± 12.6	28.1 ± 13.1	0.965
Proportion of thrombus	0.3 (0.1, 0.5)	0.2 (0.1, 0.4)	0.011
α angle	32.5 ± 27.3	35.1 ± 30.5	0.410
β angle	48.2 ± 29.8	49.6 ± 30.6	0.671
Diameter of right CIA	18.9 ± 9.2	19.5 ± 9.7	0.515
Diameter of left CIA	17.3 ± 7.6	18.3 ± 10.1	0.242
Diameter of right IIA	10.9 ± 5.9	11.6 ± 5.5	0.332
Diameter of left IIA	11.2 ± 6.7	12.3 ± 8.1	0.143
Diameter of MSA	0.9 ± 0.9	1.1 ± 0.9	0.040
Diameter of LA	2.5 ± 0.6	2.6 ± 0.6	0.015
Diameter of IMA	2.3 ± 2.5	2.7 ± 1.2	<0.001
Complicated with CIA	125 (24.8)	28 (28.6)	0.427
Complicated with IIA	78 (15.4)	10 (10.2)	0.179
Number of patent LA	6.0 (4.0, 6.0)	6.0 (6.0, 7.0)	0.019
Diameter of right ILA	2.3 ± 0.7	2.4 ± 0.6	0.052
Diameter of Left ILA	2.3 ± 0.7	2.5 ± 1.4	0.068

Data are presented as *n* (%) or mean ± standard deviation.
CIA, celiac internal artery; MSA, median sacral artery; IMA, inferior mesentery artery; IIA, internal iliac artery; LA, lumbar artery; ILA, ilioiliac lumbar artery.

TABLE 4 Characteristics of the internal iliac artery and ILA.

	T2EL (−)	T2EL (+)	*p*
Internal iliac intervention			0.224
No intervention	372 (73.7%)	71 (72.4%)	
Unilateral stent coverage	54 (10.7%)	6 (6.1%)	
Bilateral stent coverage	9 (1.8%)	1 (1.0%)	
Unilateral stent coverage with embolization	48 (9.5%)	11 (11.2%)	
Bilateral stent coverage with embolization	22 (4.4%)	9 (9.2%)	
Primary internal iliac occlusion			0.723
No occlusion	473 (93.7%)	94 (95.9%)	
Unilateral occlusion	25 (5.0%)	4 (4.1%)	
Bilateral occlusion	7 (1.4%)	0 (0%)	
Left origin of ilio-lumbar artery			0.26
Posterior division of IIA	167 (33.1%)	41 (41.8%)	
The trunk of IIA	313 (62.0%)	51 (52.0%)	
Left CIA	14 (2.8%)	4 (4.1%)	
Right origin of ilio-lumbar artery			0.223
Posterior division of IIA	109 (21.6%)	15 (15.3%)	
The trunk of IIA	385 (76.2%)	79 (80.6%)	
Right CIA	4(0.8%)	2(2.0%)	

Data are presented as *n* (%).

association with T2ELs. In Table 5, our multivariate analysis showed the number of LAs (before, OR: 1.351, 95% CI: 1.144–1.597, $p < .001$. After, OR: 1.349, 95% CI: 1.140–1.595, $p < .001$), and diameter of IMA (Before, OR: 1.330, 95% CI: 1.08–1.637, $p = .007$. After, OR: 1.328, 95% CI: 1.078–1.636, $p = .008$) were identified to be significantly associated with T2Els, which was consistent after adjusting for the IIA.

ROC analysis (Figure 1) showed that the cutoff value for the number of LAs was 6 (AUC = 0.640, 95% CI: 0.587–0.693, sensitivity = 0.714, specificity = 0.522) and for the diameter of the IMA was 2.5 mm (AUC = 0.642, 95% CI: 0.584–0.699, sensitivity = 0.786, specificity = 0.48).

The Kaplan–Meier curves in Figures 2, 3 show that there were no differences between the T2EL group and N-T2EL group in overall survival (T2EL, 71.9%, N-T2EL, 59.9% at 8 years, $p = 0.45$) and freedom from AAA-related death (T2EL, 95%, N-T2EL, 91.3% at 8 years, $p = 0.61$). The reintervention-free survival rates at 8 years were 96.1% and 77.3% in patients with and without T2ELs, respectively, which were significantly different between the two groups ($p = 0.049$, Figure 4).

Variables of PSM included all anatomical data, age, sex, and preoperative comorbidities (Table 6, univariable analysis after PSM). The propensity score matching (PSM) included 391 patients (T2ELs vs. non-T2ELs: 91 vs. 297), and the multivariate analysis after PSM in Table 5 indicated that the independent risk factors for T2ELs were still the number of LAs (OR: 1.349, 95% CI: 1.140–1.595, $p < 0.001$) and the diameter of the IMA (OR: 1.328, 95% CI: 1.078–1.636, $p = 0.008$). There was no significant difference between the intervention modes of IIA and ILA in the two groups. Additionally, the Kaplan–Meier curves after PSM found that T2ELs group had a higher rate of reintervention ($p = 0.034$) in Supplementary Figure S3, but there was no difference in overall survival and AAA-related death between the two groups (Supplementary Figures S1 and S2).

Discussion

The management of T2EL remains controversial in the current literature, and it has several definitions, including “early”, “late”, “persistent” and “isolated” type II endoleaks. T2ELs were observed in 10.2% of patients after EVAR (9), and 30% to 50% of these resolved spontaneously (9, 26). In a Japanese nationwide analysis, persistent T2EL was defined as T2EL detected after EVAR on initial contrast-enhanced CT and during follow-up or new T2EL not documented at the end of EVAR but reported at any point during follow-up (27). A correlation between persistent T2ELs (p-T2ELs) and late adverse events, including aneurysm sac enlargement, reintervention, rupture, and abdominal aortic aneurysm-related mortality after endovascular aneurysm repair, was demonstrated. In addition to p-T2ELs, older age, female sex, chronic kidney disease, and dilated proximal neck were associated with sac enlargement.

Wang et al. (28) analyzed 10-year follow-up results and found that T2ELs were significantly associated with aneurysm sac growth, but no association with survival was observed. The low overall survival rate in our analysis may be related to COVID-19.

Current guidelines, such as the 2019 European Society for Vascular Surgery (ESVS) guideline and Society for Vascular Surgery implementation of clinical practice guidelines, have recommended conservative management, and intervention was indicated for significant sac expansion (≥10 mm or 5 mm) (1, 29). Although reintervention for T2ELs after EVAR could achieve some clinical effects (30–32), a study (33) found that embolization procedures were generally ineffective in preventing further expansion of abdominal aortic aneurysms in patients with T2ELs after EVAR. The risk of repeated intervention after

TABLE 5 Multivariate analysis before (M1) and after (M2) adjusting for primary hypogastric artery condition.

	Before		After		PSM	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
CKD	2.596 (0.983–6.855)	0.054	2.612 (0.986–6.920)	.053	0.383 (0.145–1.015)	0.053
Diameter of MSA	1.102 (0.854–1.422)	0.497	1.095 (0.847–1.415)	.489	1.095 (0.847–1.415)	0.489
Diameter of IMA	1.330 (1.08–1.637)	.007	1.328 (1.078–1.636)	.008	1.328 (1.078–1.636)	0.008
Numbers of patent LA	1.351 (1.144–1.597)	<.001	1.349 (1.140–1.595)	<.001	1.349 (1.140–1.595)	<.001
Proportion of thrombus	0.423 (0.157–1.179)	.100	0.424 (0.152–1.182)	.101	0.424 (0.152–1.182)	0.101
Diameter of right ILA	1.389 (0.957–2.017)	.084	1.394 (0.958–2.028)	.083	1.394 (0.958–2.028)	0.083
Primary internal iliac occlusion						
Unilateral occlusion	—	—	0.821 (0.227–2.976)	.764	1.606 (0.146–17.641)	0.698
Bilateral occlusion	—	—	0.623 (0.057–6.840)	.698	1.319 (0.143–12.128)	0.807
Internal iliac intervention						
Unilateral stent coverage	0.569 (0.230–1.407)	.222	0.706 (0.155–3.224)	.653	0.281 (0.023–3.460)	0.321
Bilateral stent coverage	0.644 (0.076–5.435)	.686	1.023 (0.042–24.696)	.989	0.198 (0.019–2.032)	0.173
Unilateral stent coverage with embolization	1.093 (0.520–2.301)	.814	1.324 (0.314–5.575)	.702	0.287 (0.030–2.773)	0.281
Bilateral stent coverage with embolization	2.247 (0.957–5.277)	.063	3.564 (0.289–43.961)	.083	0.372 (0.033–4.237)	0.425

CIA, celiac internal artery; MSA, median sacral artery; IMA, inferior mesentery artery; IIA, internal iliac artery; LA, lumbar artery; ILA, ilioiliac lumbar artery.

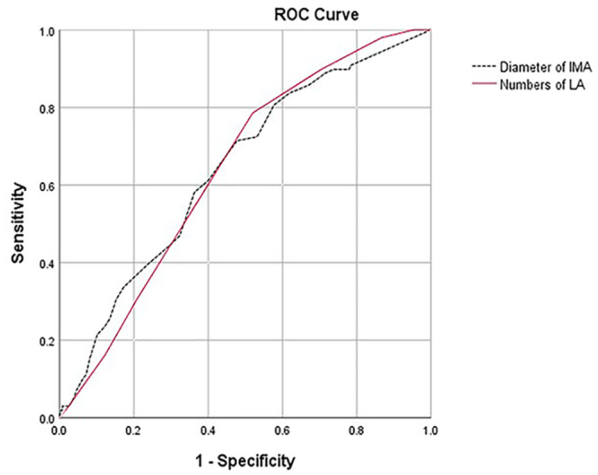

FIGURE 1
ROC analysis showed that there was no difference in predictive value between the number of LAs (AUC = 0.640, 95% CI: 0.587–0.693, sensitivity = 0.714, specificity = 0.522) and the diameter of the IMA (AUC = 0.642, 95% CI: 0.584–0.699, sensitivity = 0.786, specificity = 0.48, $p = 0.972$).

reintervention for T2ELs exists, and the key to treating T2ELs has shifted from reintervention to prevention.

Therefore, identifying risk factors for T2ELs and early intervention in high-risk patients are key to treatment. Our study found that the IMA diameter and the number of LAs were independent risk factors, which was consistent with most studies (8, 13, 22, 34). Through ROC curve analysis, this study determined the number of lumbar arteries (≥6) and the cutoff of IMA diameter (≥2.5 mm). Some studies have identified IMA ≥3 mm as a risk factor for T2ELs (11, 12).

IIA embolization has also been suggested as a risk factor for T2ELs in some studies (35, 36). They thought IIA embolization was more likely to increase the redistribution of blood flow from the lumbar arteries and IMA branches than IIA stent coverage alone. The formation of collateral circulation may also be associated with ILA. Meishi et al. (22) thought that the iliolumbar artery arising from the IIA was a major source of T2ELs. In their study, no significant impact of IIA embolization on T2ELs was observed after analyzing 375 patients. Of all 603 patients in our article, 9.8% received unilateral and 5.1% bilateral IIA embolization. The multivariate analysis showed that the different interventions for IIA were not associated with T2ELs, regardless of the IIA status. Currently, iliac branch devices are used to preserve at least one IIA. From existing studies (37, 38) and the limited evidence presented in our article, preservation of the IIA does not appear to increase the incidence of T2ELs (22).

In addition, the relationship between ILA and T2ELs has not been compared, although it has sometimes been found to be the source of T2ELs during follow-up (**Figure 5**). In our study, the right ILA diameter measured based on abdominal CTA was 2.31 ± 0.65 mm, and the left ILA was 2.30 ± 0.66 mm, which was similar to previous results based on human anatomy, which reported that the diameter was 2.7 ± 0.6 mm (39). We found that 28.0% of ILAs originated from the posterior of the IIA, 69.9% from the main trunk of the IIA, and 0.2% from the CIA. Kiray et al. (40) reported an average ILA diameter of 3.7 ± 0.7 mm, and Teli et al. (25) reported an average ILA diameter of 3.5 ± 0.5 mm. Koc et al. (23) reported that the ILA diameter originating from the main trunk of the IIA was smaller than that originating from the posterior branch of the IIA. In addition, the iliac lumbar artery mainly originates from the main internal iliac artery and less from the posterior branch of the IIA and CIA (25, 39, 40). This finding was similar to our study.

In the T2ELs caused by ILA, we found that ILA tended to be backward and upward, but only 2% of T2ELs were caused by ILA. There was no significant difference in the anatomical characteristics of the ILA in univariate analysis, and the right

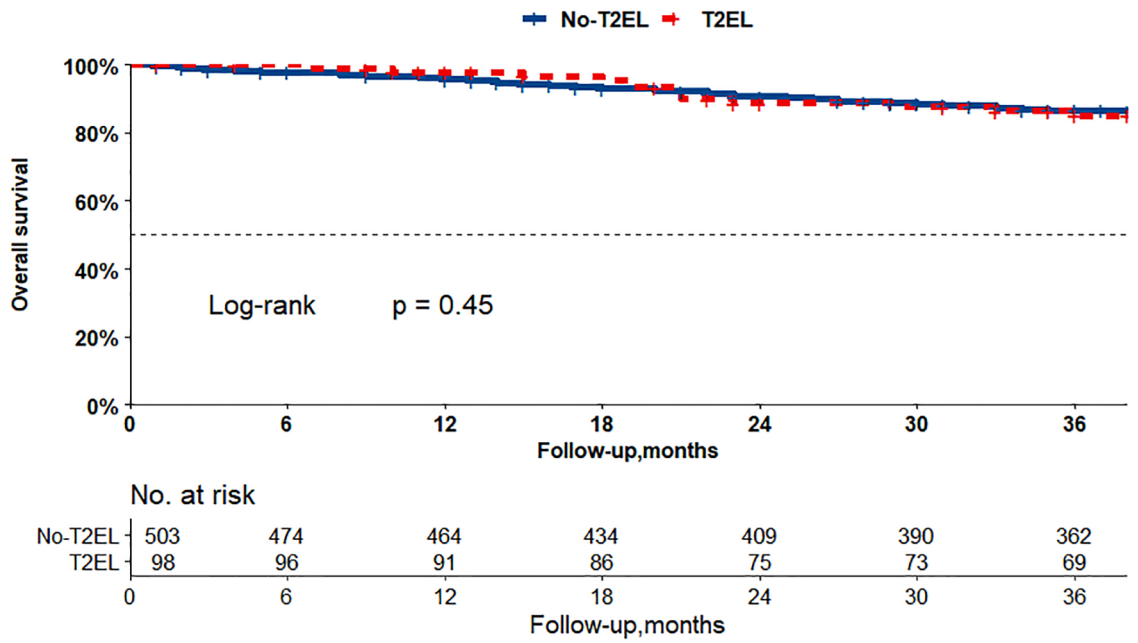

FIGURE 2
Overall survival did not differ between the patients with T2ELs and those without T2ELs. (p = 0.45, log rank test).

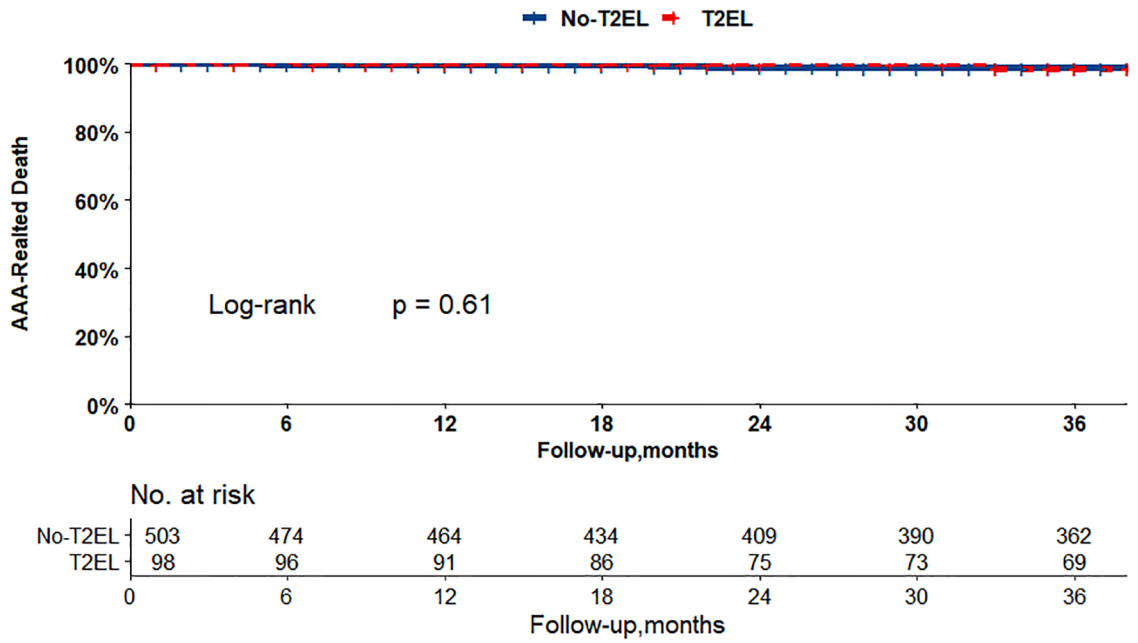

FIGURE 3
AAA-related survival did not differ between the patients with T2ELs and those without T2ELs. (p = 0.61, log rank test).

ILA diameter also showed no difference in multivariate analysis (p = 0.83). T2ELs from the IIA reported in the past are relatively rare, and the incidence of most previous report series is between 0% and 3.8% (21, 41), and no correlation was demonstrated in previous studies (22, 42). Other risk factors associated with T2ELs include chronic kidney disease, advanced age, aneurysm sac volume, and aneurysm sac thrombus volume (34, 43–46). Although our study did not find a statistical correlation between ILA and T2ELs, T2ELs caused by ILA still deserve attention.

Pre-embolization for the IMA or aneurysm sac in high-risk patients seems to be of greater benefit (14, 47, 48), and it could suppress aneurysm sac expansion and reduce the reintervention rate. A network meta-analysis (49) suggested that IMA embolization demonstrated benefits in achieving long-term

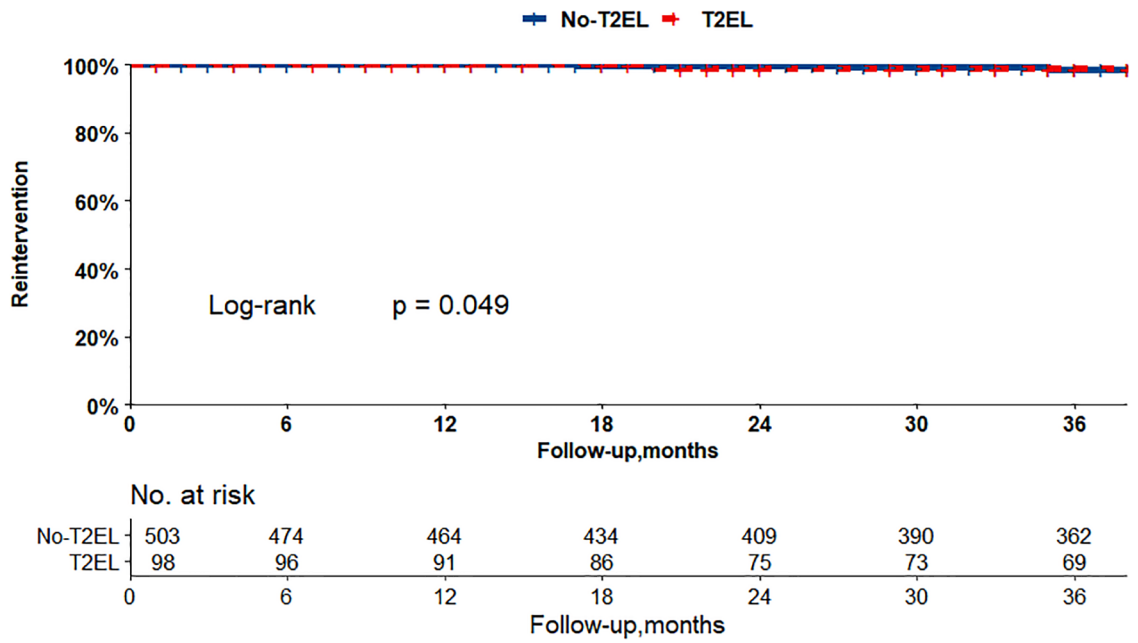

FIGURE 4
Patients with T2ELs had more reinterventions than those without T2ELs ($p = 0.049$, log rank test).

TABLE 6 Univariable analysis of patients with or without T2EL after EVAR after PSM.

	Univariable analysis Hazard ratio (95% CI)	*p*
Age	0.993 (0.967–1.020)	0.616
Max-diameter of AAA (mm)	1.004 (0.988–1.021)	0.606
diameter of AAA neck (mm)	1.035 (0.95–1.128)	0.427
Length of AAA neck (mm)	0.998 (0.980–1.016)	0.804
Proportion of thrombus	0.72 (0.262–1.977)	0.523
α angle	1.00 (0.992–1.009)	0.908
β angle	1.00 (0.992–1.008)	0.994
Diameter of right CIA	1.008 (0.985–1.032)	0.513
Diameter of left CIA	1.020 (0.999–1.042)	0.068
Diameter of right IIA	1.016 (0.981–1.053)	0.374
Diameter of left IIA	1.021 (0.991–1.052)	0.168
Diameter of MSA	0.962 (0.746–1.242)	0.767
Diameter of LA	1.161 (0.775–1.740)	0.468
Diameter of IMA	1.137 (0.919–1.407)	0.236
Numbers of patent LA	1.100 (0.927–1.306)	0.273
Diameter of right ILA	1.164 (0.810–1.673)	0.412
Diameter of left ILA	1.101 (0.865–1.401)	0.433

CIA, celiac internal artery. MSA, median sacral artery. IMA, inferior mesentery artery. IIA, internal iliac artery. LA, lumbar artery. ILA, ilio-iliac lumbar artery.

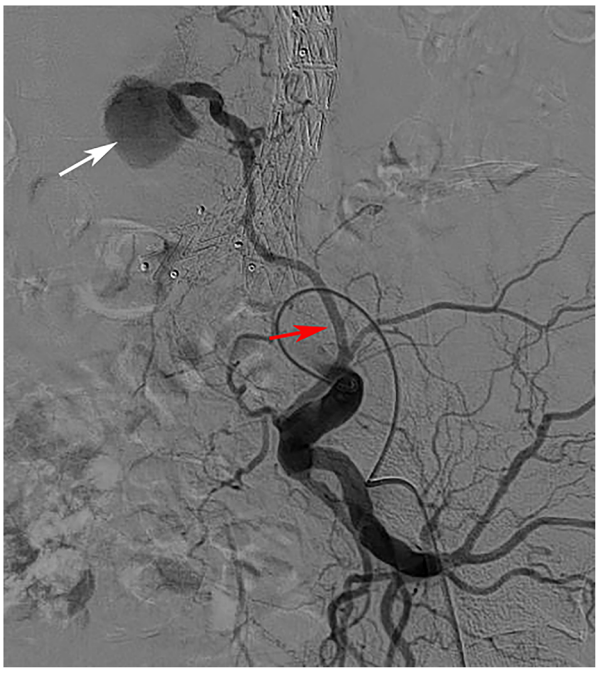

FIGURE 5
The iliolumbar artery was a source of type 2 endoleak. (Red arrow is the ILA, white arrow is the aneurysm cavity).

aneurysm sac stability and lowering the risk of secondary surgery. Nonselective embolization of aneurysm sac side branches more effectively reduces the incidence of T2ELs, while IMA embolization alone or in combination with aneurysm sac coil embolization enhances the clinical benefits of EVAR. Sun et al. (49) analyzed whether nonselective preemptive aneurysm sac embolization could prevent T2ELs in the short and mid-term, and they interestingly found that the IMA diameter showed continuous regression in the embolization group.

However, Kontopodis et al. (50) in their meta-analysis that included four random studies, suggested that preemptive embolization confers no clinical benefits in EVAR, but their data were limited and had low certainty. Additionally, Väärämäki et al. (51) found that the strategy of routinely embolizing the

IMA does not seem to yield any significant clinical benefit and should therefore be abandoned. Therefore, more standardized, and high-quality studies are needed to explore the therapeutic effects of preemptive embolization.

There are several other limitations that should be noted. The present study excluded patients with type I and III endoleaks at any time during follow-up. This may reduce the number of patients with T2ELs because some patients with T2ELs may also have type I or type III endoleaks. Another limitation is the definition of T2EL. Previous reports use various terms, such as "early", "late", and "persistent" T2ELs. However, we did not classify T2ELs in this study. On the one hand, there was recall bias during the telephone follow-up; on the other hand, some patients did not have regular follow-up after surgery, so the occurrence time of endoleaks was not clear.

Finally, the mode of IIA embolization was not a routine procedure and was only performed in a relatively specialized anatomical population. Aortoiliac aneurysms with insufficient distal anchor area of the common iliac artery may lead to type Ib endoleaks (52). In some aortoiliac abdominal aortic aneurysms or AAA with internal iliac aneurysms and with a short common iliac artery, stents need to extend to the external iliac artery or even embolize the ipsilateral internal iliac artery. Future studies may need to collect the anatomical characteristics of the patent lateral branches after EVAR to identify the risk factors further accurately for type II endoleaks through the changes before and after surgery.

Conclusion

The iliolumbar artery and the different internal iliac artery interventions may not increase the incidence of T2Els. But the number of patent lumbar arteries (≥6) and the diameter of the inferior mesenteric artery (≥2.5 mm) were independent risk factors for T2ELs. More rigorous studies are still needed to explore the risk factors for T2ELs.T2ELs was associated with the reintervention but did not affect long-term survival or increase aneurysm-related mortality after EVAR.

Data availability statement

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving humans were approved by the Ethics Committee of West China Hospital, Sichuan University. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

GC and DL are joint first authors and wrote the manuscript. JZ, as the corresponding author, was responsible for the review and submission of the manuscript. CC and CW were responsible for the data analysis and data inspection and were in charge of statistical method correction. JW was responsible of the telephone follow-up. TW, DY and BH were responsible for anatomic data verification. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary Material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2023.1210248/full#supplementary-material

SUPPLEMENTAL FIGURE 1
Overall survival did not differ between T2ELs group and non-T2Els group after PSM (p = 0.58, log rank test).

SUPPLEMENTAL FIGURE 2
AAA-related survival did not differ between T2ELs group and non-T2Els group after PSM (p = 0.6, log rank test).

SUPPLEMENTAL FIGURE 3
Patients with T2ELs had more reinterventions than those without T2ELs. (p = 0.034, log rank test).

SUPPLEMENTAL FIGURE 4.
Flow chart of cases inclusion and expulsion.

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Superior mesenteric artery-related outcomes in fenestrated/branched endografting for complex aortic aneurysms

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Aim: Early/follow-up durability of superior mesenteric artery (SMA) stent-grafts is crucial after fenestrated/branched endografting (FB-EVAR) in complex abdominal aortic aneurysms (CAAAs) and thoracoabdominal aortic aneurysms (TAAAs). The study aimed to report early/midterm outcomes of SMA incorporated during FB-EVAR procedures.

Methods: FB-EVAR procedures performed between 2016 and 2021 in a single institution were reviewed. Anatomical SMA characteristics were analyzed. The SMA configuration was classified into three types according to the angle between the SMA main trunk and the aorta: (A) perpendicular, (B) downward, and (C) upward. SMA-related technical success (SMA-TS: cannulation and stenting, patency at completion angiography without endoleak, stenosis/kinking, dissection, bleeding, and 24-h mortality) and SMA-adverse events (SMA-AEs: one among bowel ischemia, stenosis, occlusion, endoleak, reinterventions, or SMA-related mortality) were assessed.

Results: Two hundred FB-EVAR procedures with SMA as the target artery were performed. The indication for FB-EVAR was CAAAs and TAAAs in 99 (49%) and 101 (51%) cases, respectively. The SMA configuration was A, B, and C in 132 (66%), 63 (31%), and 5 (3%) cases, respectively. SMA was incorporated with fenestrations and branches in 131 (66%) and 69 (34%) cases, respectively. Directional branch ($P < .001$), aortic diameter ≥35 mm at the SMA level ($P < .001$), and ≥2 SMA bridging stent-grafts ($P = .001$) were more frequent in TAAAs. Relining of the SMA stent-graft with a bare metal stent was necessary in 41 (21%) cases to correct an acute angle between the stent-graft and native artery (39), stent-graft stenosis (1), or SMA dissection (1). Relining was associated with type A or C SMA configuration (OR: 17; 95% CI: 1.8–157.3; $P = .01$). SMA-TS was achieved in all cases. Overall, 15 (7.5%) patients had SMA-AEs [early: 9 (60%), follow-up: 6 (40%)] due to stenosis (2), endoleak (8), and bowel ischemia (5). Aortic diameter ≥35 mm at the SMA level was an independent risk factor for SMA-AEs (OR: 4; 95% CI: 1.4–13.8; $P = .01$). Fourteen (7%) patients died during hospitalization with 10 (5%) events within the 30-postoperative day. Emergency cases (OR: 33; 95% CI: 5.7–191.3; $P = .001$), peripheral arterial occlusive disease (OR: 14; 95% CI: 2.3–88.8; $P = .004$), and bowel ischemia (OR: 41; 95% CI: 1.9–87.9; $P = .01$) were risk factors for 30-day/in-hospital mortality. The mean follow-up was 32 ± 24 months; estimated 3-year survival was 81%, with no case of late SMA-related mortality or occlusion. The estimated 3-year freedom from overall and SMA-related reinterventions was 74% and 95%, respectively.

Conclusion: SMA orientation determines the necessity of stent-graft relining. Aortic diameter ≥35 mm at the SMA level is a predictor of SMA-AEs. Nevertheless, SMA-related outcomes of FB-EVAR are satisfactory, with excellent technical success and promising clinical outcomes during the follow-up.

KEYWORDS

superior mesenteric artery (SMA), thoracoabdominal aneurysm repair, complex aortic aneurysm, fenestrated endograft, branched endograft

Introduction

Fenestrated and branched endografting (FB-EVAR) is an established technique for the endovascular treatment of complex abdominal aortic aneurysms (CAAAs: juxta/pararenal aneurysms) and thoracoabdominal aortic aneurysms (TAAAs) where anatomically feasible, and particularly in patients at high risk for open repair (1). Single- and multicenter experiences have reported satisfactory and reproducible early and mid-term outcomes (2–5) in both standard and challenging clinical/anatomical scenarios, including emergency settings, cases involving previous aortic surgery and postdissection TAAAs, and those with hostile aortic-iliac anatomy (6–12).

The durability of renal, mesenteric, and celiac arteries [target arteries (TAs)] or stent-graft patency is one of the key factors contributing to the technical and clinical success of FB-EVAR procedures since the loss of these arteries can be life-threatening (13). Suppose it should be considered true for renal and celiac arteries (14–18). In that case, it becomes particularly important for the superior mesenteric artery (SMA) because the acute loss of this vessel causes a direct fatal event.

Previous experiences reported outcomes and risk factors for technical/clinical failure in managing renal and celiac arteries (13–18) during F/B-EVAR. However, this aspect has been rarely analyzed in previous literature studies dedicated to SMA, and few data are currently available.

The present study aimed to report and analyze the SMA-related outcomes of FB-EVAR to treat CAAAs and TAAAs.

Methods

Study design and patient selection

This single-center observational study was performed without funding from companies or other organizations and approved by the local review board (T.Ev.AAA-155/2015/U/Oss). All patients undergoing FB-EVAR (Cook Zenith platform, Cook Medical LLC, Bloomington, IN, USA) for CAAAs and TAAAs (degenerative or postaortic dissection) between 2016 and 2021 were prospectively grouped and retrospectively analyzed. FB-EVAR repair was proposed for patients with CAAAs or TAAAs, where standard endovascular endografting was not possible, at high risk for open repair if anatomically suitable (1). An infrarenal neck length <10 mm was usually adopted to indicate F/B-EVAR repair. Each patient signed dedicated informed consent for endovascular aortic repair and anonymous data analysis for retrospective clinical studies. According to the European General Data Protection Regulation (GDPR), all cases were deidentified with a coding number and clustered in an electronic database. Anatomical, procedural, and postoperative data were analyzed and reported.

Endograft sizing and planning

Custom-made and off-the-shelf devices were used according to clinical and anatomical patient's characteristics. Patient-specific endografts were planned for elective cases by the same surgical team performing procedures and confirmed by the Cook Zenith Planning Center for fenestrated and branched endografts. Since 2012, the Cook Zenith off-the-shelf multibranched thoracoabdominal device (T-Branch) has been used for patients under emergencies (symptomatic, rupture, diameter >80 mm) or elective cases with anatomical feasibility and without adjunctive healthy aortic coverage other than a custom-made implant (7).

The proximal sealing zone was evaluated, measuring at least 2 cm the length of the healthy aortic wall (regular cylindrical shape—with no posterior bulging) in the multiplanar reconstructions. In this segment, a circumferential apposition between the endograft and aortic wall was expected (no scallop design in these 2 cm), and the main-body oversize was usually about 20%. TAs were analyzed (diameter and main trunk length) during preoperative computed tomography angiography (CTA) to select the most appropriate bridging stent-graft. The patency of the hypogastric artery was consistently preserved through endovascular (considered the primary choice) or surgical planned adjunctive maneuvers.

Preoperative superior mesenteric artery evaluation

Preoperative thoracoabdominal CTAs were retrospectively reviewed. Postprocessing evaluations were performed using dedicated software for advanced vessel analysis (3-Mensio, Vascular Imaging, Bilthoeven, The Netherlands). The main trunk length (linear distance between the SMA origin and the first branch) and diameter of the superior mesenteric artery were evaluated along with the presence of ostial stenosis, thrombosis, and calcification. The aneurysm diameter and aortic diameter at the SMA origin were also assessed. Using the electronic angular caliper provided by 3-Mensio software in the volume rendering reconstructions (**Figure 1**), the angle between the longitudinal axis of the aorta and the SMA main trunk was evaluated to define the SMA configuration, which was classified as perpendicular (A), downward (B), or upward (C) (**Figure 2**).

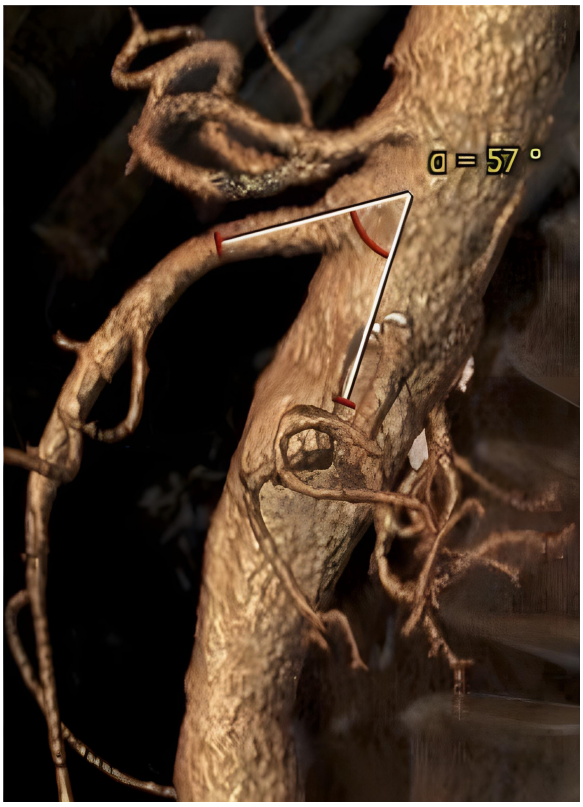


FIGURE 1
Volume rendering reconstruction of preoperative computed tomography angiography; angle between the longitudinal axis of the aorta and the main superior mesenteric artery trunk was evaluated by an electronic caliper provided by the 3-Mensio software.

Superior mesenteric artery incorporation

Superior mesenteric artery revascularization was performed by fenestration or external directional branch design according to the aortic diameter at the level of vessel's origin (1). Balloon-expandable stent-grafts were always used in fenestration design as bridging stents, while balloon- or self-expandable stent-grafts were used in branched design according to the TAs' anatomical characteristics and physicians' preference. The length and diameter of the bridging stent-grafts were preoperatively evaluated according to the anatomical SMA features. Relining with bare metal stents (balloon- or self-expandable) was performed in case of residual stenosis/kinking of the bridging stent-graft, acute angle between the stent-graft and native vessels (not smooth/natural angle at the level of transition between the bridging stent-graft and the distal native vessel), or distal dissection of the arteries.

Definitions and endpoints

Preoperative, intraoperative, and postoperative data, definitions, and outcomes were reported and classified according to the current Society of Vascular Surgery (SVS) reporting standard (1). Superior mesenteric artery-technical success (SMA-TS) and SMA-adverse events (SMA-AEs) were defined as primary outcomes of the study. Secondary outcomes were mortality and freedom from re-interventions (FFRs—overall and SMA-related) during the follow-up.

For the present study, SMA-TS was defined as successful SMA cannulation and stenting, SMA patency at completion angiography without SMA-related type I–III endoleaks, stenosis/kinking, dissection, rupture, and 24-h mortality. SMA-AE was defined as one among bowel ischemia (clinical or radiological manifestations), SMA-related stenosis, occlusion, endoleak, reintervention, and mortality.

Follow-up

Laboratory evaluations of renal, hepatic, pancreatic function, and thoracoabdominal CTA were performed before discharge (19). The follow-up surveillance program consisted of Doppler ultrasound (DUS) or contrast-enhanced DUS (CEUS) at 6, 12 months, and yearly after that. In case of diagnostic doubts, a CTA was always performed. Patients received dual antiplatelet therapy from discharge to the first 6 postoperative months.

Statistical analysis

Continuous variables were reported as means and standard deviations, while categorical ones were reported as numbers and

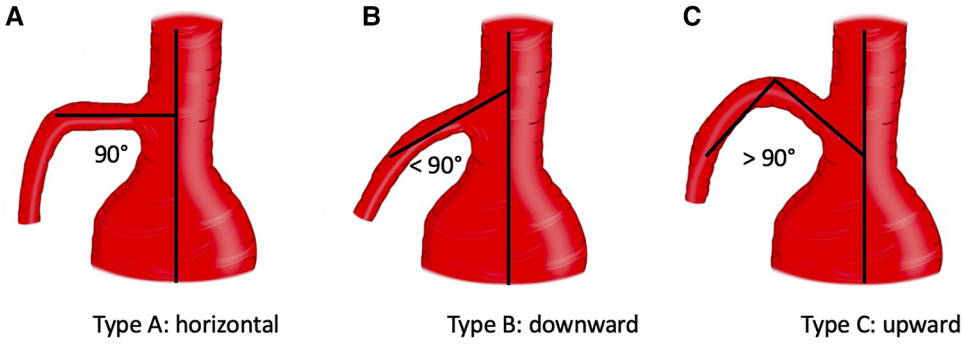


FIGURE 2
Configuration of superior mesenteric artery according to the orientation. Three types were identified: A (perpendicular), B (downward), C (upward).

percentages. Uni- and multivariate analyses were performed to evaluate potential risk factors for the study endpoints. Preoperative anatomical characteristics of the SMA and the aorta, endograft design (fenestration vs. external branch), setting of repairs (elective vs. emergency), and procedural data (fenestration/branch, number, and type of bridging stent-grafts, need of relining) were considered as risk factors for this analysis. Survival and FFR were evaluated using Kaplan–Meyer analysis. Statistical analysis was performed using SPSS 28.0 (SPSS statistical software, Chicago, IL, USA).

Results

Patient selection

In total, 228 consecutive patients underwent FB-EVAR for CAAAs and TAAAs. Among them, 14 (6%) patients were excluded for unavailability of preoperative CTA and 14 (6%) were excluded because the FB-EVAR implant did not require SMA incorporation. Finally, 200 (88%) cases met the study's inclusion criteria and were considered for the analysis. Of the 200, 17 (9%) patients were managed in an emergency clinical setting (rupture with stable hemodynamic parameters: 13; symptomatic: 4). The demographics, cardiovascular risk factors, and preoperative comorbidities of the 200 cases considered for the present study are summarized in Table 1.

Preoperative aortic and SMA anatomical details

The indication for FB-EVAR repair was CAAAs, TAAAs, and a failed previous EVAR in 91/200 (45%), 101/200 (51%), and 8/200 (4%) cases, respectively. Sixty-four (32%) patients had a previous aortic surgery (open: 38, endovascular: 17, both open and endovascular: 9), and 7 (4%) were chronic postdissection TAAAs. Five (3%) patients had a history of previous perivisceral aortic repair, and there was no case of previous SMA stenting. The mean aneurysm diameter and aortic diameter at the SMA origin were 64 ± 13 mm and 33 ± 12 mm, respectively. The mean SMA diameter and main trunk length were 8 ± 1.5 mm and 43 ± 16 mm, respectively. There were 3/200 (1%) cases of severe (>50%) SMA ostial stenosis, and the aorta had thrombotic (>50% of circumference) apposition at the level of the SMA origin in 23/200 (12%) patients. The SMA configuration was A, B, and C in 63/200 (31%), 132/200 (66%), and 5/200 (3%) cases, respectively. No SMA was involved in the dissection or originating from the false lumen in chronic postdissection TAAAs.

TABLE 1 Demographics, cardiovascular risk factors, and preoperative comorbidities.

	N	%
Male	194	97
Hypertension	182	91
Smoke	154	77
Dyslipidemia	148	74
Diabetes	32	16
Chronic obstructive pulmonary disease	82	41
Coronary artery disease	77	39
Atrial fibrillation	23	12
Peripheral artery occlusive disease	24	12
Stroke	23	12
Body mass index >30	40	20
Chronic renal failure	85	43
Dialysis	3	2
Previous aortic surgery	64	32
American Society of Anesthesiologists score 3	72	36
American Society of Anesthesiologists score 4	128	64
	N	SD
Mean age (years)	73	5

Endograft configuration

Custom-made and off-the-shelf devices were used in 140 (70%) and 60 (30%) patients, respectively. Endograft design with a fenestration branch, a directional branch, or both fenestration and directional branches was planned in 128/200 (64%), 60/200 (30%), and 12/200 (6%) cases, respectively. A superior mesenteric artery was incorporated using a fenestration in 131/200 (66%) cases, and a directional branch was incorporated in 69/200 (34%) cases. Directional branches were used more commonly to incorporate the SMA in patients with TAAAs [OR 12 (95% CI: 3.9–34.8), $P < .001$] or aortic diameter >35 mm at the level of SMA [OR: 5 (95% CI: 2.0–19.9), $P < .001$] and in patients needing ≥2 stents for SMA incorporation [OR: 8 (95% CI: 2.3–24.2), $P = .001$].

Procedure

Balloon-expandable or a combination of balloon- and self-expandable stent-grafts were used as SMA bridging stent-grafts in 194/200 (97%) and 6/200 (3%) cases, respectively (Table 2). Two stent-grafts were necessary as bridging devices for incorporating the SMA in 44/200 (22%) patients (excluding relining by bare metal stents). Relining of the SMA stent-graft using bare metal stents was performed in 41/200 (21%) cases due to an acute angle between the stent-graft and native vessel (39 cases), stent-graft stenosis (1 case), or SMA dissection (1 case), as shown in Figures 3–5. In these cases, SMA relining was performed with a self-expandable bare metal stent in 40 cases and a balloon-expandable bare metal stent in 1 case. Type A or C SMA configuration was an independent risk factor for SMA stent-graft

TABLE 2 Types of stent-grafts implanted as bridging stents in the superior mesenteric artery for fenestrated and branched endografts.

	N	%
Overall cases	200	100
Atrium Advanta	119	59
Bentley Begraft plus	3	2
Gore VBX	72	35
Atrium Advanta + Gore Viabahn	3	2
Gore VBX + Gore Viabahn	3	2

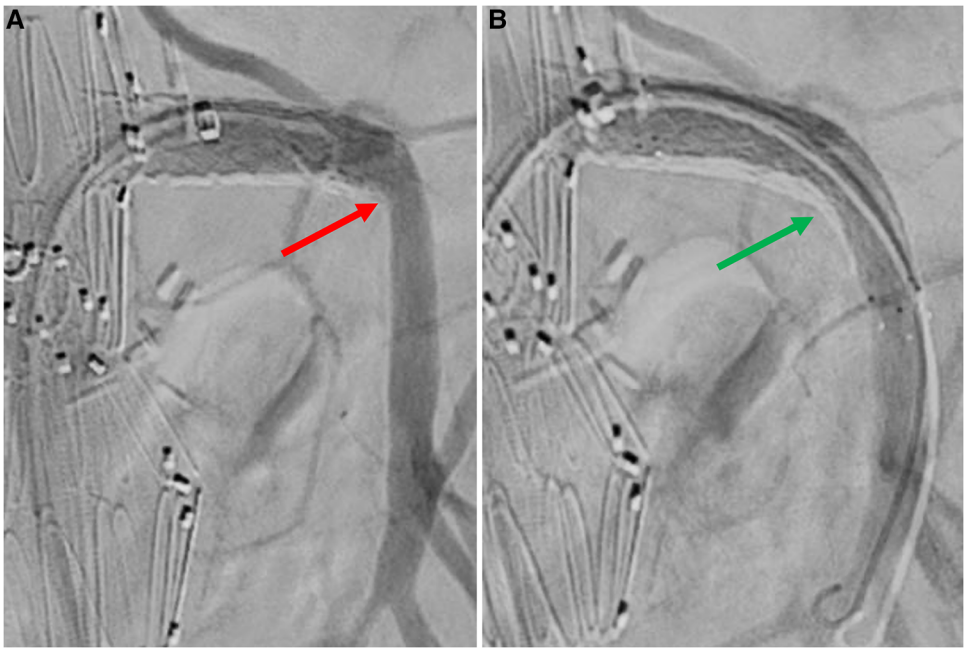


FIGURE 3
Selective angiography of superior mesenteric artery after bridging stenting. A: angiography without Rosen guidewire identifies an acute angle between SMA stent-graft and native vessel (red arrow). B: angiography without Rosen guidewire after relining by self-expandable bare metal stent does not identify any angle (green arrow).

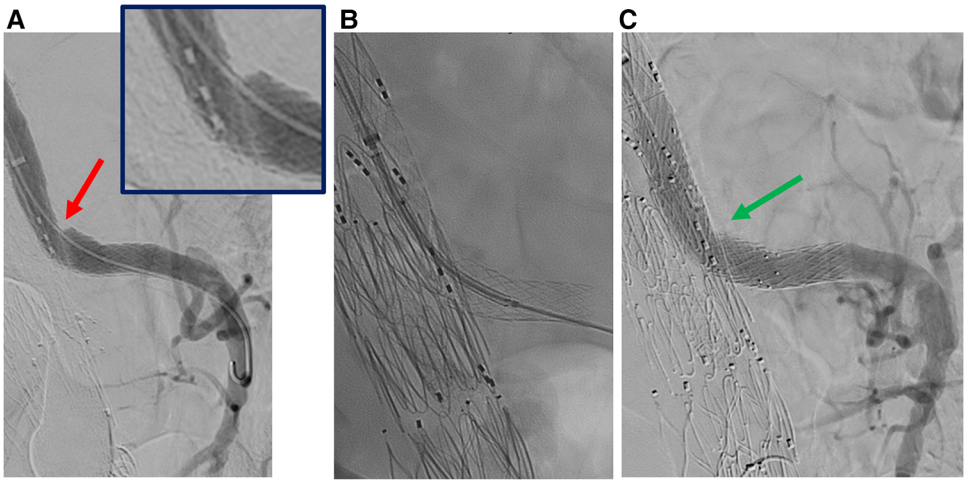


FIGURE 4
Selective angiography of superior mesenteric artery after bridging stenting. A: stenosis of the stentgraft (red arrow). B: relining by balloon expandable stent. C: angiography without Rosen guidewire after relining does not identify any stenosis (green arrow).

relining with bare metal stents [OR: 17 (95% CI: 1.8–157.3), $P = .01$]. For the superior mesenteric artery, technical success was achieved in all cases.

The mean procedural and fluoroscopy times were 325 ± 120 and 93 ± 20 min, respectively. The mean amount of iodinated contrast agent used was 185 ± 40 ml. At the end of the procedure, all patients were admitted to the intensive care unit (ICU) with a subsequent mean hospitalization in ICU of 24 ± 18 h.

Early results

Five (2.5%) patients had postoperative clinical and radiological signs of bowel ischemia. In all cases, preoperative anatomical challenging characteristics (stenosis, calcification, thrombus) were noted, and no defect in the native SMA and SMA stent-graft patency (stenosis, occlusion, dissection) was detected at the postoperative CTA. Moreover, they had no defects in celiac trunk patency. Three of them required a bowel

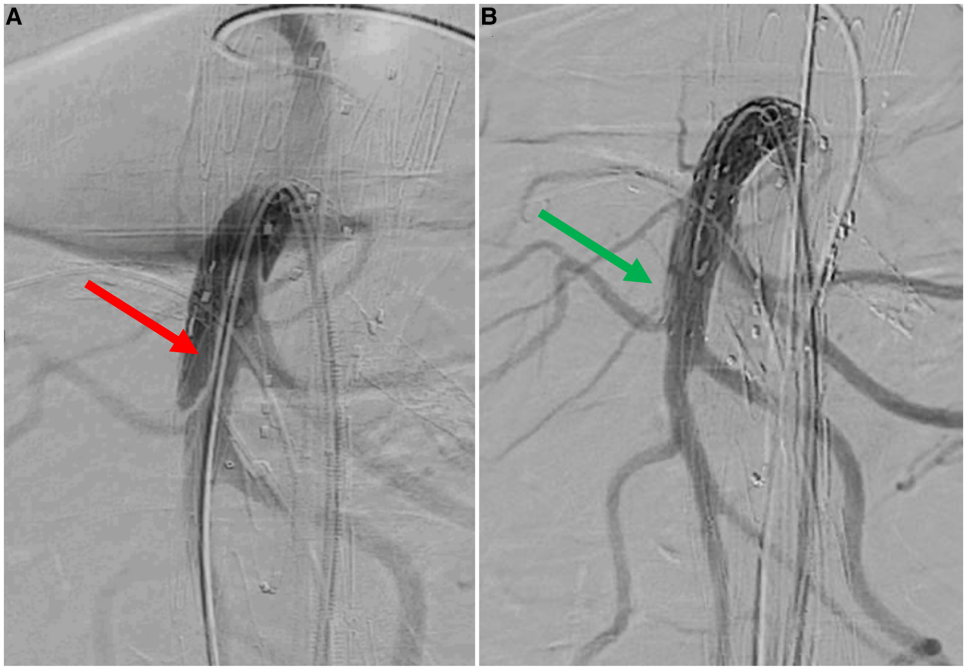


FIGURE 5
Selective angiography of superior mesenteric artery after bridging stenting. A: dissection of native superior mesenteric artery distally to the stentgraft (red arrow). B: angiography without Rosen guidewire after relining by self-expandable bare metal stent does not identify any defect (green arrow).

resection. In total, 32/200 (16%) patients required reinterventions within 30 days, which were mostly surgical access-related in 17/32 (53%) cases. Fourteen (7%) patients died during the hospitalization, with 10 (5%) events within 30 postoperative days. The causes of mortality are summarized in **Table 3**. Emergency cases [OR: 33 (95% CI: 5.7–191.3), $P = .001$], peripheral arterial occlusive disease [OR: 14 (95% CI: 2.3–88.8), $P = .004$), and bowel ischemia [OR: 41 (95% CI: 1.9–87.9), $P = .01$] were independent risk factors for 30-day/in-hospital mortality.

Midterm results

The mean follow-up time was 32 ± 24 months. The estimated 3-year survival was 81% (**Figure 6**), with no case of SMA-related mortality or occlusion at follow-up. The values for estimated 3-year freedom from overall and SMA-related reinterventions were 74% and 95% (**Figures 7A,B**), respectively. In total, 15 (7.5%) patients had SMA-AEs; 9 (60%) and 6 (40%) events occurred within 30 postoperative days and during the follow-up, respectively. They were classified into bowel ischemia (five cases), endoleaks (eight cases), and stent-graft stenosis/compression (two cases). **Table 4** summarizes each of these patients, the timing of event occurrence, management, and the result. Aortic diameter ≥35 mm at the SMA origin was an independent risk factor for SMA-AEs [OR: 4 (95% CI: 1.4–13.8), $P = .01$].

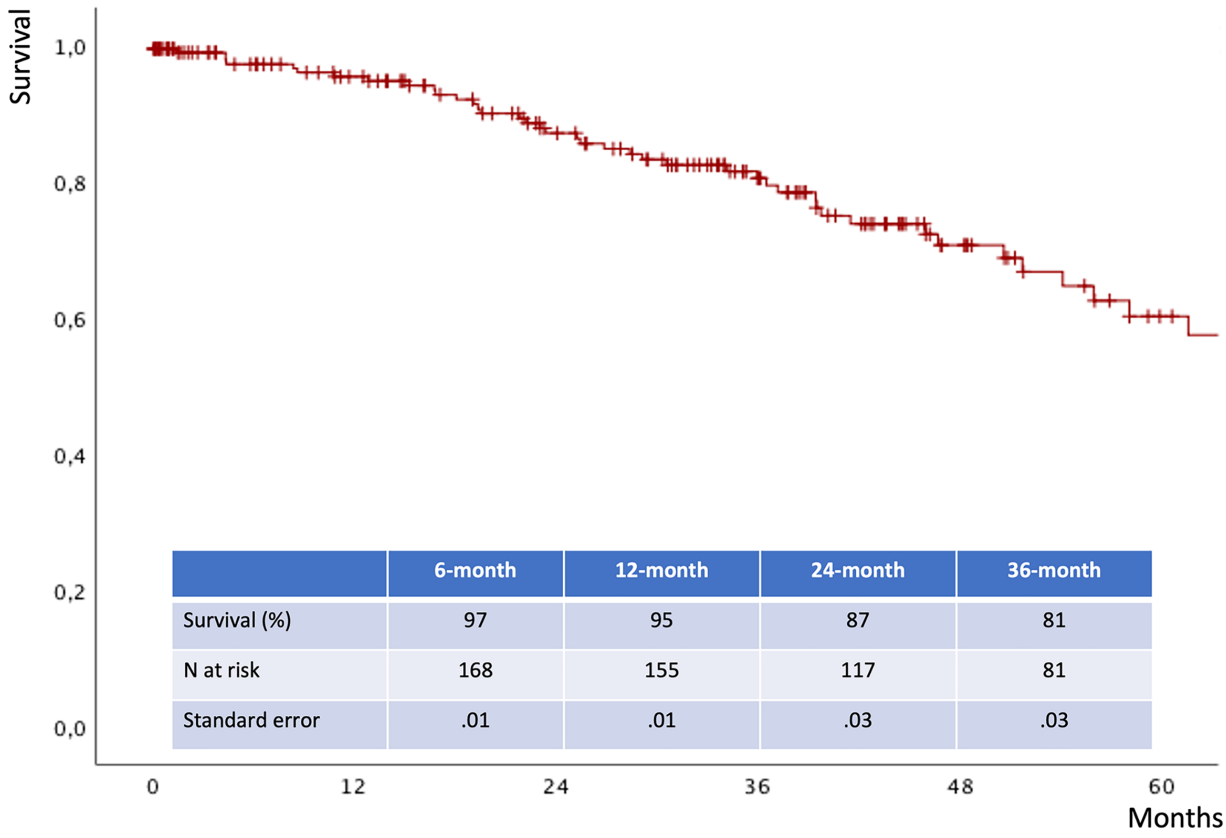
TABLE 3 Final causes of 30-day/in-hospital mortality.

	N	%
Cardiac morbidity	5	36
Cerebral hemorrhage	1	7
Hemorrhagic shock	1	7
Multiorgan failure/bowel ischemia	3	21
Pulmonary morbidity	4	29
Overall	14	100

Discussion

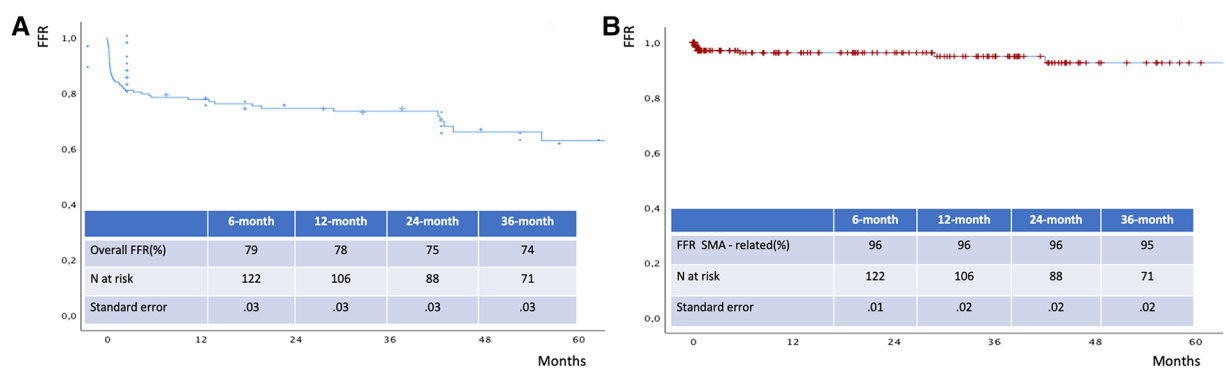
In this study, we have reported a single-center 6-year experience of 200 FB-EVAR procedures to manage CAAAs or TAAAs with a mean follow-up of 32 months. Results were satisfactory in terms of early postoperative morbidity, 30-day/in-hospital mortality, freedom from reinterventions, and survival during the follow-up. These outcomes are in line with the findings of previous single and multicenter studies conducted by European and US aortic centers over the last few decades (1–12). These results support the rationale behind the widespread use of FB-EVAR as the primary endovascular solution for CAAAs/TAAAs in high-risk patients with anatomical feasibility.

The technical and clinical success of FB-EVAR is strictly related to TAs' cannulation/stenting and to guarantee their patency during a life-long follow-up (13). Previous studies focused on intraoperative, early, or late occlusions of celiac and renal arteries, especially if the latter are incorporated using the directional branch design (14–18). Currently, comprehensive and dedicated data on SMA results are lacking, and this absence of data is relevant since most recent FB-EVAR experiences report a



	6-month	12-month	24-month	36-month
Survival (%)	97	95	87	81
N at risk	168	155	117	81
Standard error	.01	.01	.03	.03

FIGURE 6
Follow-up survival estimated by Kaplan Meier analysis.



	6-month	12-month	24-month	36-month
Overall FFR(%)	79	78	75	74
N at risk	122	106	88	71
Standard error	.03	.03	.03	.03

	6-month	12-month	24-month	36-month
FFR SMA - related(%)	96	96	96	95
N at risk	122	106	88	71
Standard error	.01	.02	.02	.02

FIGURE 7
Freedom from overall (A) and SMA - related (B) reinterventions estimated by Kaplan Meier analysis. FFR: freedom from reintervention.

wide use of 3–4 fenestrated (or branched) endograft configurations (20). Even though these designs ensure a safe and reliable proximal sealing zone in CAAAs over long-term follow-up, they also may create potential and life-threatening complications in the case of serious SMA-related adverse events (20–22).

The present study aimed to report specific data about the SMA-related outcomes in FB-EVAR for CAAAs and TAAAs. Significant epidemiological and intraoperative information was discovered in the current analysis. The most frequent orientation of the SMA main trunk is perpendicular (type A—66%) or downward (type B—31%). In only 3% of cases, the orientation of the SMA was upward. It is an important detail to consider during endograft planning when choosing a fenestration or directional branch design for the SMA. In most cases, caudal direction branches can be safely utilized to allocate arteries oriented horizontally or in a downward direction. On the other hand, in the 3% of upward-oriented SMA cases, fenestrations or retrograde branches may be considered to facilitate SMA cannulation and stenting. However, fenestrations and branches were designed to accommodate 66% and 34% of SMA anatomies, respectively. Obviously, this result

TABLE 4 Superior mesenteric artery-adverse events: timing, management, and clinical outcomes.

N	Timing	SMA-AE	Management	Outcome
1	Within 30-day	Bowel ischemia	Left hemicolectomy	In-hospital mortality
2	Within 30-day	Endoleak Ic	Relining	Sealed
3	Within 30-day	Endoleak Ic	Relining	Sealed
4	Within 30-day	Stenosis	Relining	Solved
5	Within 30-day	Endoleak III	Relining	Sealed
6	Within 30-day	Bowel ischemia	Right hemicolectomy	In-hospital mortality
7	Within 30-day	Bowel ischemia	Left hemicolectomy	In-hospital mortality
8	Within 30-day	Bowel ischemia	Conservative	In-hospital mortality
9	Within 30-day	Bowel ischemia	Conservative	In-hospital mortality
10	After 30-day	Stenosis	Relining	Solved
11	After 30-day	Endoleak III	Relining	Sealed
12	After 30-day	Endoleak III	Relining	Sealed
13	After 30-day	Endoleak III	Relining	Sealed
14	After 30-day	Endoleak Ic	Relining	Sealed
15	After 30-day	Endoleak III	Relining	Sealed

SMA-AE, superior mesenteric artery-adverse event.

reflects our philosophy of endograft planning that prefers an external branch in the case of large aortic diameter at the level of the SMA to avoid a long gap distance between the hypothetical fenestration and the origin of vessels, reducing the possibility of TA instability during the follow-up. Once again, another finding from our statistical analysis confirms that a directional branch design for the SMA is more frequently adopted in patients with TAAAs ($P < .001$) or aortic diameter ≥35 mm at the SMA origin ($P < .001$) and those needing ≥2 stent-grafts ($P = .001$) as bridging stents for SMA.

As regards the choice of the bridging stent-graft, the most frequent option was the balloon-expandable type (97%), with only a few cases (3%) managed using a combination of balloon- and self-expandable stent-grafts and no cases managed with only a self-expandable stent-graft.

However, relining of the SMA stent-graft using a bare metal stent was reported in a not negligible rate of cases (21%). The main reason for relining was the correction of an acute angle between the stent-graft and the native SMA (95% of cases). Most of the relining was performed using self-expandable bare metal stents, which could be attributed to the high rate of balloon-expandable stent-grafts implanted. Moreover, SMA relining was associated with type A or C SMA configuration [OR: 17 (95% CI: 1.8–157.3), $P = .01$]. Unfortunately, the low rate of adverse events during the follow-up and the absence of a control group (acute angle without relining) did not allow for a subanalysis of the real efficacy of this adjunctive stenting. At the moment, it is an empiric adjunctive maneuver performed to correct a not ideal radiological image, and we have no data to confirm whether it is effective in the prevention of acute SMA stent-graft occlusions or stenosis during the follow-up. Nevertheless, no complications related to the relining stents were reported in either the procedural or follow-up results.

Overall, procedural results were excellent, with no case of intraoperative SMA-related technical failure. It seems obvious but is a crucial point in the FB-EVAR procedure because an acute intraoperative SMA loss is a lethal complication that should always be avoided. For this reason, it is mandatory to underline how all considerations about preoperative planning and sizing and procedural maneuvers (cannulation, manipulations, stent-grafting, and flaring) aim to achieve successful SMA management. The facilities of a modern hybrid room, such as intraoperative cone beam CT and intravascular ultrasound, are essential tools to be used in case of any diagnostic doubts to optimize the intraoperative control of quality (23, 24).

SMA patency is not the only aspect to evaluate for perioperative patient safety. We have reported five cases of bowel ischemia with SMA patency and the absence of any stent-graft defect at postoperative CTA. Three of these events were serious and required a bowel resection, while the remaining two cases were managed by conservative medical therapy. The origin of these events is probably multifactorial and can be explained by distal embolization during catheterization maneuvers, postoperative hypotensive status caused by other clinical postoperative complications, or multiorgan failure. It was an independent risk factor (OR: 41) for 30-day/in-hospital mortality as well as emergency TAAA repair (OR: 33) and preoperative PAOD (OR: 14). Overall, 30-day/in-hospital mortality was 7%; these data are in line with the most recently published FB-EVAR European and US experiences, and they can be considered satisfactory due to the presence of both emergency and elective repairs (1–12).

The estimated 3-year survival was 81%, which is comparable with the previous data available in the literature (1–12). There were no cases of aortic- or SMA-related deaths at the follow-up. Satisfactory results were also reported in terms of freedom from overall and SMA-related reinterventions, which were 74% and 95%, respectively.

In total, 15 (7.5%) patients had SMA-AEs: 60% in the postoperative period and 40% during the follow-up. They were caused by bowel ischemia (five cases), endoleaks (eight cases), and stenosis (two cases). As reported above, all cases of bowel ischemia occurred during the perioperative period and were not associated with defects in SMA patency. A surgical repair was required in three of five cases, and it had a negative impact on patient survival. Among the endoleak cases, three were detected at postoperative CTA and were successfully treated before discharge. They were not detected at the completion of angiography, but they should probably be considered a suboptimal technical result. The other five endoleak cases were detected during the follow-up (four in routine tests and one in a symptomatic patient) and were successfully managed by stent-graft relining. Both SMA stent-graft compressions were detected (one early and one at follow-up) at CTA and managed by an adjunctive balloon-expandable stent-graft. It is important to underline that biplanar intraoperative angiography may underestimate these findings. Therefore, it is crucial to emphasize the importance of dedicated intraoperative imaging tools for high-quality control. Interestingly, there was no case of native SMA stenosis distally to the bridging stent-graft or stent-graft fracture. An important finding in our analysis was that aortic diameter ≥35 mm at the level of the SMA was an independent risk factor for SMA-AEs.

Several limitations must be considered in the present study. First, it is a single-center, retrospective study with a relatively small cohort of patients and mid-term follow-up. However, it should be considered that it is one of the largest single-center series reported in the last years and FB-EVAR is a relatively new technology with no big data about long-term follow-up. The small sample size may be associated with a theoretical statistical type B error, reducing the strength of study's conclusions. Second, the operator's learning curve was not considered, and it is crucial to optimize technical and clinical results in these challenging cases. In our department, the FB-EVAR program started in 2010, and the patients included were treated after 5 years of experience by using well-standardized pre-, intra-, and postoperative protocols in a hybrid room with all the available facilities (vessel navigator, CO_2 angiography, cone beam CT, and IVUS). Third, the protocol of home surveillance consists of different imaging modalities (DUS, CEUS, and CTA) with different sensitivity and specificity levels to detect TVV-related endoleaks, stent-graft stenosis/kinking, or other complications. This may be reason for a part of undetected or underestimated adverse events during the follow-up and the subsequent underestimate of the rate of SMA-related reinterventions. Fourth, a dedicated analysis of stent-grafts of different brands used to incorporate the SMA was not performed because the number of cases was too small to guarantee a significant subgroup analysis. We report data dividing SMA managed by SE or a combination of SE and BE stent-grafts with similar results in terms of SMA-AEs and follow-up patency. Finally, it is impossible to exclude that acute SMA thrombosis was the real cause of death during the follow-up in cases of unknown cause of mortality.

Conclusion

The orientation of the superior mesenteric artery determines the necessity of stent-graft relining. Aortic diameter >35 mm at the level of the SMA is a predictor of SMA-AE. However, SMA-related outcomes of FB-EVAR are satisfactory, with excellent technical success and encouraging clinical outcomes during the follow-up.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Materials, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by IRCCS Sant'Orsola, Vascular Surgery, University of Bologna, Italy. The studies were conducted in accordance with the local legislation and institutional requirements. The human samples used in this study were acquired from primarily isolated samples as part of our previous study for which ethical approval was obtained. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

EG: conception, data analysis, writing. GF: conception, critical revision. AV: data collection, data analysis, critical revision. ML: data collection, critical revision. AC: data collection, critical revision. AL: data collection, critical revision. MF: data collection, critical revision. RP: data collection, data analysis, critical revision. MG: conception, critical revision. All authors contributed to the article and approved the submitted version.

Conflict of interest

MG, GF, and EG are clinical proctors for fenestrated branched endografts with the CooK Zenith platform. MG is the Principal Investigator of the Expand Registry (Gore VBX stent-graft).

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Efficacy of prognostic nutrition index in combination with D-dimer in predicting postoperative clinical adverse events after acute type A aortic dissection: a single center retrospective study

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Background: The aim of this study was to identify the predictive factors for adverse clinical events after surgery in patients with acute type A aortic dissection (AAAD), and to explore the predictive value of preoperative prognostic nutritional index (PNI) combined with D-dimer for these events.

Methods: This study was a retrospective analysis of clinical data of 153 patients with AAAD who underwent emergency surgery at our center from January 2019 to January 2022. Patients were divided into adverse event group and non-adverse event group based on whether they experienced adverse clinical events after surgery. Univariate and multivariable logistic regression analyses were performed to identify the risk factors for adverse events, and the predictive efficacy was evaluated by the area under the receiver operating characteristic curve (ROC-AUC).

Results: A total of 153 AAAD patients were included in the study, and were divided into the adverse event group ($n = 46$) and the non-adverse events group ($n = 107$) based on whether or not they experienced clinical adverse events after surgery. The optimal cutoff value was determined using ROC curves, and multivariate logistic regression analysis was performed. Ultimately, it was found that preoperative PNI < 42.45 and D-dimer > 15.05 were independent predictors of postoperative clinical adverse events in AAAD patients. The odd ratios (OR) value for preoperative PNI < 42.45 is 3.596 [95% Confidence Interval (CI): 1.508–8.923, $p = 0.004$], while the OR value for D-dimer > 15.05 is 7.572 [95% CI: 3.094–20.220, $p < 0.001$]. The combination of these two indicators has a high predictive value (AUC = 0.843, 95% CI: 0.774–0.912, $p < 0.001$) and is superior to using either variable alone.

Conclusion: Preoperative PNI < 42.45 and D-dimer > 15.05 are independent predictive factors for postoperative adverse events during hospitalization in patients with AAAD. The combination of these two indicators can improve the predictive accuracy, which is superior to using either variable alone.

KEYWORDS

acute type A aortic dissection, prognostic nutrition index, D-dimer, clinical adverse events, predictive efficacy

Introduction

Acute aortic dissection is a highly lethal and high-risk cardiovascular emergency. Among them, acute type A aortic dissection (AAAD) is the most dangerous situation (1–3). The previous research results showed that the overall incidence rate of AAAD is approximately 4.7 per 100,000 population, but there are significant regional variations in the incidence rates (4). A study by Meszaros et al. indicated that the average age of onset of AAAD is around 50 years old (5). Its clinical features include an acute onset, rapid progression, and high mortality rate. Some studies have reported that the in-hospital mortality rate associated with AAAD is approximately 22% (6), and without surgical treatment, it is as high as 82% at 1 year (7). The only effective treatment for AAAD is emergency surgical repair. Although surgical techniques and perioperative management have made great progress compared to the past, the prognosis of AAAD after surgery is significantly worse compared to conventional cardiovascular surgery due to the characteristics of the disease and the complexity of the surgery (7–9). Therefore, it is necessary to identify sensitive preoperative prognostic indicators to predict the prognosis of AAAD patients, which can effectively improve perioperative treatment measures and help clinical doctors better evaluate the early outcomes after AAAD surgery.

Inflammatory responses and changes in coagulation function are integral to the development of aortic dissection and are closely related to its pathogenesis and prognosis (10, 11). Previous studies have shown that some inflammation-related biomarkers, such as C-reactive protein (CRP) and D-dimer, are considered to be associated with an adverse prognosis after AAAD surgery (12–14). The prognostic nutritional index (PNI) is a new systemic inflammation marker calculated based on serum albumin levels and peripheral lymphocyte count. It was originally widely used to evaluate the long-term outcomes and prognosis of gastrointestinal cancer patients (15, 16). In recent years, PNI has been shown to be associated with the prognosis of heart failure and coronary heart disease patients (17–19). Studies have found that a low PNI during the perioperative period is a risk factor for in-hospital mortality in AAAD patients (20, 21). However, as a single indicator, the accuracy of using PNI to predict postoperative outcomes after AAAD surgery is not sufficient. Therefore, it is necessary to combine other indicators for a systematic evaluation. Previous studies have shown that the coagulation function is closely associated with the prognosis of AAAD. D-dimer, as a major indicator reflecting the coagulation status of the body, can serve as a key biomarker for predicting postoperative outcomes (22). Through univariate and multivariate regression analysis, we found that PNI and D-dimer are independent risk factors for clinical adverse events after AAAD surgery. Therefore, we speculate that the composite index formed by PNI combined with D-dimer can provide effective clinical predictive information for clinical adverse events after AAAD surgery. The aim of this study is to explore the application of two indicators combined in predicting the risk of adverse clinical events after AAAD surgery.

Materials and methods

Study design and setting

A single center retrospective study was used to investigate the clinical data of AAAD patients admitted to our center. These patients were admitted to hospital for emergency surgery from January 2019 to January 2022. Since this is a retrospective study and there is no need to obtain informed consent, this study was approved by the Ethics Committee of the affiliated Union Hospital of Fujian Medical University, which is in line with the Helsinki Declaration.

The inclusion criteria of this study were: AAAD diagnosed by computed tomography thoracic aortography or magnetic resonance imaging; over 18 years of age; emergency surgical treatment after admission. Patients with the following conditions are excluded: patients whose time from onset to hospitalization is more than 48 h; patients with long-term use of drugs that affect blood cell count; patients with malignant tumors, autoimmune diseases, severe infectious diseases and chronic organ dysfunction. The serological samples of all patients were drawn from venous blood without medication before emergency operation.

By measuring the level of D-dimer, serum albumin and lymphocyte count, the formula ($10 \times$ serum albumin (g/dL) + $0.005 \times$ lymphocyte count (per mm^3)) was used to calculate PNI (16), and the relationship between PNI, D-dimer and clinical adverse events after operation was analyzed.

Definition of clinical adverse events

Clavien–Dindo grading is a general surgical complication grading system, which can also be used to grade the severity of complications after cardiovascular surgery (23). The postoperative clinical adverse events in this study were defined as complications of Clavien–Dindo grade III or above, including single or multiple organ dysfunction and postoperative death (24). Single organ dysfunction includes renal insufficiency requiring dialysis treatment, cardiac dysfunction requiring left ventricular assist device or intra-aortic balloon pump (IABP) therapy, neurological deficits requiring reintubation, tracheostomy or radiological and neurosurgical interventions, irreversible spinal cord injury, and intestinal ischemia requiring surgical intervention. Multiple organ dysfunction is defined as simultaneous or sequential dysfunction of two or more organs or systems caused by various clinical factors (25).

Data collection

We collected clinical data of each patient from the hospital's medical record system and observed and summarized various indicators before and during surgery. Preoperative indicators include: (1) demographic data: gender, age, body mass index

(BMI); (2) past medical history: smoking history, drinking history; (3) comorbidities: hypertension, diabetes, coronary artery disease, history of cerebrovascular disease, chronic obstructive pulmonary disease, Marfan syndrome, hepatic dysfunction and renal insufficiency; (4) preoperative general condition: aortic valve regurgitation (moderate or above), pericardial effusion (moderate or above), left ventricular ejection fraction (LVEF). Preoperative laboratory tests: red blood cell count, white blood cell count, leukomonocyte, hemoglobin, platelet, albumin, alanine aminotransferase, aspartate aminotransferase, serum creatinine, D-dimer, prothrombin time (PT), B-type natriuretic peptide, C-reactive protein, troponin-I. Intraoperative indicators include: processing method of the aortic root, total operation time, cardiopulmonary bypass time, aortic cross-clamp time, cerebral perfusion time time, deep hypothermic circulatory arrest time and intraoperative blood product input (red blood cells, plasma, platelets). The postoperative complications were classified into two groups based on whether or not Clavien–Dindo grade III or higher surgical complications occurred: the no-adverse events group and the adverse events group.

Surgical technique

The surgery was performed under general anesthesia and cardiopulmonary bypass support. The specific surgical procedure was described in detail in Chen et al.'s previous study, including reconstruction of the aortic root, replacement of the ascending aorta, and implantation of a modified triple-branch stent graft (26, 27).

Statistical analysis

All statistical analyses were performed using SPSS 23.0 and R software (4.2.2). Continuous variables were expressed as mean ± standard deviation or interquartile range, while categorical variables were expressed as frequency, ratio, and percentage. The Kolmogorov–Smirnov test was used to check the normality of the distribution of continuous variables. Student t-tests were used for intergroup comparison of continuous variables that followed a normal distribution, while Mann–Whitney U tests were used for those that did not follow a normal distribution. The chi-square test or Fisher's exact test was used for categorical variables. Predictive variables with $p < 0.05$ in the univariate analysis were included in a multivariate logistic regression analysis to identify independent risk factors for postoperative adverse events. Receiver operating characteristic (ROC) curves were constructed to determine the optimal cutoff values for PNI, D-dimer, and combination variables in predicting postoperative adverse events, and the area under the curve (AUC) was calculated. The predictive performance of the combined indicators will be evaluated using AUC, net reclassification improvement (NRI), and integrated discrimination improvement index (IDI). A difference was considered statistically significant when $p < 0.05$.

Results

This study diagnosed a total of 214 patients with AAAD between January 2019 and January 2022. Among them, 36 cases were excluded due to the onset-to-hospitalization time exceeding 48 h, 9 cases were excluded due to death caused by a ruptured aortic dissection, 6 cases were excluded due to concurrent chronic hepatic or kidney dysfunction, and 10 cases were excluded due to failure to undergo emergency surgical treatment. In the end, a total of 153 patients were included in this study (**Figure 1**).

The baseline data comparison of the patients showed that the two groups of patients had similar baseline data such as gender, age, and body mass index (BMI), but the preoperative PNI of the adverse event group was significantly lower than that of the non-adverse event group (39.60 ± 5.68 vs. 44.55 ± 4.63, $p < 0.001$). Laboratory examination results showed that the leukomonocyte [0.71 (0.56, 1.02) vs. 1.01 (0.83, 1.37)], albumin (35.49 ± 5.13 vs. 39.00 ± 3.84), and platelet [151.00 (128.00, 196.00) vs. 176.00 (145.00, 206.00)] of the adverse event group were significantly lower than those of the non-adverse event group, while D-dimer (17.40 ± 5.47 vs. 9.83 ± 7.28), AST [33.00 (22.00, 71.00) vs. 24.00 (19.00, 34.00)], PT [14.30 (13.50, 15.80) vs. 13.80 (13.10, 14.50)], and troponin-I [0.013 (0.004, 0.165) vs. 0.005 (0.002, 0.033)] were significantly higher than those of the non-adverse event group. The differences in the clinical indicators between the two groups were statistically significant ($p < 0.05$) (**Tables 1**, **2**). The intraoperative comparison results showed that there were no significant differences in the total operation time, cardiopulmonary bypass (CPB) time, aortic cross-clamp (ACC) time, cerebral perfusion time, and deep hypothermic circulatory arrest (DHCA) time between the two groups of patients. The aortic root handling methods and intraoperative blood product transfusion were also similar between the two groups (**Table 3**). The occurrence of postoperative complications in the adverse event group is shown in **Table 4**.

The optimal cut-off values of the clinical characteristic variables for which there were statistically significant differences between groups were calculated by drawing a ROC curve. Subsequently, univariate and multivariate logistic regression analyses were performed, and the results are presented in **Table 5**. A forest plot depicting the odds ratio (OR) and their 95% confidence interval (CI) was generated based on the results, as shown in **Figure 2**.

We found that when the optimal cutoff value was 42.45, the sensitivity of preoperative PNI was 0.692, specificity was 0.696, and the AUC value was 0.752; the optimal cutoff value for D-dimer was 15.05, with a sensitivity of 0.826, specificity of 0.701, and an AUC value of 0.770. The results of the multivariate logistic regression analysis showed that a PNI < 42.45 and a D-dimer > 15.05 μg/ml were independent risk factors for postoperative clinical adverse events in AAAD patients.

In order to better predict postoperative clinical adverse events, we combined the above clinical indicators (preoperative PNI combined D-dimer) and calculated the AUC of the combined index to be 0.843 (95% CI was 0.774–0.912, $p < 0.001$), with a sensitivity of 0.826 and specificity of 0.738. The AUC value of the combined index was more predictive than using a single

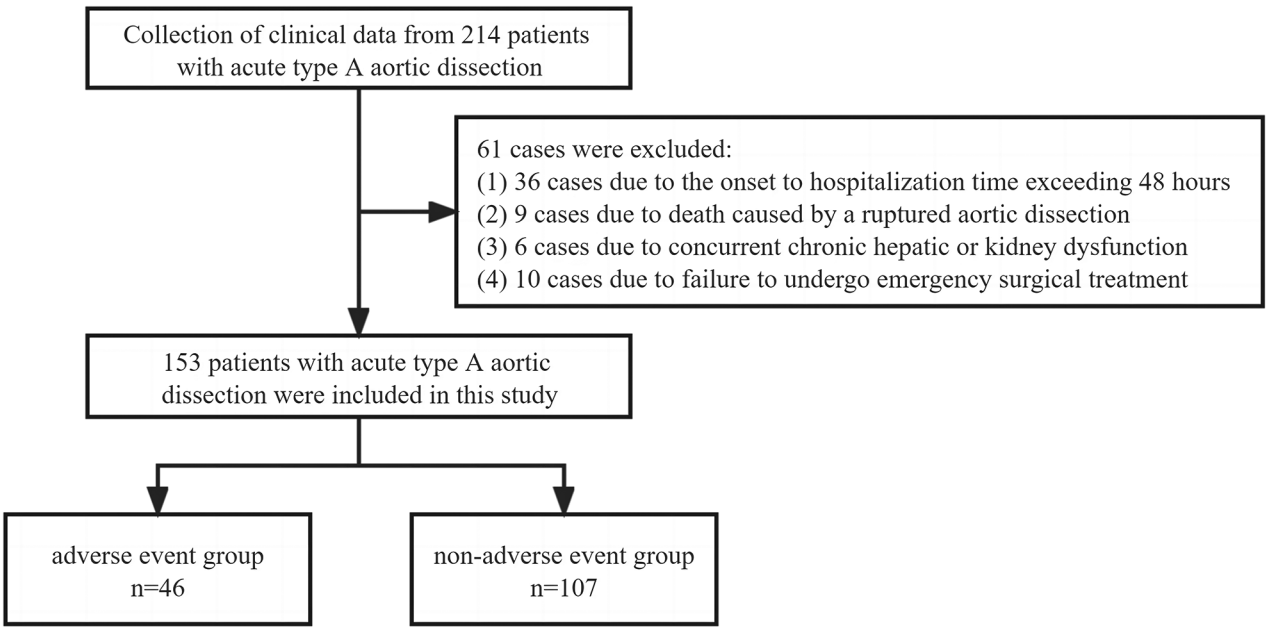

FIGURE 1
Grouping process and exclusion criteria for AAAD patients.

TABLE 1 Comparison of preoperative condition between the two groups.

Valuables	Non-adverse event group ($n = 107$)	Adverse event group ($n = 46$)	P value
Gender (male), *n* (%)	84 (78.5%)	35 (76.1%)	0.742
Age (year), mean (±SD)	53.15 ± 12.46	55.09 ± 12.97	0.388
BMI (Kg/m^2), median [IQR]	23.97 [21.27, 25.67]	23.26 [21.63, 25.10]	0.510
Smoking history, *n* (%)	54 (50.5%)	17 (37.0%)	0.124
Drinking history, *n* (%)	52 (48.6%)	20 (43.5%)	0.561
Hypertension, *n* (%)	64 (59.8%)	29 (63.0%)	0.707
Diabetes, *n* (%)	5 (4.7%)	1 (2.2%)	0.465
Coronary artery disease, *n* (%)	4 (3.7%)	2 (4.3%)	0.859
History of cerebrovascular disease, *n* (%)	7 (6.5%)	2 (4.3%)	0.597
Chronic obstructive pulmonary disease, *n* (%)	1 (0.9%)	2 (4.3%)	0.163
Marfan syndrome, *n* (%)	3 (2.8%)	2 (4.3%)	0.622
Hepatic dysfunction, *n* (%)	1 (0.9%)	2 (4.3%)	0.163
Renal insufficiency, *n* (%)	3 (2.8%)	3 (6.5%)	0.277
LVEF (%), median [IQR]	63.70 [60.70, 67.10]	63.50 [60.20, 67.80]	0.827
Pericardial effusion (medium or above), *n* (%)	19 (17.8%)	6 (13.0%)	0.470
Aortic valve regurgitation (medium or above), *n* (%)	32 (29.9%)	13 (28.3%)	0.838
Prognostic nutritional index, mean(±SD)	44.55 ± 4.60	39.60 ± 5.61	**<0.001**

SD, standard deviation; IQR, interquartile range; BMI, body mass index; LVEF, left ventricular ejection fractions.
Bold values indicate a *p*-value less than 0.05, indicating a statistically significant difference between groups.

indicator alone (Table 6). We also assessed the effectiveness and accuracy of the combined indicators in clinical prediction using the NRI and IDI. The results, shown in Table 7, indicate that the combined indicators have higher predictive accuracy compared to traditional individual predictors such as PNI or D-dimer. In order to compare the predictive performance of the combined index with traditional single biochemical indicators, we drew ROC curves to compare the combined index (preoperative PNI combined D-dimer) with commonly used clinical indicators of inflammation severity (WBC, CRP) and nutritional status (ALB). The results are shown in Figure 3, and the combined index still outperforms the single biochemical indicators in predicting outcomes.

In summary, preoperative PNI and D-dimer are effective predictive indicators for adverse events after AAAD surgery, and their combined use is more accurate.

Discussion

AAAD is an extremely dangerous cardiovascular emergency. If damaged aorta is not repaired by surgery in a timely manner, the

TABLE 2 Comparison of preoperative laboratory examination between the two groups.

Valuables	Non-adverse event group ($n = 107$)	Adverse event group ($n = 46$)	*P* value
White blood cell count ($\times 10^9$/L), mean (±SD)	12.47 ± 3.56	12.79 ± 3.85	0.622
Red blood cell count ($\times 10^{12}$/L), mean(±SD)	4.36 ± 0.52	4.31 ± 0.65	0.578
Leukomonocyte ($\times 10^9$/L), median [IQR]	1.01 [0.83, 1.37]	0.71 [0.56, 1.02]	**<0.001**
Heamoglobin (g/L), mean (±SD)	132.28 ± 17.21	128.59 ± 17.29	0.226
Platelet ($\times 10^9$/L), median [IQR]	176.00 [145.00, 206.00]	151.00 [128.00, 196.00]	**0.025**
Albumin (g/L), mean (±SD)	39.00 ± 3.84	35.49 ± 5.13	**<0.001**
ALT (IU/L), median [IQR]	20.00 [13.00, 31.00]	24.00 [15.00, 44.00]	0.084
AST (IU/L), median [IQR]	24.00 [19.00, 34.00]	33.00 [22.00, 71.00]	**0.005**
Serum creatinine (μmol/L), median [IQR]	89.00 [72.00, 114.00]	93.00 [67.00, 143.00]	0.474
D-dimer (μg/ml), mean (±SD)	9.83 ± 7.28	17.40 ± 5.47	**<0.001**
PT (s), median [IQR]	13.80 [13.10, 14.50]	14.30 [13.50, 15.80]	**0.040**
B-type natriuretic peptide (pg/ml), median [IQR]	224.00 [110.00, 678.00]	345.00 [156.00, 895.00]	0.123
Troponin-I (μg/L), median [IQR]	0.005 [0.002, 0.033]	0.013 [0.004, 0.165]	**0.004**
CRP (mg/L), median [IQR]	10.41 [3.51, 36.88]	8.46 [3.24, 25.63]	0.586

SD, standard deviation; IQR, interquartile range; PT, prothrombin time; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, c-reactive protein.
Bold values indicate a *p*-value less than 0.05, indicating a statistically significant difference between groups.

TABLE 3 Comparison of intraoperative conditions between the two groups.

Valuables	Non-adverse event group ($n = 107$)	Adverse event group ($n = 46$)	*P* value
Intraoperative time			
Operative time (min), median [IQR]	285.00 [255.00, 334.00]	300.00 [271.00, 330.00]	0.183
Cardiopulmonary bypass time (min), median [IQR]	139.00 [120.00, 160.00]	138.00 [128.00, 151.00]	0.794
Aortic cross-clamp time (min), median [IQR]	62.00 [53.00, 83.00]	62.00 [53.00, 81.00]	0.967
Cerebral perfusion time (min), median [IQR]	9.00 [5.00, 11.00]	7.00 [6.00, 10.00]	0.577
DHCA time (min), median [IQR]	4.00 [3.00, 5.00]	4.00 [3.00, 5.00]	0.186
Intraoperative blood transfusion			
Red blood cell transfusion volume (U), median [IQR]	4.00 [2.00, 4.00]	4.00 [2.00, 4.50]	0.831
Plasma transfusion volume (ml), median [IQR]	400.00 [200.00, 500.00]	400.00 [0, 600.00]	0.327
Platelet transfusion volume (U), median [IQR]	2.00 [0.80, 10.00]	1.00 [0, 10.00]	0.306
Aortic root concomitant procedure 0.759			0.759
No treatment, *n* (%)	48 (44.9%)	18 (39.1%)	
Sinus forming, *n* (%)	40 (37.4%)	20 (43.5%)	
Bentall, *n* (%)	19 (17.8%)	8 (17.4%)	

SD, standard deviation; IQR, interquartile range; DHCA, deep hypothermic circulatory arrest.

TABLE 4 In-hospital postoperative clinical adverse events in patients with AAAD.

Postoperative clinical adverse events ($n = 153$)	Number	Percentage
Renal failure (need CRRT)	27	17.65%
Respiratory failure	7	4.58%
Gastrointestinal bleeding	6	3.92%
Low cardiac output syndrome (need IABP)	2	1.31%
Ventricular fibrillation	5	3.27%
Permanent neurological deficits	14	9.15%
Sepsis	11	7.19%
Secondary thoracotomy	1	0.65%
Secondary intubation	7	4.58%
Tracheotomy	3	1.96%
Pericardial effusion	6	3.92%
Myocardial ischemia	2	1.31%
Death	12	7.84%

AAAD: acute type A aortic dissection; CRRT: continuous renal replacement therapy; IABP: intra-aortic balloon pump.

mortality rate within 48 h is about 50% (28). Despite emergency surgery being performed, the mortality rate remains high due to numerous postoperative complications. Therefore, early risk prediction of clinical adverse events and taking timely and effective measures for treatment can greatly help reduce in-hospital mortality. It is crucial to identify predictive factors that can forecast the risk of clinical adverse events after AAAD surgery. Currently, many studies have shown that certain blood biochemical indicators may have important significance in predicting the postoperative prognosis of AAAD, such as inflammatory factors and coagulation function indicators (29, 30). However, the clinical accuracy of predicting with a single indicator still needs to be improved. Therefore, this study aims to explore the clinical application value of combining multiple indicators to predict clinical adverse events after AAAD surgery.

Previous studies have shown that local and systemic inflammatory responses play a crucial role in the development of

TABLE 5 Univariate and multivariate analysis of postoperative clinical adverse events.

Valuables	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
PNI < 42.45	5.126	[2.421, 10.853]	**<0.001**	3.596	[1.508, 8.923]	**0.004**
Platelet < 154 ($\times 10^9$/L)	2.791	[1.371, 5.683]	**0.005**	1.529	[0.601, 3.884]	0.369
AST > 32 (IU/L)	3.078	[1.496, 6.333]	**0.002**	1.675	[0.641, 4.373]	0.289
D-dimer > 15.05 (μg/ml)	9.635	[4.169, 22.270]	**<0.001**	7.572	[3.094, 20.220]	**<0.001**
PT > 15.3(s)	2.562	[1.145, 5.732]	**0.022**	1.225	[0.391, 3.700]	0.721
Troponin-I > 0.007 (μg/L)	2.486	[1.213, 5.095]	**0.013**	2.245	[0.886, 5.891]	0.092

PNI, prognostic nutritional index; PT, prothrombin time; AST, aspartate aminotransferase.
Bold values indicate a *p*-value less than 0.05, indicating a statistically significant difference between groups.

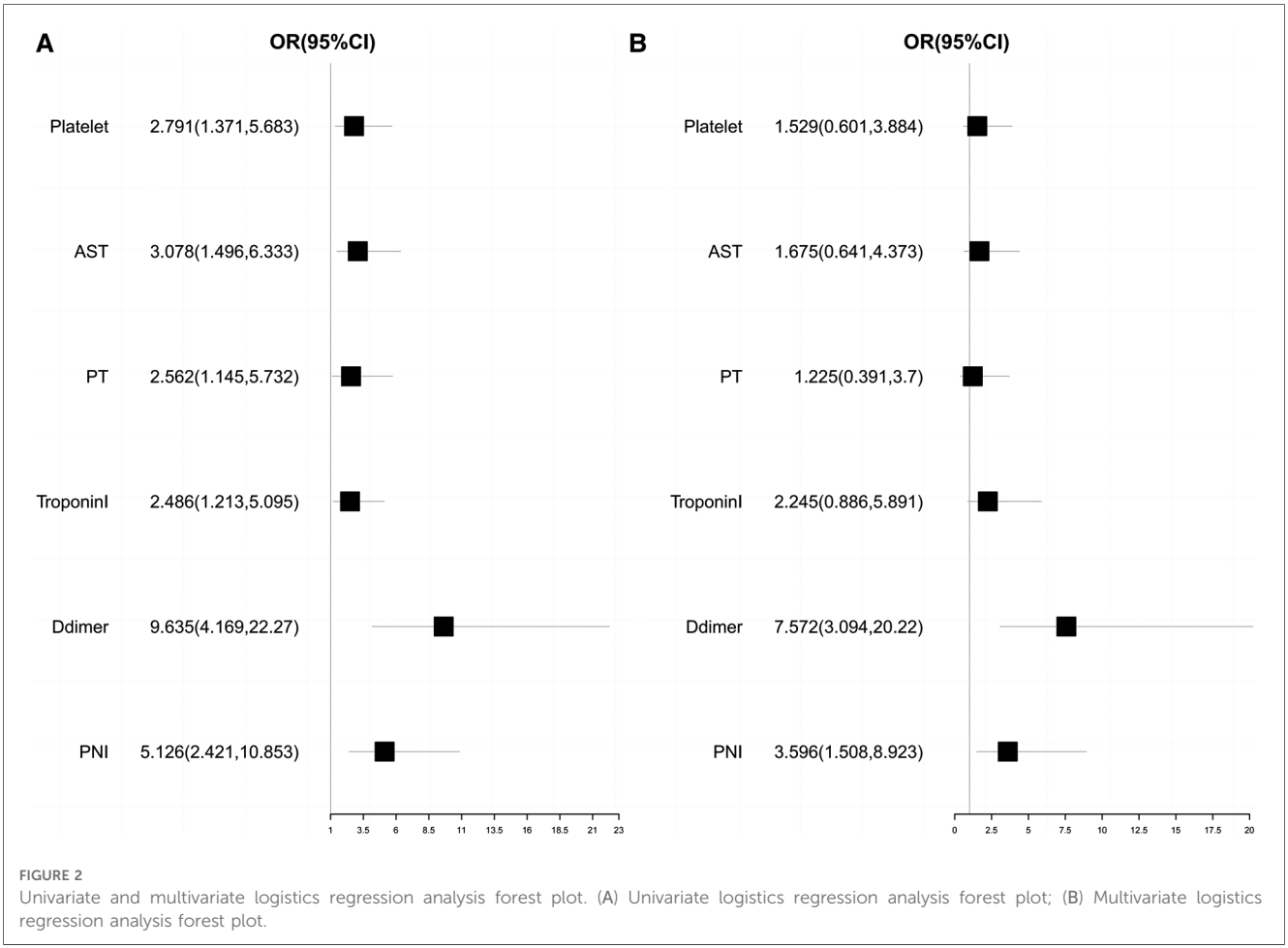

FIGURE 2
Univariate and multivariate logistics regression analysis forest plot. (A) Univariate logistics regression analysis forest plot; (B) Multivariate logistics regression analysis forest plot.

TABLE 6 Predictive value of preoperative PNI combined D-dimer for postoperative clinical adverse events.

Valuables	AUC	Cut-off value	95% CI	*P* value
PNI	0.752	42.45	[0.665, 0.839]	**<0.001**
D-dimer	0.770	15.05	[0.694, 0.847]	**<0.001**
PNI combined D-dimer	0.843	/	[0.774, 0.912]	**<0.001**

PNI, prognostic nutritional index.
Bold values indicate a *p*-value less than 0.05, indicating a statistically significant difference between groups.

AAAD (31–33). Inflammatory factors such as interleukin-6, procalcitonin, CRP are significantly elevated in the serum of most AAAD patients, and the degree of inflammatory response is often closely related to the prognosis (34, 35). As a composite index of systemic inflammation, PNI takes into account the degree of current inflammatory response and corresponding nutritional status, and the immune and nutritional status is closely related to the progression and prognosis of cardiovascular disease (36, 37). In recent years, in addition to being an independent predictor of postoperative mortality and prognosis in gastrointestinal tumors, the potential application value of PNI in cardiovascular diseases has also been increasingly recognized (17, 19). Although some studies have shown that PNI can be used to predict short-term prognosis for certain heart surgeries, due to the urgency and complexity of AAAD disease, the predictive value of PNI in such cardiovascular emergencies is still unknown. Our study is also the

TABLE 7 Comparison of the predictive performance of combined indicators vs. single indicators.

Valuables	NRI [95% CI]	*P* value	IDI [95% CI]	*P* value
PNI combined D-dimer vs. PNI	0.354 [0.157, 0.552]	**<0.001**	0.142 [0.089, 0.195]	**<0.001**
PNI combined D-dimer vs. D-dimer	0.348 [0.182, 0.515]	**<0.001**	0.115 [0.055, 0.175]	**<0.001**

NRI, net reclassification index; IDI, integrated discrimination improvement index; PNI, prognostic nutritional index.
Bold values indicate a *p*-value less than 0.05, indicating a statistically significant difference between groups.

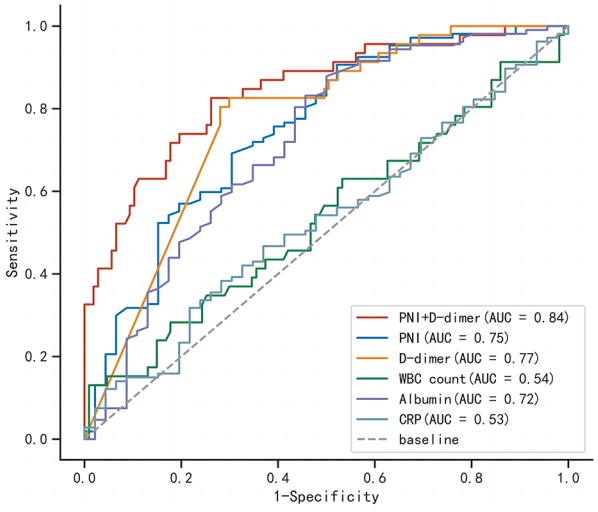

FIGURE 3
Comparison of receiver operating characteristic curves for combined indicators and single indicators.

first retrospective study on the predictive value of PNI for postoperative clinical adverse events in AAAD (38, 39).

Currently, the pathogenesis of aortic dissection (AD) is not clear. Many studies believe that the degradation of extracellular matrix in the middle layer of the aorta is closely related to the occurrence of AD (40). Activated lymphocytes can induce matrix metalloproteinase expression in smooth muscle cells of the aortic media, which is an important factor in promoting extracellular matrix degradation and plays an important role in the inflammatory response of AD, closely related to its prognosis (41, 42). Therefore, we believe that lymphocyte counts have potential value in predicting the prognosis of AD outcomes. At the same time, albumin, as an important indicator in clinical biochemistry testing, is usually used to evaluate the current nutritional status of the body, and can also indirectly reflect the degree of consumption of the body caused by disease, as most patients with inflammation-related diseases have acute or chronic consumption in their bodies (43). In this study, the PNI calculated by combining lymphocyte count and serum albumin was used to predict postoperative clinical adverse events. We believe that PNI has more accurate predictive value than its individual components. Currently, we have found that preoperative PNI < 42.45 is an independent risk factor for clinical adverse events after AAAD surgery. This finding can help clinicians make more appropriate clinical decisions in emergency situations of AAAD.

D-dimer is a non-specific fibrin degradation product that can reflect hyperfibrinolysis and hypercoagulable state in the human body. It is widely used for the diagnosis, efficacy evaluation, and prognosis prediction of thrombotic diseases (44, 45). During the occurrence of AD, due to the tearing and damage of the inner layer of the aorta, the coagulation system is rapidly activated, forming a false lumen thrombus, triggering a cascade reaction of coagulation, and activating the fibrinolysis system, leading to a rapid increase in the level of D-dimer in the serum. This has a good reference value in the diagnosis and differential diagnosis of AAAD (46). However, due to the fact that D-dimer is a highly sensitive but low-specificity detection indicator, its levels will significantly increase in cancer, infections, or any condition that may affect the body's coagulation function. Therefore, the reliability of using it as a prognostic indicator for AAAD still needs further verification. Research has also reported a correlation between the risk of in-hospital mortality in AAAD and the level of D-dimer (47). This may be due to the association between elevated D-dimer levels and serious complications such as postoperative acute renal failure, severe infection, and gastrointestinal bleeding. The level of elevated D-dimer can reflect the degree of disorder in the body's coagulation function to some extent. Although using D-dimer alone to predict the clinical outcome of AAAD has low specificity, our research results indicate that D-dimer > 15.05 μg/ml is an independent risk factor for postoperative clinical adverse events in AAAD, and has potential value in predicting the prognosis of AAAD. Therefore, we hope to increase its predictive reliability by combining it with other clinical indicators.

The results of this study indicate that preoperative PNI combined D-dimer are effective indicators for predicting postoperative clinical adverse events in patients with AAAD. Preoperative PNI < 42.45 and D-dimer > 15.05 μg/ml are independent risk factors for patients to experience postoperative clinical adverse events, which may provide more valuable predictive evaluation for the prognosis of patients with AAAD. This study is the first to apply PNI to the prediction of prognosis outcomes in cardiovascular emergencies such as AAAD. This composite inflammation-related indicator comprehensively considers the current nutritional status of the body, which can more reliably evaluate the prognosis outcomes. At the same time, we also found that the combination of PNI and the coagulation function indicator D-dimer had a significantly better predictive effect than using any single indicator alone (AUC = 0.843). The combination of the two indicators mentioned above for predicting the postoperative outcomes of AAAD patients has clear advantages, mainly because these clinical indicators do not increase the patient's medical costs or cause additional trauma, and are easy to obtain results in practical operations. This advantage also increases the clinical application value of these indicators.

The limitations of this study are as follows: (1) This is a single-center retrospective study, and the results may be limited by factors such as sample size, only representing the experience of this center in predicting adverse events of AAAD. In the future, more multi-center randomized controlled trials with larger sample sizes are needed to further verify the conclusions of this study; (2) This study only explored the relationship between preoperative PNI and D-dimer levels and postoperative adverse events, without further studying whether they have practical value in predicting the mid-to-long-term prognosis of AAAD, which is our next research direction.

Conclusion

Preoperative PNI < 42.45 and D-dimer > 15.05 are independent predictive factors for adverse clinical events in patients with AAAD after surgery, and have potential application value for predicting postoperative prognosis. The combined use of these two indicators can further improve their predictive value.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Ethics Committee of the affiliated Union Hospital of Fujian Medical University. The studies were conducted in accordance with the local legislation and institutional requirements. The Ethics Committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because this is a retrospective study and there is no need to obtain informed consent. Written informed consent was not obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article because this is a retrospective study and there is no need to obtain informed consent.

Author contributions

LX, JH, and DJ designed the study, and drafted the manuscript. XL, XZ, and ZZ collected the clinical data and performed the statistical analysis. LX and DJ provide technical support. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Hybrid total arch replacement via ministernotomy for Stanford type A aortic dissection

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Background: Type A aortic dissection (TAAD) is a cardiovascular emergency condition with high mortality rate. Hybrid total aortic arch replacement using endovascular graft for the descending aorta repair results in favorable outcomes and has been recommended as an alternative procedure for the higher-risk category patients. Our institution started applying the upper ministernotomy incision technique for the hybrid procedures back in 2018.

Methods: We collected patients who underwent hybrid total arch replacement (HTAR) via ministernotomy (96) and total arch replacement with frozen elephant trunk (TAR + FET) procedures (99), between 2018 and 2021. The baseline information, intraoperative and postoperative characteristics have been compared. Kaplan-Meier analysis was used for survival evaluation. Cox regression were applied to identify the independent predictor of mortality.

Results: The baseline characteristics between the two patient groups were compared and found similar, except that RBC counts were higher ($p = 0.038$) and the ascending aorta diameter was smaller ($P = 0.019$) in the "HTAR" group relative to the "TAR + FET" group. The cardiopulmonary bypass time ($P < 0.001$), the aortic cross clamp time ($P < 0.001$), the operation duration ($P = .029$), ICU ($P = 0.037$) and postoperative hospital stay ($P = 0.002$) were shorter in the "HTAR" group. The "HTAR" group exhibited also significantly lower levels of intraoperative transfusion (all <0.001) characteristics than the "TAR + FET" group. The hospital mortality and 1-year mortality revealed similar patterns in both groups.

Conclusion: HTAR via ministernotomy have similar short term prognosis, and also reduced the ICU and postoperative hospital stay. In all, The application of the ministernotomy technique in HTAR was safe and technically feasible and may benefit individual patients as well as hospitals in general.

KEYWORDS

Stanford type A aortic dissection, total arch repair, hybrid total arch repair, frozen elephant trunk, ministernotomy

Abbreviations

TAAD, type A aortic dissection; HTAR, hybrid total arch replacement; TAR, total arch replacement; FET, frozen elephant trunk; CTA, computed tomography angiography; IHM, intramural hematoma; PAU, penetrating aortic ulcer; TBAD, Stanford type B aortic dissection; HCA, hypothermic circulatory arrest; DSA, digital subtraction angiography; ICU, intensive care unit; ACCT, aortic cross clamp time; PSM, propensity-score matching; BMI, body mass index; IQR, interquartile range; RBC, red blood cell; HCT, Hematocrit; WBC, white blood cell; INR, international normalized ratio; APTT, activated partial thromboplastin time; LVEF, left ventricular ejection fraction; CAD, coronary atherosclerosis disease; CKD, chronic kidney disease; CPB, cardiopulmonary bypass; SCPT, selective cerebral perfusion time; CABG, coronary artery bypass grafting; PLT, platelets; IABP, intra-aortic balloon pump; ECMO, extracorporeal membrane oxygenation; CRRT, continuous renal replacement therapy; HR, hazard ratio; CI, confidence interval.

Introduction

Type A aortic dissection (TAAD) is a devastating disease with a high degree of mortality if not intervened promptly (1). TAAD, with its rapid progression, requires a multidisciplinary diagnosis in combination with a proper and timely surgical intervention. A poor prognosis for the disease is mostly associated with the aortic rupture and organ malperfusion (2, 3). Timely surgical reconstruction of aortic aneurysm and its dissection are the mainstays of the TAAD therapy. Total arch replacement with frozen elephant trunk (TAR + FET) has achieved desirable long-term outcomes and been widely used for TAAD treatment in China (4, 5). Nonetheless, the operative mortality of the disease remained high, owing to the inevitably large surgical invasions and long operation times (6).

While endovascular total arch repair is a new technique of limited utility (7), hybrid total arch replacement (HTAR) currently represents a more practical and extensive therapeutic strategy for TAAD (8). Initially, short and long-term outcomes of HTAR were reported by single-center clinical studies (9, 10), however, the small sample size in those studies has led to different experiences and conclusions. Subsequently, various institutions have successively utilized HART as one of the TAAD main treatments, and some even attempted to further improve the technique (8, 11).

Having benefited from the implementation and improvement of the TAAD repair procedures and the cerebral protection methods, surgeons have advocated for utilization of a minimally-invasive approach involving an upper ministernotomy, which had been used in cardiac surgery for nearly two decades (12), especially in aortic valve surgery, and, according to numerous studies, provided satisfactory outcomes (13, 14). Utilization of upper ministernotomy for the HTAR procedure has been initiated also at our institution. This study was aimed at determining if the use of upper ministernotomy for HTAR is safe for patients, as compared to the conventional TAR + FET intervention, and further advisable.

Patients and method

Study populations

We retrospectively included 195 patients who underwent surgery at Union Hospital between December 2018 and December 2021. All patients initially experienced sudden chest/back pain and were diagnosed with Stanford type A aortic dissection on the basis of computed tomography angiography (CTA). The morphology of the patients' heart valves was assessed by using transthoracic echocardiography. Patients with intramural hematoma (IHM), aortic aneurysm, penetrating aortic ulcer (PAU), or Stanford type B aortic dissection (TBAD) were excluded from this study (**Figure 1**). All the patients included in this study underwent aortic dissection repair surgery. The patients were divided into two study groups based on the surgical method used in their treatment: 96 (49.2%) patients who underwent hybrid total arch repair via upper ministernotomy, and 99 (50.7%) who received a conventional TAR with FET. The "TAR + FET" group included only patients above age 50. At our center, Stanford Type A aortic dissection repair surgery is being performed by three staff chief physicians with similar surgical skills and experience. We collected medical history and examined clinical information, including test results, surgical records as well as the follow-up information for each patient enrolled in the study by using the Union Hosptial Records System. This study was approved by the ethics committee of Wuhan Union Hospital, Huazhong University of Science and Technology (UHCT22975) and complied with the World Medical Association Code of Ethics (Declaration of Helsinki) adopted in 1975.

Surgical indication

In our hospital, hybrid total arch repair (HTAR) via ministernotomy and TAR + FET are currently the standard treatment options for Stanford type A aortic dissection. HTAR via ministernotomy is the most commonly used treatment of this disorder in the following circumstances: (i). in patients of old age (above 50) with multiple comorbid conditions who are at higher risk of hypothermic circulatory arrest (HCA); (ii) in patients with routine distal FET anastomosis that is a challenging condition when massive intimal tears or dissected pseudoluminas affect the distal portion of the descending aorta; (iii) in patients with high aesthetic wound requirements as HTAR via ministernotomy can shorten the period of wound healing.

Surgical techniques

"TAR + FET" group

After induction of general anesthesia, the right axillary artery was cannulated for cardiopulmonary bypass (CPB) and ACP, and a standard median sternotomy was performed. Then CPB was carried out through the right axillary artery and right atrium, while the cooling process was initiated. When the patient was cooled down to 33°C or the heart suffered from a ventricular fibrillation, the ascending aorta was clamped. At this time, the surgical procedures in the aortic root were carried out. Then, the patient was continuously cooled down to about 25°C, at which circulatory arrest would be performed. The bilateral ACP was initiated through the left common carotid artery during the circulatory arrest. Meanwhile, the left subclavian, left common carotid and innominate arteries were clamped. The stented elephant trunk was inserted into the true lumen of the descending aorta, which was anastomosed to the distal end of the four-branched graft (Maquet M00202175728APO). As required, air was removed from the descending aorta after anastomosis. Blood perfusion of the lower body was initiated by the infusion limb of the four-branched graft. The left subclavian artery was anastomosed to one limb of the vascular graft. As a result, CPB gradually resumed to normal flow, and the

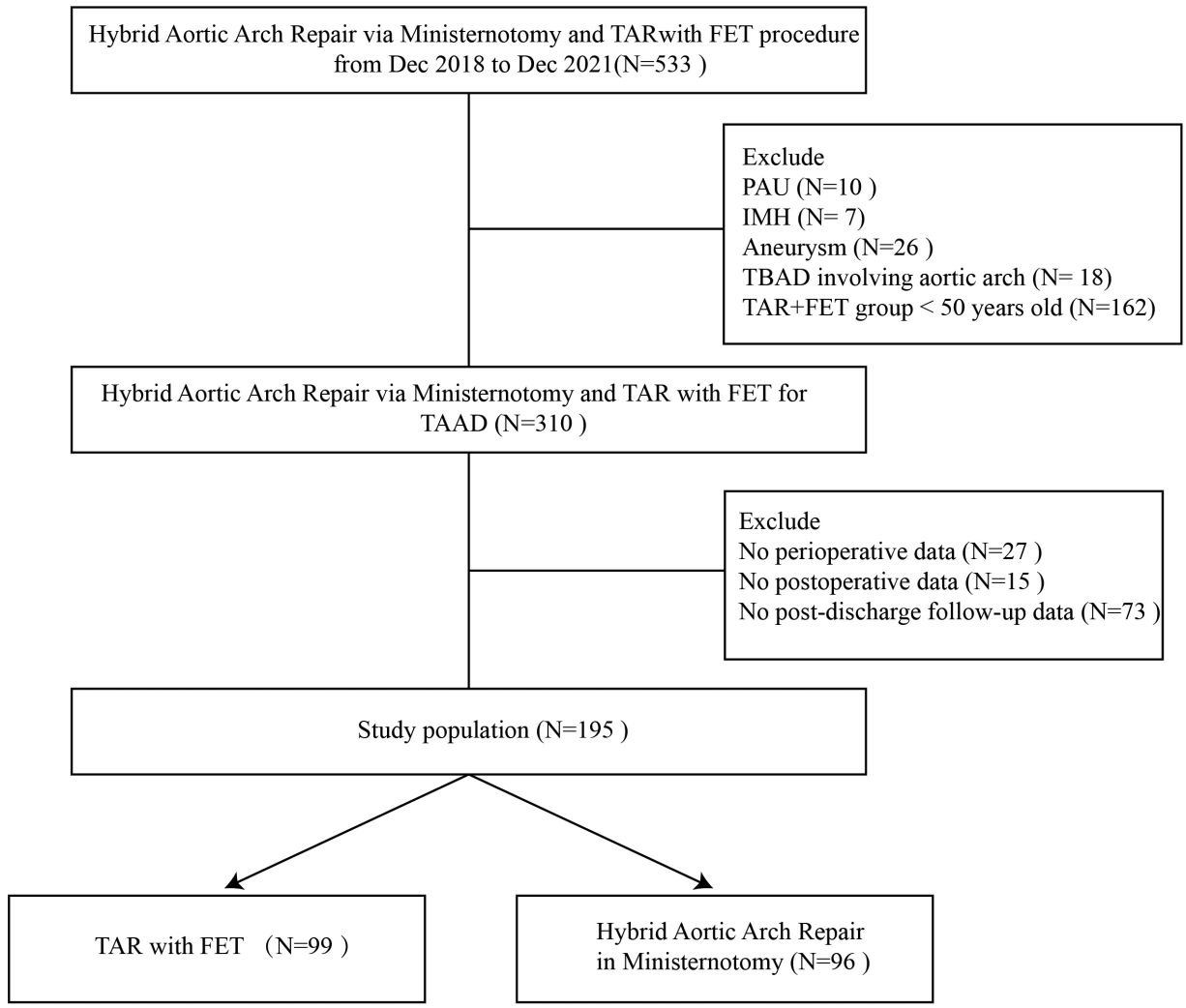

FIGURE 1
Flow diagram of the study cohort. Inclusion and exclusion criteria and population of this study. Five hundred thirty-three patients who underwent HTAR or TAR with FET procedure for TAAD from Dec 2018 to December 2021 were included. PAU, penetrating aortic ulcer; IMH, Intramural hematoma; TAAD, type A aortic dissection; TBAD, Stanford type B aortic dissection; FET, frozen elephant trunk.

rewarming started. The left common carotid artery was anastomosed end-to-end with the innominate artery. Anastomosis of the proximal end was carried out during the rewarming step. When the lung was reventilated, the ascending aorta was reopened to resume the cardiac perfusion.

When the patients were cooled down to the temperatures below 28°C, a PH steady-state blood gas management was used, while an alpha steady-state blood gas management was applied when the temperature was above 28°C. The whole process of cooling and rewarming was carried out at a slow and uniform rate, in a step-by-step process. Following the operation, CPB was stopped when the blood gas analysis results were satisfactory.

"Hybrid total arch repair via ministernotomy" group

Our small-incision hybrid aortic repair is a single-stage procedure that was performed in a hybrid operating room and consisted of two phases: an open repair and an endovascular repair phase. The operation involved hybrid aortic arch repair without MHCA. In the open repair phase, a midline ministernotomy incision was made from the suprasternal fossa to the third intercostal (about 12–16 cm) (Figure 2A). Then the right femoral artery and the right atrium were used for cardiopulmonary bypass, and cooled to 32°C–28°C. The aortic cross-clamp placement was proximal to the opening of the anonymous artery and followed by the aortic root repair. Subsequently, a bilateral cerebral perfusion was initiated through the left common carotid artery and innominate artery catheterization. Meanwhile, the left subclavian carotid and innominate arteries were clamped. The aortic cross-clamp was used between the opening of the anonymous artery and the left common carotid artery. The aortic arch was transected proximal to the left common carotid artery. The distal end of the graft was then sutured end-to-end to the aortic arch, proximal to the left common carotid. An antegrade perfusion of the lower body was initiated by the branch of the artificial vessel, followed by rewarming and proximal anastomosis of the artificial vessel trunk (Figure 2B). The vessels in the parietal region were sequentially anastomosed with the left common artery,

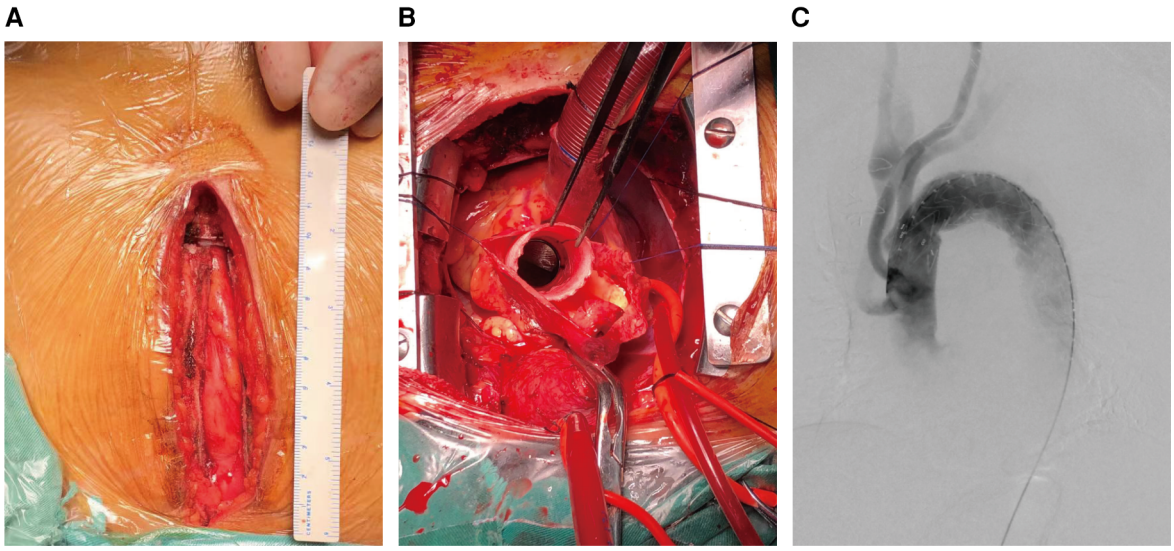

FIGURE 2
Incision of upper ministernotomy and HTAR technique. (A) Upper ministernotomy incision. (B) Intra-operative surgical filed of view: proximity of tetrafurcate vascular prosthesis graft was anastomosed to the sinotubular junction (aortic root has been repaired). (C) Endovascular portion: a stent graft implantation to exclude the entire lesioned aortic arch.

left subclavian artery, and anonymous artery. CPB was discontinued and wound hemostasis was achieved after protamine was administered to neutralize heparin. This is followed by endoluminal repair on digital subtraction angiography (DSA) (Figure 2C).

In the endovascular repair phase, the proximal stent was anchored to the artificial vessel to complete the arch repair. Angiography showed that there was no endoleak or contrast agent inside the false lumen of the thoracic aorta. A computed tomography performed prior to discharge showed aortic remodeling with complete thrombosis of the false lumen of the stented thoracic aorta. A postoperative transfer of the patients was made first to the intensive care unit (ICU) and then to a general ward, depending on the state of their recovery. After discharge, patients were advised to undergo a total aortic CTA examination in 3 months and 12 months after surgery, and annually thereafter.

Outcome criteria

The primary outcome was a 1-year survival rate. The secondary outcome included such postoperative criteria as in-hospital mortality, postoperative complications, tracheotomy, extracorporeal membrane oxygenation (CRRT) secondary insertion pipe, tracheal intubation time, ICU stay, and postoperative hospital stay.

Statistical analysis

Statistical analysis was performed by SPSS 25.0 software. Descriptive statistics was presented as frequency and percentage for categorical variables. For continuous variables, data was reported as mean ± SD or median with interquartile range after normal distribution testing. The non-normal distribution of the data necessitated the use of non-parametric tests. The Kaplan Meier survival estimate was calculated using Kaplan Meier analysis and Kaplan Meier curves were plotted. Cox univariable and multivariable regression analyses were performed and screened to show predictors of mortality. The variables used have been established in previous literature as predictors of the total arch replacement outcome.

Results

Baseline characteristics

The median age of patients in the "hybrid total arch replacement (HTAR) via ministernotomy" group was 60 (IQR:55–66) with 76 (79.2%) patients being males, whereas the median age of the patients in the "TAR + FET" group was 60 (IQR:53–67) with 78 (78.8%) being males. A moderate to severe aortic regurgitation occurred in 44 (45.8%) patients in HTAR and 42 (42.4%) in TAR + FET groups, respectively. RBC was statistically different between the two groups (4.18 vs. 3.97, $p = 0.038$). In addition, the results of the patients' echocardiography analysis have shown that the ascending aorta diameter in the "HTAR via ministernotomy" group was smaller than that in the "TAR + FET" group (4.75 vs. 5.0, $P = 0.019$). Apart from the above, the baseline characteristics of both groups were identical, which is evident from Table 1. As shown in Table 2, there were no significant differences in coronary atherosclerosis disease ($P = 0.268$), hypertension ($P = 0.154$), or diabetes ($P = 0.050$) between the "HTAR via ministernotomy" and the "TAR + FET" groups. Moreover, there was no statistically significant difference between the two groups in terms of comorbidities.

TABLE 1 Baseline variables.

Variables	Hybrid total arch replacement ($n = 96$)	TAR + FET ($n = 99$)	P Value
Male sex, n (%)	76 (79.2)	78 (78.8)	0.948
Age, year, median (IQR)	60 (55–66)	60 (53–67)	0.549
BMI, kg/m^2, mean ± SD	25.35 ± 8.76	25.69 ± 9.96	0.509
Smoking, n (%)	38.00 (39.60)	39.00 (39.40)	0.978
Alcohol drinking, n (%)	21.00 (21.90)	24.00 (24.20)	0.695
Systolic pressure, mmHg, mean ± SD	137.96 ± 21.91	135.20 ± 23.17	0.366
Diastolic pressure, mmHg, median (IQR)	80.00 (69.00–88.00)	80.00 (70.00–89.00)	0.988
Emergency operation, n (%)	59 (61.5)	69 (69.7)	0.226
Moderate to severe aortic regurgitation, n (%)	44.00 (45.80)	42.00 (42.40)	0.632
Hydropericardium, n (%)	31.00 (33.70)	26.00 (27.70)	0.372
RBC, 10^{12}/L, median (IQR)	4.18 (3.65–4.50)	3.97 (3.36–4.45)	**0.038**
HCT, %, median (IQR)	37.10 (32.23–40.78)	36.30 (33.05–39.95)	0.419
Platelet, 10^9/L, median (IQR)	152.50 (122.50–191.50)	146.50 (110.00–188.00)	0.234
WBC, g/l, median (IQR)	9.56 (7.72–12.13)	9.12 (6.55–12.21)	0.171
Ratio of lymphocytes, %, median (IQR)	9.15 (5.90–12.78)	10.10 (6.25–13.30)	0.444
Hemoglobin, g/L median (IQR)	124.50 (109.00–138.00)	121.00 (109.00–132.50)	0.286
Albumin, g/L, median (IQR)	35.75 (32.33–38.78)	37.00 (34.20–38.98)	0.153
Scr, μmol/L, median (IQR)	79.25 (65.40–109.30)	82.90 (68.90–125.95)	0.202
Bun, mmol/L, median (IQR)	6.76 (5.35–8.48)	7.16 (5.53–8.98)	0.400
Blood glucose, mmol/L, median (IQR)	6.30 (5.46–7.67)	6.21 (5.61–7.31)	0.883
Troponin I, ng/L, median (IQR)	27.80 (5.05–143.35)	16.60 (5.35–79.30)	0.257
INR, median (IQR)	1.10 (1.05–1.22)	1.10 (1.05–1.20)	0.590
APTT, s, median (IQR)	38.80 (34.40–41.33)	36.85 (34.65–42.18)	0.566
LVEF, %, median (IQR)	62.00 (60.00–65.00)	62.00 (60.00–65.00)	0.920
Aortic sinus diameter, cm, median (IQR)	3.90 (3.63–4.30)	4.05 (4.55–5.45)	0.355
Ascending aorta diameter, cm, median (IQR)	4.75 (4.30–5.13)	5.00 (4.55–5.45)	**0.019**
Aortic arch diameter, cm, median (IQR)	3.70 (3.40–4.13)	3.90 (3.50–4.30)	0.062
Distal diameter of the arch, cm, mean ± SD	3.47 ± 0.212	3.59 ± 0.173	0.071
Descending aorta diameter, cm, median (IQR)	3.90 (3.50–4.20)	3.90 (3.65–4.15)	0.635

BMI, body mass index; IQR, interquartile range; RBC, red blood cell; HCT, hematocrit; WBC, white blood cell; INR, international normalized ratio; APTT, activated partial thromboplastin time; LVEF, left ventricular ejection fraction.
Bold values indicated significance in statistical analysis.

TABLE 2 Comorbidities.

Variables	Hybrid total arch replacement ($n = 96$)	TAR + FET ($n = 99$)	P Value
History of heart surgery, n (%)	3 (3.1)	6 (7.1)	0.241
Hypertension, n (%)	72 (75.0)	65 (65.7)	0.154
Diabetes, n (%)	14 (14.6)	6 (6.1)	0.050
CAD, n, (%)	10 (10.4)	6 (6.1)	0.268
Pulmonary embolism, n, (%)	2 (2.1)	0 (0)	0.241
Stroke, n, (%)	4 (4.2)	8 (12.1)	0.111
CKD, n (%)	3 (3.1)	5 (5.1)	0.752
Chronic liver disease, n, (%)	3 (3.2)	0 (0)	0.223
Dialysis, n (%)	2 (2.1)	3 (3.0)	>0.999
Malperfusion, n (%)	3 (3.2)	5 (5.1)	0.753
Pericardial tamponade, n (%)	2 (2.1)	3 (3.0)	>0.999

CAD, coronary atherosclerosis disease; CKD, chronic kidney disease.

Intraoperative data

Intraoperative data are detailed in Table 2. The CPB time (155 vs. 216 min, $P < 0.001$), the aortic cross clamp time (ACCT) (100 vs. 118.5 min, $P < 0.001$) and the operation duration (462.5 vs. 484.0 min, $P = .029$) times were shorter in the "HTAR via ministernotomy" group than in the "TAR + FET" group (Table 3). Besides, the "HTAR via ministernotomy" group exhibited also significantly lower values in intraoperative blood transfusion: RBC (6 vs. 9.5 units, $P < 0.001$), plasma (600 vs. 950 ml, $P < 0.001$), PLT (2 vs. 3 units, $P < 0.001$) compared with the "TAR + FET" group. Besides, the "HTAR via

TABLE 3 Intraoperative variables.

Variables	Hybrid total arch replacement ($n = 96$)	TAR + FET ($n = 99$)	P Value
CPB time, min, median (IQR)	155.00 (129.00–190.00)	216.00 (171.50–263.75)	**<0.001**
ACCT, min, median (IQR)	100.00 (78.25–119.00)	118.50 (97.25–164.50)	**<0.001**
Operation duration, min, median (IQR)	462.50 (386.25–530.25)	484.00 (420.00–600.00)	**0.029**
SCPT, min, median (IQR)	0 (0.0)	16.00 (0–20.00)	**<0.001**
Intraoperative RBC transfusion, unit, median (IQR)	6.00 (4.13–7.88)	9.50 (7.25–11.50)	**<0.001**
Intraoperative plasma transfusion, ml, median (IQR)	600.00 (500.00–800.00)	950.00 (675.00–1,050.00)	**<0.001**
Intraoperative PLT transfusion, unit, median (IQR)	2 (2.00–3.00)	3 (3.00–4.00)	**<0.001**
Entry location envolvement of aortic root or sinotubular junction	8 (8.3)	21 (21.2)	**0.004**
Aortic root management, all, *n* (%)	17 (17.7)	40 (40.4)	**<0.001**
David, *n* (%)	0 (0.0)	2 (2.0)	0.491
Bentall, *n* (%)	13 (13.5)	37 (37.4)	**<0.001**
Wheat, *n* (%)	4 (4.2)	1 (1.0)	0.347
CABG, *n* (%)	9 (9.4)	6 (6.1)	0.385

CPB, cardiopulmonary bypass, ACCT, aortic cross clamp time; SCPT, selective cerebral perfusion time; CABG, coronary artery bypass grafting.
Bold values indicated significance in statistical analysis.

ministernotomy" and the "TAR + FET" groups revealed a difference with regard to the simultaneous surgical aortic root management by Bentall operation (13.5% vs. 37.4%, $P < 0.001$).

Short-term postoperative outcomes

There were no significant differences in the outcomes of post-surgical continued treatment such as ECMO, secondary thoracotomy operation, tracheotomy, tracheal intubation time, secondary insertion pipe, and CRRT ($P > 0.05$). However, the length of the patients' ICU stay (129 vs. 153 h, $P = 0.037$) and the length of postoperative hospital stay (20 vs. 24 days, $P = 0.002$) were shorter for the "HTAR via ministernotomy" group relative to the "TAR + FET" group. As far as the postoperative complications are concerned, no difference between the groups was noted, as from the 12 patients who died during the immediate postoperative period, 6 were from the "HTAR via ministernotomy" group and 6 from the "TAR + FET" group (6.3% vs. 6.1%, P = 0.941), while no patients exhibited a postoperative stent endoleak or stent displacement. The percentage of postoperative pulmonary complications, however, was lower in the "HTAR via ministernotomy" group than in the "TAR + FET" group (60.4% vs. 83.7%, $P < 0.001$). Nonetheless, there were no significant differences in postoperative pericardial effusion ($P = 0.360$), postoperative neurological complications ($P = 0.421$), and postoperative renal or liver dysfunctions ($P = 0.539$).

Survival analysis

All patients were followed up until October 10th, 2022, and the median follow up time was 29.0 (16.5–40.7) months for the "TAR

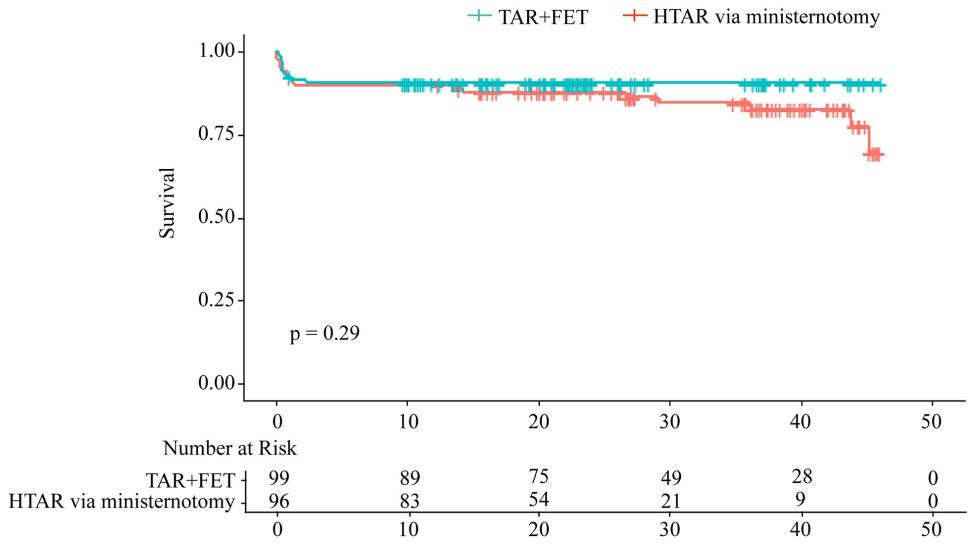

FIGURE 3
Kaplan–Meier analysis for overall survival stratified by HTAR via ministernotomy and TAR + FET, and log-rank test showed no significant difference between two group ($P = 0.29$).

+ FET" group and 20.8 (10.3–27.3) months for the "HTAR via ministernotomy" group, respectively. In Kaplan–Meier survival analysis, no significant differences were found between the "HTAR via ministernotomy" group and the "TAR + FET" group ($p = 0.29$) (**Figure 3**). Separate analyses of hospital mortality (5.2% vs. 5.1%, $p = 0.960$) and 1-year mortality (10.4% vs. 11.1%, $p = 0.876$) revealed similar patterns (**Table 4**). The variables were selected according to the previous studies and the baseline variables that have a significant bias between the two groups for univariable Cox analysis (**Figure 4A**). On the basis of Cox multivariable regression analysis, we found that the application of ministernotomy for HTAR was safe [HR 0.671 (0.331–1.444); $p = 0.307$] (**Figure 4B**). Furthermore, older age [HR 1.072 (1.030–1.115); $p = 0.001$], cardiopulmonary bypass time [HR 1.008(1.005–1.012); $p < 0.001$] and Scr [HR 1.002 (1.001–1.003); $p = 0.001$] represented significant independent predictors of mortality in both univariable and multivariable models. The Schoenfeld residuals analysis was performed and showed no significance (**Figure 4C**).

Conclusion

HTAR via ministernotomy have similar short term prognosis, and also reduced the ICU and postoperative hospital stay. In all, The application of the ministernotomy technique in HTAR was safe and technically feasible and may benefit individual patients as well as hospitals in general.

Discussion

This retrospective study on acute TAAD patients has led to the following findings: primarily, the application of the ministernotomy for HTAR was safe and technically feasible compared with the traditional aortic repair. Second, the differences in intraoperative variables have indicated that the HTAR via ministernotomy procedure has shortened duration of the operation, CPB, and ACC, as well as reduced the intraoperatively needed blood transfusion volume of RBC, plasma, and PLT. More importantly, the ministernotomy for HTAR procedure *per se* was not an independent risk factor for the patient mortality. However, older age, the cardiopulmonary bypass time, and the Scr level remained independent risk factors after adjusting for covariates.

As the technology improving the sensitivity of diagnostic for TAAD advances, more and more patients receive timely surgical interventions before the aortic rupture occurs. A prompt surgical treatment along with improved surgical techniques and perioperative patient care make the TAAD disease increasingly curable. Despite the advances in all the above fields, the operative and perioperative morbidity and mortality for TAAD remains high. In this regard, the goal of clinical TAAD treatment has not only been to improve the patients' survival, but also to obtain a better long-term prognosis for those patients. Since the traditional total aortic repair surgery was still a highly-invasive and risky procedure, the endovascular treatment of the thoracic aortic disease is emerging as a less invasive alternative to open surgery (15, 16). With the steadily increasing use of EAVR, it has been the mainstay of the descending aortic disease treatment (17, 18). Since the HTAR approach was first implemented in 2000 by J.A. Macierewicz et al. (19), many cardiovascular centers applied it for over a decade and their data show that HTAR has achieved desirable early and long-term clinical outcomes (9, 20). Our method of HTAR via upper ministernotomy procedure has similar indications as the conventional HTAR approach. Our data also indicated a favorable outcome after adjusting for age, which is the factor of the greatest bias from the TAR group (10). A meta-analysis of 38 studies reported that the hospital mortality associated with HTAR for TAAD was 5.5% lower than that in the case of traditional total arch repair (11). While a 12-year retrospective study involving the HTAR treatment of 209 patients in China demonstrated an early mortality rate of 10.0% (9), our

TABLE 4 Short-term postoperative outcomes.

Variables	Hybrid total arch replacement ($n = 96$)	TAR + FET ($n = 99$)	*P* Value
Secondary thoracotomy operation, *n* (%)	2 (2.1)	1 (1.0)	0.979
Tracheotomy, *n* (%)	4 (4.2)	10 (10.1)	0.109
Secondary insertion pipe, *n* (%)	5 (5.2)	13 (13.1)	0.056
Tracheal intubation time, hour, median (IQR)	67.00 (41.25–118.25)	80.00 (54.50–155.50)	0.085
ICU stay, hour, median (IQR)	129.00 (88.50–209.00)	153.00 (111.00–260.25)	0.037
Postoperative hospital stay, day, median (IQR)	20.00 (16.00–24.75)	24.00 (18.00–35.00)	**0.002**
CRRT, *n* (%)	14 (14.6)	11 (11.1)	0.468
Postoperative pericardial effusion, *n* (%)	60 (63.2)	68 (69.4)	0.360
Postoperative paraplegia, *n* (%)	3 (3.1)	2 (2.0)	0.972
Postoperative pulmonary complications, *n* (%)	58 (60.4)	82 (83.7)	**<0.001**
Postoperative neurological complications, *n* (%)	5 (5.2)	8 (8.1)	0.421
Postoperative renal dysfunction, *n* (%)	30 (28.6)	28 (29.4)	0.862
Postoperative liver dysfunction, *n* (%)	40 (49.4)	41 (50.6)	0.971
False lumen patency persisted, *n* (%)	5 (5.2)	8 (8.1)	0.421
Hospital mortality, *n* (%)	5 (5.2)	5 (5.1)	0.960
1-year mortality, *n* (%)	10 (10.4)	11 (11.1)	0.876

PLT, platelets; IABP, intra-aortic balloon pump; ECMO, extracorporeal membrane oxygenation; CRRT, continuous renal replacement therapy.
Bold values indicated significance in statistical analysis.

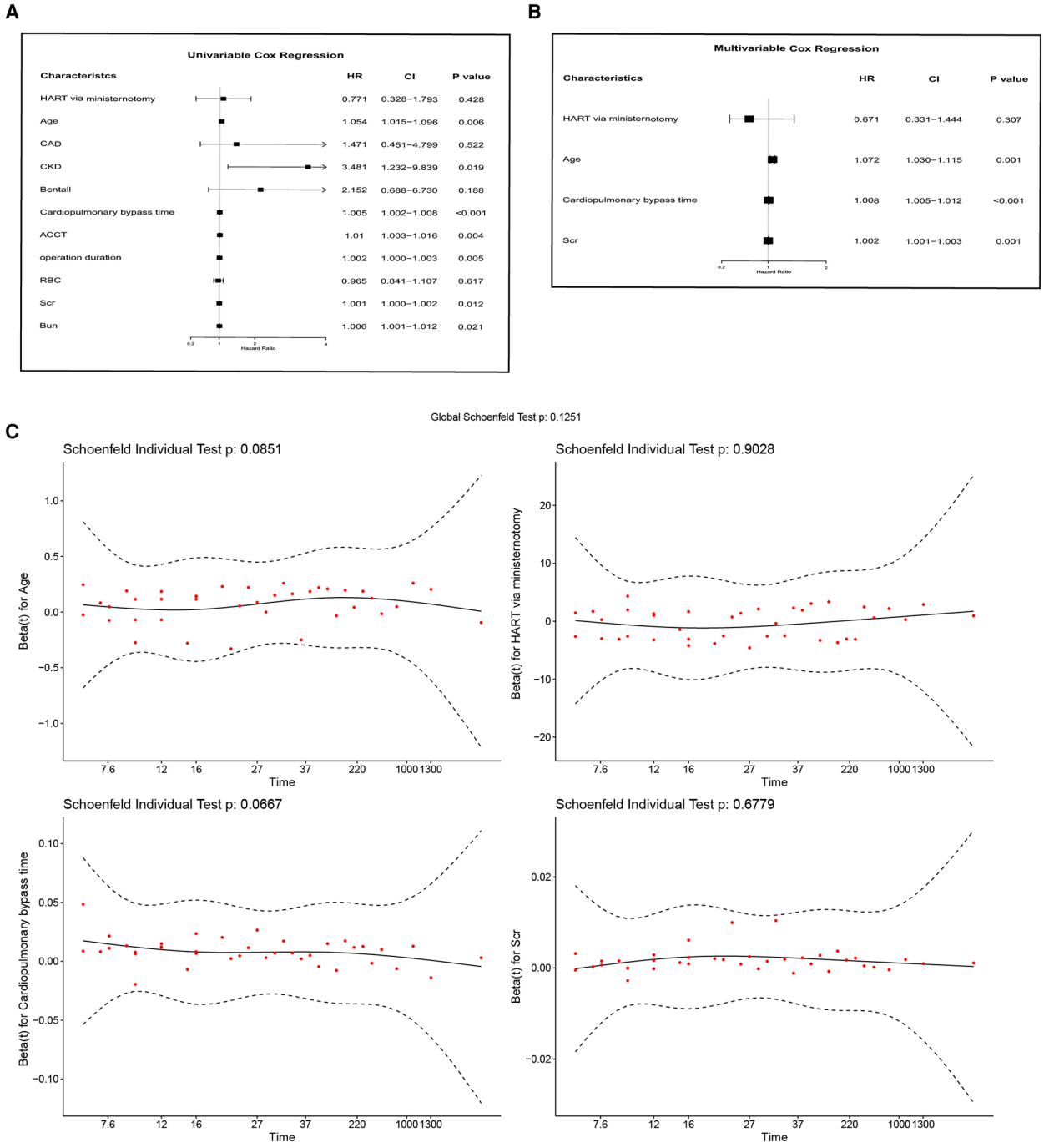

FIGURE 4
Cox proportional hazards regression models. (**A**) Univariable *Cox* regression analysis; (**B**) multivariable *Cox* regression analysis. (**C**) Schoenfeld residuals analysis. HR, hazard ratio; CI, confidence interval.

study's early mortality associated with HTAR via ministernotomy was only 5.2%, (5.1% in the "TAR + FET" group), and a 1-year mortality was 10.4% (11.1% for the "TAR + FET" group). The rate of early mortality associated with our ministernotomy for HTAR technique was similar to that resulting from the conventional invasion of HTAR procedure. The two procedures compared in our study significantly differed in such characteristics, as post-operative in-hospital time (20 vs. 24; $p = 0.002$) and post-operative pulmonary complications (60.4% vs. 83.7%; $p < 0.001$). Except for the comparable short-term outcomes, the two groups exhibited significant differences in intraoperative variables, in line with the previous studies demonstrating that the HTAR procedure decreased the time of CPB, ACC, as well as the operation duration time (20). Besides, the use of HTAR via ministernotomy reduced the intraoperatively needed blood transfusion volume.

It is noteworthy that "HTAR" reported by some earlier studies was referred to as a "TAR with FET" procedure. Actually, TAR

with FET that is also called Sun's procedure, has been widely used for the TAAD treatment in China for over 20 years (21). In our institution HTAR has been utilized as an alternative option for TAR with FET, especially for the high-risk patient category. In this case, there was a notable discrepancy in patients' age between the two groups. We excluded patients under the age of 50 from the "TAR with FET" treatment group also because the indication age for the HTAR treatment in our institution was 50 years of age and over. Patients' age has been previously reported as an independent predictor for mortality and used as such also in our study [HR 1.072 (1.030–1.115); $p = 0.001$]. This, to some extent, decreased the risk of potential bias. Besides, our results were consistent with those of an earlier study, reporting that, after propensity-score matching (PSM), the early mortality and post-operational complication rates in the "HTAR" group were not significantly different from the "TAR + FET" group (10).

The upper ministernotomy approach was first implemented for aortic valve operations in 1996, and since 1997 its use was extended to more complex cardiac surgery procedures (13, 22, 23). A surgical department from Italy with 11 years of experience in applying upper ministernotomy for the ascending aorta procedures, has found that this technique can reduce the postoperative bleeding and thereby the number of transfused RBC units in patients, as well as reduce their hospital stay (14). These outcomes were similar to those of our study and demonstrated that the utilization of upper ministernotomy provides substantial clinical advantages (24, 25). Both the satisfactory clinical outcomes and patients' requests facilitated application of ministernotomy for HTAR. To date the usage of this technique has been limited to a few large cardiovascular centers. More time is obviously needed for this technique to be widely and more commonly used in complex cardiac surgeries. A center in China has applied upper ministernotomy for the conventional TAR with FET procedure, but their results showed no difference in ICU and total hospital stay (26). Besides, they selected low-risk patients for this minimally-invasive surgery, and this made the above study different from ours. Our purpose thus was to further decrease the risk of infection and improve the poor surgical wound healing, since the HTAR procedure was indicated for the high-risk category patients. To our delight, our study revealed that the use of HTAR via ministernotomy has led to less post-operative pulmonary complications, which would mainly involve a pulmonary infection and excessive or moderate pleural effusions. In conclusion, practicing upper ministernotomy for HTAR in our institution proved safe and feasible, alleviated both patients' and hospital's burden and provided a minimal invasiveness to the surgical process.

Study limitations

There are few limitations to this study. First, this was a single-center based retrospective observational study, which can only provide a limited clinical and statistical information. A multi-center study with larger sample size may be needed. Second, we didn't include a perfect control group because, since 2018, almost all the patients with HTAR indication received surgery using the upper ministernotomy approach at our institution. However, the data of HTAR via ministernotomy in this study was discussed and compared with previous studies of conventional invasion of HTAR procedure above. Third, since the use of this approach in our institution has not been long enough, the data on the long-term outcomes of this study are not yet available, and the patients from our study should still be followed up in the future.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving humans were approved by Wuhan Union Hospital, Huazhong University of Science and Technology (UHCT22975). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin because Retrospective study have no intervention on human or need any coordination.

Author contributions

XL, XYL, JL, and HL contributed to conception and design of the study. JS, FL, PL, CD, XH, LW, JL, and HL Performed development of surgery methodology. XL, XYL, HY, YY, QZ, and KW organized the database. XL, XYL, and HY performed the statistical analysis. XL and XYL wrote the first draft of the manuscript. HY, QZ, KW, JS, JWL, and HL performed review and revision of the paper. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Intramural hematoma in the proximal sealing zone of the thoracic endovascular aneurysm repair: frequency and safety in acute and subacute type B dissections

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Introduction: To assess the outcomes after thoracic endovascular aneurysm repair (TEVAR) in the presence of intramural hematoma (IMH) in the proximal sealing zone.

Material and methods: Patient data were retrospectively extracted from the hospital records of patients treated with TEVAR for acute and chronic aortic dissection type B in one single center. The initial, preoperative, first postoperative, and last follow-up CT scans were evaluated in the aortic 3D multiplanar reformats and the centerline regarding IMH presence in the proximal sealing zone, anatomical preconditions, and the morphological TEVAR complications including migration and bird-beak. Groups with (IMH) and without IMH (no-IMH) were compared.

Results: Overall, 84 patients (IMH:42; no-IMH:42) were treated at the age of 63(55; 72) years, of whom 23/84 (27%), 34/84 (40%), and 27/84 (32%) were in the hyperacute, acute and subacute dissection phases, respectively. The bovine arch was found in 10/84(12%) and the type III arch was most common (43/84;51%). IMH maximum extent was found in zones 0, 1, 2, and 3 in 14/84 (17%), 17/84 (20%), 18/84 (21%), and 6/84 (7%), respectively. Sealing was achieved in zone II in 71/84 (85%) and LSA was revascularized in 66/84 (79%) of the overall cohort. Early mortality and paraplegia were 2/84 (2%) each; stroke rate was 3/84 (4%). During the 22 months median follow-up (22;4;43) no RTAD was observed. Migration ≥10 mm (IMH: 11/82; no-IMH: 10/82; $P = 1.0$) and bird-beaks (IMH: 10/82; no-IMH: 12/82; $P = 0.8036$) were comparable in both groups and accompanied by a low aorta related mortality (1/82) in both groups.

Conclusion: The presence of the IMH in the proximal TEVAR sealing zone is frequent and may not be relevant for the occurrence of the RTAD, stent-graft migration, or bird-beak formation.

KEYWORDS

aorta, dissection, endovascular, thoracic, stent-graft, migration, TEVAR

Abbreviations

BCT, brachiocephalic trunk; CABG, coronary artery bypass graft; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CT, computed tomography; dSINE, distal stent-induced new entry; ESVS, European Society for Vascular Surgery; ICU, intensive care unit; IMH, intramural hematoma; LCCA, left common artery; LSA, left subclavian artery; OR, odds ratio; RTAD, retrograde type A dissection; STROBE, strengthening the reporting of observational studies in epidemiology; TBD, type B dissection; TEVAR, thoracic endovascular aortic repair.

Introduction

The endovascular treatment of type B dissections (TBD) has evolved to the invasive therapy of choice in the current guidelines (1). Thus, an increasing number of patients are treated in the hyperacute and acute phases due to complicated TBD with acute life-threatening states including organ malperfusion, rupture, and conservatively unmanageable recurrent pain or uncontrollable hypertension. Furthermore, in the presence of the risk factors for aortic growth during the follow-up, TEVAR should be considered in the subacute phase to ensure aortic remodeling and prevent rupture and mortality at a later stage (2, 3).

However, TEVAR may also be associated with a higher perioperative risk, particularly when performed in the acute and hyperacute phases (4). Retrograde type A dissection (RTAD) is one of the most serious complications, associated with high mortality (4). Responsible for the occurrence of RTAD may be the vulnerability of the aortic wall in and proximal to the TEVAR sealing zone in the aortic arch in combination with excessive oversizing (4, 5). Therefore, reduced proximal oversizing has been recommended and broadly applied (6). However, reduced oversizing may create new challenges after the absorption of the IMH in the proximal sealing zone, and result in proximal stent graft malapposition, proximal sealing zone dilatation and stent-graft migration (7).

The aim of our study was to evaluate the rate of IMH in the proximal TEVAR sealing zone and to examine the impact of its presence on the occurrence of RTAD, the remodeling of the descending aorta, and the development of migration and the bird-beak configuration.

Materials and methods

The study was approved by the local ethical committee of the University medical center Tübingen (322/2022BO2). Patient consent was waived due to the retrospective character of the study.

TBD treatment protocol and cohort specifications

The center's protocol provides the TEVAR treatment of all complicated TBD with rupture or malperfusion in the hyperacute phase. In case of complicated TBD with uncontrolled hypertension, recurrent pain, or early aortic diameter progress of 5 mm in the CT scan 48 h after the diagnosis the invasive treatment is performed in the acute phase. Uncontrolled hypertension is defined as the inability to control blood pressure with intravenous antihypertensive therapy (targeted blood pressure <120/80 mmHg) or to substitute intravenous antihypertensive therapy with oral medication after 1-week post admission. Uncomplicated TBD patients with the presence of aortic growth risk factors including proximal entry tear diameter >10 mm, or aortic diameter >40 mm are discharged from the hospital after the oral blood pressure control has been established. Those patients are subjected to elective TEVAR in the subacute phase. All patients with acute TBD are followed up with contrast-enhanced CT scans at 48 h and 7 days on a regular base. The further follow-ups are performed at 3, 6, 12 months and yearly thereafter.

This retrospective cohort study included patients with hyperacute (<24 h), acute (day 1–14), and subacute (day 15–90) TBD treated between 2016 and 2023 with TEVAR in a tertiary referral hospital. The procedures were isolated through the search of the center's database (SAP, Walldorf, Germany). The patients were assigned to 2 study groups: The no-IMH group without the IMH in the proximal TEVAR sealing zone, and the IMH group where sealing was performed in the presence of the IMH (**Figure 1**). Furthermore, at least 10 mm of IMH-free sealing zone was defining the no-IMH group (8). The study design and the manuscript were organized according to the STROBE guidelines for observational studies (9).

Population demographics, co-morbidities, and procedural specifications

Demographic data included age and sex. The co-morbidities were obtained from the hospital records: hypertension, current nicotine abuse, orally or insulin-treated diabetes, dyslipoproteinemia, COPD, previous percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG), and previous ascending aorta replacement.

Procedural details including the indication for treatment, the Ishimaru landing zone (zone 0-III), stent-graft type and diameter, the revascularization of the left subclavian artery, the presence of a bovine arch, the arch type (type I-III) (10), and the technical success were drawn from the operation protocols, intraoperative imaging, and the pre-and postoperative CT scans (11). Our procedural protocol includes the proximal oversizing in dissections of 10% and the standard use of Relay NBS (Terumo Aortic, Inchinnan, UK) and Gore C-TAG conformable (Gore Medical, Flagstaff, AZ, USA) stent-grafts without a long proximal bare stent. In the case of Relay NBS, tapered stent-grafts are used in dissections by default to reduce distal oversizing. Our preference for the Relay NBS graft can be explained by the proximal deployment mechanisms of this endograft which include the proximal to distal deployment, stabilization wires, and the V-patch in the inner aortic curvature to stabilize the endograft and to prevent the bird-beak during the deployment, respectively (12). Thanks to the V-patch the inner portion of the endograft can be securely apposed to the inner aortic curvature. In comparison to the Relay NBS, C-TAG conformable device with the active control system allows for the inner curvature apposition by the active endograft orientation feature in the proximal landing zone (13). C-TAG conformable is predominantly used in our center for patients with high true lumen tapering to address the risk of distal stent-induced new entry due to the fact that this endograft may have a reduced risk of this complication during the follow-up in comparison to the ring stent design (14).

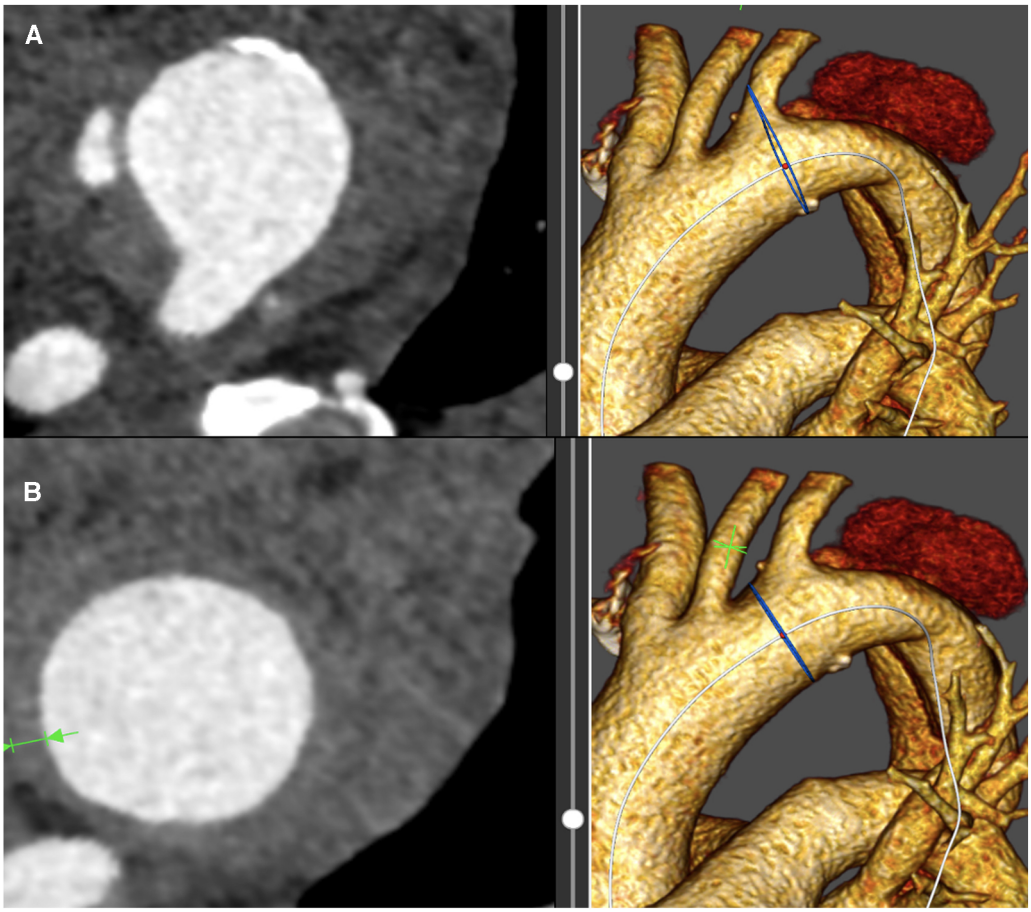

FIGURE 1
(A) Shows the intramural hematoma with proximal dissection extent in the aortic centerline at the site of the left subclavian artery. (B) demonstrates the intramural hematoma extent in the proximal landing zone II between the left carotid and left subclavian artery.

According to our protocol, the left subclavian artery (LSA) is revascularized in all hemodynamically stable patients during the same procedure. All patients treated electively in the subacute phase receive a cerebrospinal fluid drain on the day before the operation. The endograft deployment was performed in all patients under the left ventricular output reduction with rapid pacing.

CT analysis

CT scan analysis of the admission/preoperative, first postoperative, and last follow-up CT scan was performed with dedicated software (Therenva, Rennes, France). All patients were subjected to a contrast-enhanced CT scan with a slice thickness of 1 mm. The post-processing of the DICOM data set included the centerline measurement of the diameter of the proximal landing zone in the preoperative CT scan and the outer-to-outer total aortic diameter and TL diameters at the level of the pulmonary artery bifurcation. Proximal oversizing was calculated according to the formula:

[*(proximal stent-graft diameter, mm/outer-to-outer proximal sealing zone diameter, mm)-1]* × *100%*.

Stent-graft migration was measured by the increase in the distance between the distal left common carotid artery (LCCA) origin and the proximal stent-graft end at the outer curvature of the aorta. The bird-beak was described by the angle between the innermost proximal stent-graft plane and the inner aortic curvature plane, as described in our previous works (15, 16). The CT morphological absence of the contrast agent in the venous phase defined the total false lumen thrombosis, whereas partial thrombosis included patent and thrombosed areas of the FL.

Outcome parameters

Early follow-up outcomes included the postoperative results within 30 days after the operation, while mid-term follow-up outcomes described the findings of the last follow-up, which consisted of a contrast-enhanced CT scan and a patient interview with the physical examination. Primary technical success was reported according to the SVS reporting standards for TEVAR (11). A stroke was defined as a new neurological event that persisted for >24 h and affected the National Institutes of Health

Stroke Scale (NIHSS) by at least 2 points (17). Any new onset of transient or permanent paraplegia or paraparesis after TEVAR, which occurred as a deficit in motor or sensory function of the lower extremity, or incontinence was assessed.

Statistical analysis

The statistical analysis was performed with JMP® 14 software (SAS, NC, USA). Categorical variables are presented as patient count (percentage), and continuous variables are reported as median (1st quartile; 3rd quartile). Fisher's exact test or x^2 $^-$test was employed for categorical variables. Continuous data were tested for normality and equality of variance by Kolmogorov-Smirnov and Levene tests, respectively. *t*-test was used for normal distribution, and the Mann-Whitney U test was applied for non-normal continuous variables. Multivariate logistic regression analysis with the Wald test and likelihood ratio test was performed to assess the risk factors for migration. $P < 0.05$ was considered significant.

Results

Patient cohort and procedural parameters

The median age of the cohort was 63 (55; 72; Table 1) years and 21/84 were female. Between the study groups there was a trend towards a higher rate of hypertension (37/ 42 vs. 42/42; $P = 0.0551$) in the IMH group and hypercholesterinemia with statin treatment was more common in the no-IMH group (9/42 vs. 2/42; $P = 0.0485$). Other comorbidity parameters were comparable between the study groups including current nicotine abuse, diabetes, COPD, previous PCI/CABG, and previous ascending aorta replacement (Table 1).

The aortic arch types I, II, and III, were found in 20/84, 21/84, and 43/84 of the cohort, respectively, and the distribution was comparable between the study groups ($P = 0.7219$). The bovine arch was present in 10/84 patients (Table 2).

TABLE 1 Demographic characteristics and co-morbidity of the cohort.

Patient characteristics	Overall	No-IMH	IMH	*p*
n	84 (100)	42 (50)	42 (50)	
Age (years)	63 (55;72)	61 (53; 71)	65 (56;73)	0.2201
Sex (female) *n* (%)	21 (25)	7 (17)	14 (33)	0.1295
Hypertension *n* (%)	79 (94)	37 (88)	42 (100)	0.0551
Current nicotin abuse *n* (%)	15 (18)	7 (17)	8 (19)	1.0
Diabetes *n* (%)	4 (5)	2 (5)	2 (5)	1.0
Hypercholesterinemia with statin treatment *n* (%)	11 (13)	9 (21)	2 (5)	0.0485
COPD *n* (%)	6 (7)	3 (7)	3 (7)	1.0
Previous PCI/CABG *n* (%)	2 (2)	2 (5)	0 (0)	0.969
Previous ascending replacement *n* (%)	2 (2)	2 (5)	0 (0)	0.969

IMH, intramural hematoma; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

The individuals were treated in the hyperacute, acute, and subacute dissection phases in 23/84, 34/84, and 27/84 of the cases, respectively. The most important TEVAR treatment indications in the hyperacute and acute phases were malperfusion (29/84), early diameter progress (19/84), rupture (18/84), recurrent pain (16/84), and uncontrolled hypertension (6/84). In the subacute phase, patients were treated due to the

TABLE 2 Planning and procedural parameters of the cohort.

Patient characteristics	Overall	No-IMH	IMH	*p*
Arch type				
I *n* (%)	20 (24)	9 (21)	11 (26)	0.7219
II *n* (%)	21 (25)	12 (29)	9 (21)	0.7219
III *n* (%)	43 (51)	21 (50)	22 (52)	0.7219
Bovine arch *n* (%)	10 (12)	4 (10)	6 (14)	0.7379
Indication for hyperacute/acute TEVAR				
Malperfusion *n* (%)	29 (35)	21 (50)	8 (19)	0.0054
Rupture *n* (%)	18 (21)	8 (19)	10 (24)	0.7909
Recurrent pain *n* (%)	16 (9)	6 (14)	10 (24)	0.4052
Uncontrolled hypertension *n* (%)	6 (7)	2 (5)	4 (10)	0.6758
Early diameter progress ≥5 mm *n* (%)	19 (23)	6 (14)	13 (31)	0.1163
Indication for subacute TEVAR				
Aortic Diameter >40 mm at dissection onset *n* (%)	27 (32)	11 (26)	16 (38)	0.3502
Entry Diameter >10 mm at dissection onset *n* (%)	23 (27)	8 (19)	15 (36)	0.1412
Temporal dissection classification at TEVAR				
Hyperacute	23 (27)	11 (26)	12 (29)	0.1541
Acute	34 (40)	21 (50)	13 (31)	0.1541
Subacute	27 (32)	10 (24)	17 (41)	0.1541
LSA revascularisation (TEVAR with LSA coverage)	66 (79)	34 (81)	32 (76)	0.7909
Intended proximal oversizing	11 (8;13)	10 (9;13)	11 (7;13)	0.6413
Stent-graft type	43 (51)			
C TAG	8 (10)	3 (7)	5 (12)	0.7126
Relay NBS	76 (90)	39 (93)	37 (88)	0.7126
Primary entry localisation (zone)				
II	30 (36)	19 (45)	11 (26)	0.1850
III	39 (46)	17 (40)	22 (52)	0.1850
IV	15 (18)	6 (14)	9 (21)	0.1850
Proximal landing zone				
I	3 (4)	1 (2)	2 (5)	0.8405
II	71 (85)	36 (86)	35 (83)	0.8405
III	10 (12)	5 (12)	5 (12)	0.8405
Most proximal IMH extent *n* (%)				
I	17 (20)	0 (0)	17 (40)	<0.0001
II	18 (21)	8 (19)	10 (24)	<0.0001
III	6 (7)	5 (12)	1 (2)	<0.0001
0 (BCT)	9 (11)	0 (0)	9 (21)	<0.0001
0 (ascending)	5 (6)	0 (0)	5 (12)	<0.0001
IMH absent	29 (35)	29 (69)	0 (0)	<0.0001
IMH dynamics in subacute dissections *n* (%)				
Extent increase	1 (4)	0 (0)	1 (6)	1.0
Extent decrease	0 (0)	0 (0)	0 (0)	1.0
Extent stability	22 (96)	7 (100)	15 (94)	1.0
Technical success	84 (100)	42 (100)	42 (100)	1.0

IMH, intramural hematoma; TEVAR, thoracic endovascular aneurysm repair; LSA, left subclavian artery; BCT, brachiocephalic trunk.

aortic diameter over 40 mm at dissection onset (27/27), and additionally, the proximal entry tear diameter over 10 mm was found in 23/27 cases.

Primary entry tear localization was zone II, III, and IV in 30/84, 39/84, and 15/84, respectively. The proximal sealing zone was zone I in 3/84, zone II in 71/84, and zone III in 10/84 of the patients. Patients acutely treated in the zone I received a carotid-carotid bypass through the ante-tracheal approach (1/84), whereas for the elective treatment in the subacute phase, a proximal scallop TEVAR for the LCCA was customized (2/84). LSA revascularization with a carotid axillary bypass was performed in 66/84 patients prior to the TEVAR but during the same intervention. The proximal oversizing of the stent-graft was 11% (8; 13), and the most common stent-graft in this study was Relay NBS (Terumo Aortic, Inchinnan, UK), which was used in 76/84 of the cohort. In 8/84 Gore CTAG conformable stent-graft was implanted. The technical success of the procedure was achieved in 84/84 (100%).

IMH extent and dynamics

The presence of the IMH in the aortic arch zones 0-III affected 55/84 individuals (**Figure 2**). The most proximal IMH extent is shown in **Table 2**. In 14/84 patients the IMH reached zone 0, of whom 5/17 had a hematoma of the ascending aorta. Zone I was affected in 31/84 cases, whereas an IMH was present in zone II in 49/84. Naturally, the extent of the IMH was more proximal in the patients from the IMH group ($P < 0.0001$) but was also found in zones II (8/42) and III (5/42) of the no-IMH group. Those patients were assigned to the no-IMH group due to an IMH-free proximal sealing zone length ≥10 mm.

The patients who were treated electively in the subacute phase (median 31 days; 21; 138) had an IMH in 23/27 cases at the diagnosis CT scan. The IMH remained stable until the treatment in 22 (96%) patients and showed an extent increase in only one case.

Early follow-up outcomes

At 30 days, mortality occurred in 2/84 (**Table 3**) patients. One patient with ruptured acute TBD died on the day of the operation, due to the continuous distal perfusion of the false lumen rupture site in the descending aorta. The second patient developed an infrarenal abdominal rupture of the false lumen on the second postoperative day. Stroke was found in 3/84 (4%), of whom all were non-disabling. One patient with vertebral artery transposition had a minor cerebellar stroke with transient vertigo. A second patient with a covered left vertebral artery arising from the aortic arch experienced postoperative delirium, which gradually disappeared, and a third patient, without LSA revascularization prior to the TEVAR, had a smaller posterior stroke, and recovered completely during the hospital stay. Furthermore, 2/84 (2%) patients showed postoperative paraplegia. In both cases, cerebrospinal fluid drainage was not implemented before TEVAR, due to the aortic rupture. Both had an aortic coverage over 25 cm and the LSA was covered without revascularization. One patient recovered during the hospital stay after the implementation of the cerebrospinal fluid drainage, whereas the other remained permanently paraplegic. During the early follow-up RTAD, and type I endoleaks were not observed. The median ICU stay was 0 (0;1) days and the incidence of bird-beaks was low (2/84; 2%; **Table 3**).

Mid-term follow-up outcomes

During the follow-up of 22 (4; 43) months, 2 more patients died (2/82; 2%) of whom one patient at 3 months with prosthesis infection, while the second had lethal bleeding from

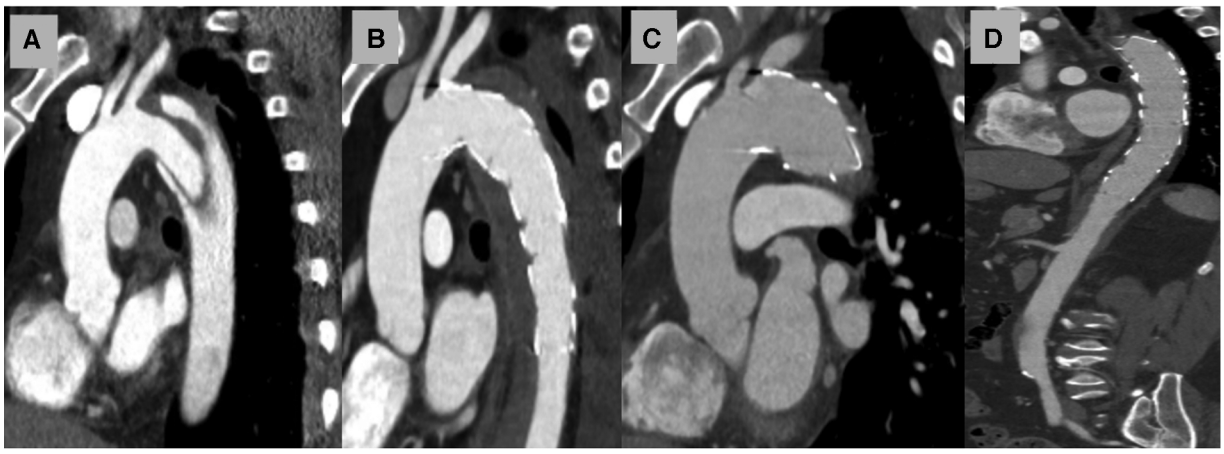

FIGURE 2
(**A**) Shows the preoperative sagittal CT scan at the time of the type B dissection diagnosis in a patient with intramural hematoma (at the site of the left subclavian artery). (**B**) demonstrates the postoperative sagittal CT scan after TEVAR in the landing zone II. (**C**) indicates the sagittal CT scan of the same patient: the stability of the proximal endograft position is well visible. The remodeling of the downstream aorta is shown in (**D**).

TABLE 3 30-day outcome of the cohort.

Patient characteristics	Overall	No-IMH	IMH	*p*
Mortality *n* (%)	2 (2)	1 (2)	1 (2)	1.0
New postoperative dialysis *n* (%)	1 (1)	1 (3)	0 (0)	0.4938
Stroke *n* (%)	3 (4)	2 (5)	1 (2)	0.5566
Paraplegia *n* (%)	2 (2)	1 (2)	1 (2)	1.0
ICU stay (d)	0 (0;1)	0 (0;1)	0 (0;1)	0.8659
Retrograde type A dissection *n* (%)	0 (0)	0 (0)	0 (0)	1.0
Bird beak *n* (%)	2 (2)	2 (5)	0 (0)	0.2407
Discharge with				
Beta-blockers *n* (%)	64 (79)	30 (75)	34 (83)	0.4241
ACE / AT 2 inhibitors	68 (84)	32 (80)	36 (88)	0.3793
Calcium channel blockers	63 (78)	30 (75)	33 (80)	0.6015
Endoleaks Type I *n* (%)	0 (0)	0 (0)	0 (0)	1.0

IMH, intramural hematoma; ICU, intensive care unit; ACE, angiotensin-converting enzyme; AT, angiotensin.

an aorto-bronchial fistula at 40 months (Table 4). Strokes, paraplegia, type I/III endoleaks, or RTAD were not observed during the follow-up. Nine patients from the no-IMH group and 7 from the IMH group have undergone a reintervention which consisted of a TEVAR extension in order to repair d-SINE, which resulted in an overall reintervention rate of 19%. Bird-beak rate significantly increased in the overall cohort during the mid-term follow-up from 2/84 to 22/82 ($P < 0.0001$), without any relevant difference between the groups (No-IMH:12/41; IMH: 10/41; $P = 0.8036$). Migration of the proximal stent-graft >10 mm was seen in 21/82 patients and the groups were equal regarding this parameter (No-IMH:10/41; IMH: 11/41; $P = 1.0$).

Complete false lumen thrombosis was present in 80/82 descending thoracic aortas, with only two patients with partial thrombosis in the IMH group. The remodeling of the true lumen was more prominent in the No-IMH group with a diameter increase from preoperative to the follow-up measurement of 14 (4; 19) mm. In comparison, the diameter increase in the IMH group was 7 (2; 15) mm ($P = 0.0225$). The aortic diameter remodeling (reduction) was less pronounced in the overall cohort 2 (−1; 5) mm, with a significantly better remodeling in the IMH group (No-IMH:0 (−2;3); IMH: 3 (0;5); $P = 0.0436$).

TABLE 4 Mid-term outcome of the cohort.

Patient characteristics	Overall	No-IMH	IMH	*p*
Follow-up time (months)	22 (4;43)	20 (4; 43)	29 (4;44)	0.8799
Mortality *n* (%)	2 (2)	1 (2)	1 (2)	1.0
Aorta related mortality	2 (2)	1 (2)	1 (2)	1.0
Endoleaks type I (total) *n* (%)	0 (0)	0 (0)	0 (0)	1.0
Stroke *n* (%)	0 (0)	0 (0)	0 (0)	1.0
Paraplegia *n* (%)	0 (0)	0 (0)	0 (0)	1.0
Retrograde type A dissection *n* (%)	0 (0)	0 (0)	0 (0)	1.0
Bird beak *n* (%)	22 (27)	12 (29)	10 (24)	0.8036
Reinterventions	16 (19)	9 (22)	7 (17)	0.78132
Median bird beak angle increase during follow-up (°)	40 (34; 52)	40 (30;50)	41 (34;54)	0.6924
Migration >10 mm *n* (%)	21 (26)	10 (25)	11 (27)	1.0
Descending aortic diameter remodeling (mm)	2 (−1;5)	0 (−2;3)	3 (0;5)	0.0436
True lumen descending aortic remodeling (mm)	9 (3;15)	14 (4; 19)	7 (2;15)	0.0225
False lumen patency				
Patent	0	0	0	0
Thrombosed	80 (98)	41 (100)	39 (95)	0.1521
Partially thrombosed	2 (2)		2 (5)	0.1521

IMH, intramural hematoma.

TABLE 5 Multivariate logistic regression to evaluate the risk factors of stent-graft migration.

Patient characteristics	OR	CI	*P* (Wald test)	Likelihood ratio test
Bird beak formation	13.3	3.9–59.3	0.0007	0.0002
dSINE occurrence	11.1	2.1–58.4	0.0045	0.0023
Proximal oversizing ≤5%	20.2	0.9–471.5	0.0614	0.0450
Arch treatment zone (I + II)	3.2	0.4–25.5	0.2738	0.2882
Arch type (III)	1.2	0.3–4.7	0.7859	0.7855
Hyperacute + acute dissection	3.3	0.7–15.3	0.1333	0.1137
Relay NBS stent-graft	2.6	0.1–51.5	0.5410	0.5149
IMH in the proximal sealing zone	1.6	0.4–6.6	0.4822	0.4784
Pronounced TL remodeling (>5 mm)	0.9	0.2–4.3	0.9227	0.9228
Pronounced aortic remodeling (>5 mm)	1.01	0.2–4.7	0.9892	0.9892

OR, odds ratio; CI, confidence interval; dSINE, distal stent-induced new entry; IMH, intramural hematoma; TL, true lumen.

Risk of stent-graft migration

The multivariate logistic regression was performed to evaluate the risk of stent-graft migration, and the results are shown in Table 5. The "whole model test" was statistically significant ($P = 0.001$). The bird beak formation was the main risk factor for stent-graft migration (OR 13.3; CI 2.9–59.3.5; $P = 0.0007$; Table 5) followed by the dSINE occurrence (OR 11.1; CI 2.1–58.4; $P = 0.0045$). Stent-graft type ($P = 0.5410$), treatment zone ($P = 0.2738$), arch type ($P = 0.7859$), the timing (dissection phase) of TEVAR ($P = 0.1333$), true lumen ($P = 0.9227$) and aortic diameter ($P = 0.9892$), remodeling, and the presence of IMH in the proximal sealing zone ($P = 0.4822$) were not significant in the multivariate logistic regression. Interestingly, proximal oversizing ≤5% was not significant in the Wald test ($P = 0.0614$), however, significant in the likelihood ratio test ($P = 0.0450$), and stood out with the highest odds ratio (OR 21.5; CI 0.9–493.8).

Discussion

Theoretically, the anticipated proximal TEVAR landing zone in TBD may consist of a completely healthy or in extremo a totally dissected aortic wall. The latter is not regarded as an adequate and sustainable proximal landing zone even though the primary entry tear may be initially covered and the false lumen thrombosis induced. The dissected proximal landing zone may lead to proximal SINE, stent-graft migration, and type IA endoleak in the short or long-term (18). Therefore,

current ESVS guidelines recommend landing in a healthy portion of the aorta ≥20 mm in length (1). However, the safety of proximal TEVAR landing in the IMH in acute/subacute TBD has rarely been reported (8). Previous reports have shown the efficacy and safety of retrograde type A IMH treatment with proximal landing in the IMH. Those smaller inhomogenous cohorts were successfully treated by TEVAR and had comparable results with open surgery going hand in hand with less postoperative morbidity (19, 20, 21). Other authors reported the occurrence of RTAD after the TEVAR treatment of the type B IMH with a diseased proximal sealing zone (affected by the IMH) (22).

The current study reports the high incidence of IMH in the proximal TEVAR landing zones in TBD, compares the outcomes of patients with and without the IMH at the proximal stent-graft end, and reports comparable results regarding RTAD, bird-beak formation, and stent-graft migration.

Our report goes in line with the previous study by Kuo et al. with considerable rates of IMH in the arch landing zones 0- III (8). The authors showed that 37% of their cohort needed zone 0 or zone I debranching to achieve at least a 10 mm IMH-free proximal TEVAR landing zone (8). Furthermore, they suspected that the occurrence of 3 RTADs may have been associated with the IMH at the proximal stent-graft end, without proving this in the multivariate analysis, due to the low patient and event numbers (8). The colleagues, therefore, recommended further evaluation of these findings in greater cohorts. We included 84 patients, and unlike Kuo et al. we excluded chronic TBD from the analysis. Furthermore, this study reports the results of a cohort with a relatively high proportion of patients treated in the hyperacute phase (27%), who may be at a higher risk of RTAD due to the fragility of the aortic wall as reported previously (4, 8). RTAD did not occur in this cohort, which may imply the safety of the proximal landing in the IMH with a moderate oversizing of approximately 10% as used in this study. Previously, oversizing of 0%–10% was recommended for the treatment of TBD to reduce the risk of RTAD (5). However, the uncertainty of the IMH fate during the follow-up (7), the result of the hematoma absorption, and its unclear effect on the dilatation of the proximal landing zone may suggest that a targeted oversizing of 10%, as applied in our study, may be reasonable in IMH-affected proximal landing zones. This is even more important due to the result of our multivariate regression analysis, which isolated an oversizing of 0%–5% as a risk factor for future stent-graft migration (OR 20.2). Furthermore, in the short term, the extent of the IMH was stable in the patients treated in the subacute phase, thus the delay of the TEVAR to the subacute phase for the purpose of IMH absorption may not be advisable. As shown by Evangelista et al. for type B IMH the absorption of the hematoma may be expected at 6 months (7) after diagnosis.

A significant increase in bird-beaks was observed in our study during the follow-up. Bird-beaks have been reported to increase the risk of type I endoleaks after TEVAR and they may lead to the instability of the stent-graft in the proximal landing zone with migration (23, 24). However, no type IA endoleaks were observed in our study and substantial migration ≥10 mm was found in 26% of the overall cohort, however, without any difference between the groups ($P = 1.0$). Furthermore, the increase of bird-beaks in the IMH and the no-IMH groups during the follow-up was equal (+10 cases). These observations may suggest that the presence of the IMH at the proximal stent-graft end does not affect the stent-graft stability in the proximal sealing zone and that migration and bird-beaks may be somewhat associated with other effects. These observations were confirmed by the multivariate analysis to identify the risk factors for migration ≥10 mm. Proximal landing in the IMH was not relevant nor were other factors including stent-graft type, treatment zone, arch type, treatment phase, and pronounced remodeling. The major risk factors for migration were the bird-beak occurrence during the follow-up ($P = 0.0007$), the occurrence of dSINE ($P = 0.0045$), and the proximal oversizing ≤5% ($P = 0.0614$).

The aortic remodeling of the true lumen was superior in the no-IMH group, which, however, may be explained by the substantially higher rate of subacute dissections with stiffer dissection membranes in the IMH group (25). Regarding the aortic diameter regression after TEVAR, the IMH group showed significantly better remodeling. Our previous works described a better diameter remodeling of subacute/chronic dissections than of those treated in the acute phase, which may be an explanation due to the higher rate of subacute dissections in the IMH group (26).

This study has several limitations. The findings of this retrospective observational study need to be confirmed by studies with a robust prospective design. Although the measurements and the study outcomes were standardized and well-defined our study may be susceptible to bias due to its retrospective and single-center design. Furthermore, the study included a limited patient number and thus, may be underpowered to determine the risk of events with a low incidence as RTAD. Nevertheless, we consider that this study may be helpful for further evaluations e.g., in a meta-analysis, due to its well-defined outcome parameters and reporting standards.

In conclusion, this study implies that the treatment of type B aortic dissections with TEVAR in the early dissection phases may be safe with a low risk of RTAD and considerable aortic remodeling in the thoracic aorta. The presence of the IMH at the proximal stent-graft end may not affect the TEVAR performance in the proximal landing zone in terms of bird-beak and migration. dSINE and bird-beak occurrence, as well as the proximal stent-graft oversizing ≤5% were identified as major risk factors for stent-graft migration.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving humans were approved by University medical center Tübingen (322/2022BO2). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

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ML: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. MM: Data curation, Formal Analysis, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing. JH: Formal Analysis, Investigation, Methodology, Resources, Validation, Visualization, Writing – review & editing. CS: Data curation, Investigation, Project administration, Resources, Supervision, Validation, Writing – review & editing. MA: Conceptualization, Data curation, Formal Analysis, Investigation, Project administration, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing.

Conflict of interest

ML has served as speaker and proctor for Terumo Aortic and Gore Medical.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Thoracic endovascular aortic repair for type B aortic dissection with aberrant right subclavian artery: a single-center retrospective study

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Objective: To evaluate the outcomes of thoracic endovascular aortic repair (TEVAR) for type B aortic dissection (TBAD) with aberrant right subclavian artery (ARSA).
Methods: A retrospective analysis was conducted on patients with TBAD and ARSA who underwent TEVAR between the period of January 2017 and December 2022. Patient demographics, computed tomography angiography (CTA) measurements, surgical procedures, and postoperative outcomes were reviewed.
Results: A total of 9 patients (6 males and 3 females) were included in the study. 4 ARSA were reconstructed, 3 by periscope technique and 1 by *in vitro* fenestration technique. 3 left subclavian arteries (LSA) were reconstructed, 1 by the chimney technique and 2 by the single-branched stent technique. 2 patients underwent reconstruction of both ARSA and LSA. The overall technical success rate was 100%, with no occurrences of stroke, paraplegia, or mortality within 30 days. 1 patient experienced immediate type Ia endoleak, which resolved after 3 months. 1 patient developed weakness in the right upper limb, while 1 patient presented mild subclavian steal syndrome (SSS); both cases showed recovery during follow-up. The average follow-up duration was 35.6 ± 11.1 months, during which no reinterventions, deaths, or strokes were observed.
Conclusion: Our limited experience involving 9 patients demonstrates that early and mid-term outcomes of TEVAR for the treatment of TBAD with ARSA are satisfactory.

KEYWORDS

type B aortic dissection, aberrant right subclavian artery, thoracic aortic endovascular aortic repair, retrospective study, outcome analysis

Introduction

The aberrant right subclavian artery (ARSA) is the most commonly observed variant of the aortic arch and its branches, originating from the aortic arch or descending aorta after the left subclavian artery (LSA). The reported incidence of ARSA ranges from 0.3% to 3% (1). In most cases, ARSA is asymptomatic, with only approximately 5% of patients experiencing symptoms such as dysphagia, dyspnea, cough, and other respiratory difficulties due to compression of the esophagus and trachea (2). In recent years, thoracic endovascular aortic repair (TEVAR) has emerged as the primary treatment for type B aortic dissection (TBAD) due to its minimal invasiveness and rapid recovery (3).

However, managing TBAD with ARSA poses challenges in TEVAR. Currently, there are no established guidelines or consensus on the management of TBAD with ARSA, and most studies available are limited to case reports. The decision to reconstruct the LSA and ARSA should take into account the proximal landing zone (PLZ), patency of the cerebral arterial circle (CAC), and dominance of the vertebral artery. In this retrospective study, we analyzed patients diagnosed with TBAD and ARSA who underwent endovascular repair to provide valuable insights for clinical treatment.

Material and methods

Patients

A retrospective analysis was conducted on patients diagnosed with TBAD and ARSA who underwent TEVAR at authors' institution between from January 2017 to December 2022. The study was approved by the Ethics Committee of Guizhou Provincial People's Hospital and the informed consents were obtained from all patients. The inclusion criteria were as follows: (1) Patients diagnosed with TBAD and ARSA; (2) Patients who underwent TEVAR with or without superior-arch artery revascularization. The exclusion criteria were as follows: (1) Presence of aortic connective tissue diseases, such as Marfan syndrome; (2) Prior history of aortic surgery; (3) Thoracic aortic aneurysm, penetrating aortic ulcers, or intramural hematoma. All patients underwent computed tomographic angiography (CTA) of the entire aorta with a slice thickness of 1 mm to assess the anatomical parameters of the aortic arch. Cerebral and cervical CTA were also performed to evaluate the CAC and identify the dominant vertebral artery. The reconstruction of the LSA and ARSA was determined based on the combination of CAC, dominant vertebral artery (DVA), and PLZ. If the CAC was patent, only the subclavian artery on the side of the DVA was reconstructed. However, in cases where the CAC was obstructed, simultaneous reconstruction of both LSA and ARSA was recommended to mitigate the risk of short-term or delayed cerebrovascular events (as shown in **Table 1**).

The indications for TEVAR included refractory hypertension, persistent chest or back pain, aortic diameter >55 mm and suspected or existing aortic rupture. The acute phase was defined as onset time of 14 days or less, the subacute phase as lasting between 15 and 90 days, and the chronic phase as exceeding 90 days (4). During the acute phase, conservative treatment was implemented by controlling blood pressure and heart rate. TEVAR was conducted during the subsequent subacute phase, except in cases requiring emergency interventions, such as rupture or impending rupture (persistent decrease in blood pressure or hemoglobin, suspected hemorrhagic pleural effusion), malperfusion syndrome, and progression of aortic dissection. The classification of TBAD was based on the location of the primary tear and the extent of involvement in the distal lesion (5).

TABLE 1 Treatment options based on circle of willis and proximal landing zone.

CAC	PLZ > 15 mm			PLZ < 15 mm		
	LVAD	RVAD	E	LVAD	RVAD	E
Fluent	AC	AR	AR	LR + AC	LC + AR	LR + AR
Obstructed	AR	AR	AR	LR + AR	LR + AR	LR + AR

PLZ, proximal landing zone; CAC, cerebral arterial circle; AC, ARSA covered; LC, LSA covered; AR, ARSA reconstruction; LR, LSA reconstruction; LVAD, LVA dominant; RVAD, RVA dominant; E, equal dominant.

TEVAR procedures

All TEVAR procedures were performed under general anesthesia. The aortic stent grafts used in the study were C-Tag (Gore, Delaware, USA), Castor (Microport Medical, Shanghai, China), and Ankura (Lifetech, Shenzhen, China), as presented in **Table 2**. The criteria for selecting the correct stent graft size allowed for an oversize of 5%–10%. The femoral artery was surgically exposed or two Perclose Proglide vascular staplers (Abbott, Chicago, United States) were pre-set. The SELDINGER technique was employed for puncturing. The stent graft was advanced using a super stiff guidewire (Lunderquist, COOK, Bloomington, USA). For the reconstruction of the ARSA or LSA, Fluency (Bard, New Jersey, USA) and Viabahn (Gore, Delaware, USA) stents were utilized. In the periscope technique, the guide wire was pre-set in ARSA, and both the stent graft and periscope stent were released simultaneously. A guide wire was inserted from the 8F sheath of the left brachial artery into the femoral artery, followed by the insertion of Castor's 4F catheter through the guide wire into the left brachial artery. Subsequently, the Castor stent guide wire was inserted into this catheter. The Castor stent graft and wire were then simultaneously moved upward, and the stent was released once it reached the planned position. During the fenestration, the anterior segment of the Castor stent was partially exposed and fenestrated *in vitro*. A short 5F sheath was placed through the right radial artery, and the guide wire from this sheath was passed through the fenestration of the Castor stent via ARSA, into the femoral artery, and retrieved from the sheath. Finally, a Viabahn stent was inserted into ARSA via the femoral artery.

Medical treatment and follow up

Discharged patients were instructed to diligently monitor and regulate their blood pressure. For patients who underwent ARSA or LSA reconstruction, a daily oral dose of 100 mg aspirin was administered. The occurrence of stroke, spinal cord ischemia, endoleak, subclavian steal syndrome (SSS), and reinterventions were considered as early and late morbidity and were included in the follow-up assessments. Follow-up appointments were scheduled for discharged patients at 1, 6, and 12 months after surgery, and annually thereafter. The end point of the follow-up period was June 2023, and data collection was conducted through outpatient medical records, CTA images, and telephone

TABLE 2 Procedures and outcomes.

Patient	Sex/age	Max diameter, mm	Classiffication	PLZ, mm	CAC	DVA	Endovascular procedures	Brand of the stent graft	Outcomes	Follow-up period, months
1	M/60	60	B3,6	10	F	R	LC + AP	Gore C-Tag		48
2	M/46	42	B3,9	16	F	L	AC	Lifetech Ankura		60
3	M/59	33	B3,9	11	F	E	LB + AP	Microport Castor		39
4	F/64	39	B3.5	6	O	L	LB + AF	Microport Castor		15
5	M/48	45	B4,9	25	F	L	AC	Gore C-Tag	weakness of the right upper limb, relieved after 5 months	51
6	M/41	37	B3,5	19	F	L	AC	Gore C-Tag	SSS, relieved after medical treatment	33
7	M/72	30	B3,9	8	F	L	LCH + AC	Gore C-Tag	Type Ia endoleak, disappeared at 3 months	28
8	M/50	44	B3,10	20	F	L	AC	Lifetech Ankura		26
9	F/55	29	B4,5	22	F	R	AP	Gore C-Tag	Lung cancer	20

PLZ, proximal landing zone; CAC, cerebral arterial circle; DVA, dominant vertebral artery; F, fluent; O, obstructed; LCH, LSA chimney; AP, ARSA periscope; LBS, LSA branched stent; AF, ARSA fenestration; AC, ARSA covered; LC, LSA covered; L, Left; R, Right; SSS, subclavian steal syndrome.

calls. The preoperative and postoperative CTA images are shown in Figure 1.

Results

A total of 9 patients, including 6 men and 3 women, were included in this study. The mean age range of patients was 55 ± 9.8 years (range 41–72). None of the patients had prior knowledge of ARSA before admission. Among the patients, 5 were in the acute stage of aortic dissection, 1 was in the subacute stage, and 3 were in the chronic stage. 1 patient experienced TBAD as a result of iatrogenic injury during coronary angiography. Further details regarding the characteristics of the patients can be found in Table 3.

Among the patients, 4 had a PLZ measuring less than 15 mm. Coverage of 1 LSA was conducted, while 2 LSA were reconstructed using single-branched stents, and 1 LSA was reconstructed

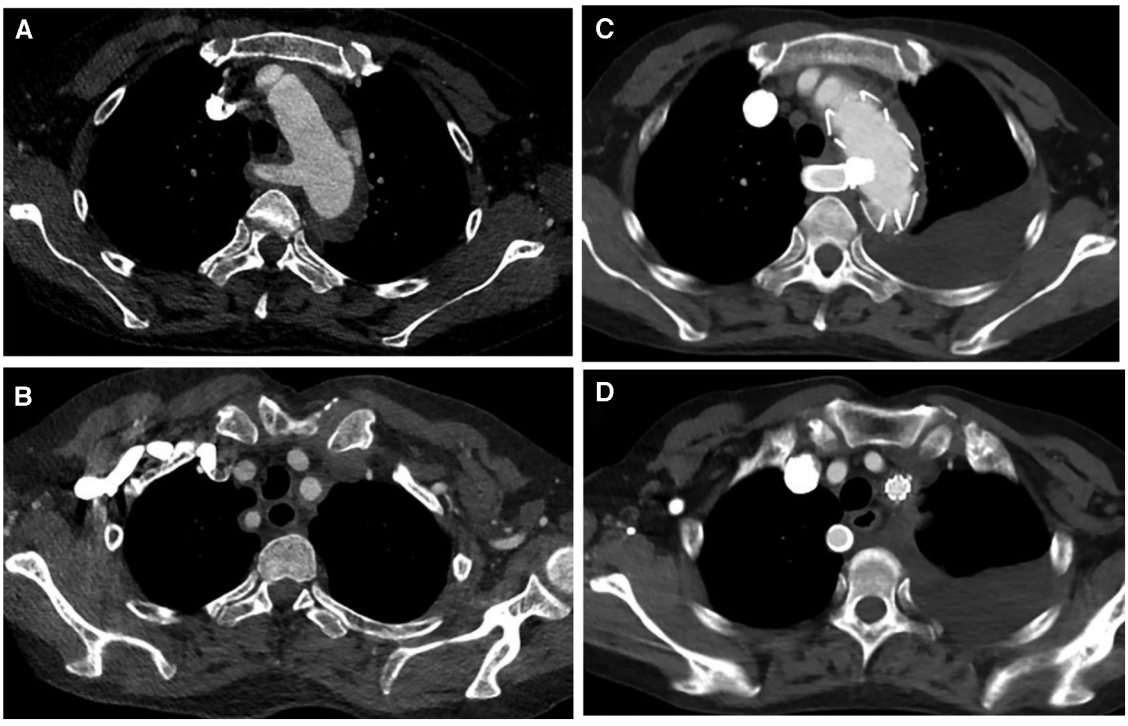

FIGURE 1
(A,B) Preoperative CT angiography of patient 4, who underwent castor stent graft and fenestration; (C,D) postoperative CT angiography, blood flow was fluent in LSA and ARSA.

TABLE 3 General and mophological characteristics of the patients.

Features	*M* or $x \pm s$	Percent or range
Age, years	55.0 ± 9.8	41–72
Sex, Male	6	66.7%
Hypertension	8	88.9%
Coronary artery disease	2	22.2%
Diabetes	1	11.1%
Chronic obstructive pulmonary disease	3	33.3%
Pleural effusion	2	22.2%
CT measurements		
Aortic diameter at the distal edge of LSA, mm	30.6 ± 1.9	28–34
Length from LSA to primary entry tear, mm	14.9 ± 6.9	6–25
Max diameter of descending aorta, mm	39.9 ± 9.5	29–60
Kommerell diverticulum	1	11.1%
Dissection of ARSR ostium	2	22.2%
Diameter of ARSR, mm	10.3 ± 1.4	9–13
Follow-up time	35.6 ± 11.1	15–60

by chimney technique. 5 ARSA were covered. 4 ARSA reconstructions were performed, 3 of which were performed by periscope technique and 1 by fenestration *in vitro* (as shown in **Figure 2**). The technical success rate achieved 100%, and there were no cases of stroke, spinal cord ischemia, death within 30 days following surgery. No patients necessitated ongoing care in the intensive care unit following the surgical procedure. Detailed information on the lesions and surgical procedures performed can be found in **Table 2**.

During follow-up, 1 patient has a slight type Ia endoleak and it disappeared 3 months later. No patients underwent reintervention and no stent occlusion, infection, or migration occured. After ARSA coverage, 1 patient developed mild SSS, confirmed by Doppler ultrasound, and manifested as mild vertigo. Significant alleviation of the vertigo was observed after medical treatment 5 months post-surgery. Another patient experienced weakness in the right upper limb, which was relieved through functional exercise. No stroke or death occurred during follow-up. 1 patient was diagnosed with lung cancer 12 months after surgery.

Discussion

ARSA is a common congenital variation in the aorta. In most cases, patients have no obvious clinical symptoms and do not require treatment (1, 2). TBAD is a clinical acute aortic syndrome with a high mortality rate. Due to its reduced trauma and faster recovery, TEVAR has gradually replaced open surgery as the preferred treatment option for TBAD (6). However, TBAD with ARSA poses additional challenges in TEVAR. Currently, there are no published treatment guidelines specifically addressing this combination. Open and hybrid procedures have been employed for the treatment of TBAD with ARSA. Di Marco et al. (7) and Abuharb et al. (8) reported the use of Frozen Elephant Trunk in patient diagnosed with aortic dissection and ARSA. The prognosis is favorable but the surgical trauma is extensive. Chen et al. (9) and Chien et al. (10) reported cases of TBAD with ARSA which are treated by hybrid technique. In a study conducted Ding et al. (11), the overall technical success rate and prognosis were satisfactory, despite a reported 12.5% incidence of brachial plexus injury among patients. Although hybrid surgery has reduced trauma compared to open surgery, TEVAR still offers significant advantages in terms of intensive care unit utilization, postoperative recovery time, and surgical trauma. With the development of interventional technology, total endovascular treatment is increasingly applicated to the treatment of TBAD with ARSA.

Currently, there remains a scarcity of guidelines or expert consensus regarding the criteria for ARSA reconstruction. Since the ARSA ostium is distal to the LSA, the stent graft will inevitably cover it. Regular TEVAR procedures that involve sacrificing the LSA are associated with a notable rise in neurological complications, including cerebral infarction and spinal cord ischemia (12, 13). In the general population, the left DVA appears more frequently compared to the right DVA. Consequently, sacrificing only the ARSA reduces the risk of neurological complications compared to sacrificing the LSA. If the length of PLZ is less than 15 mm, LSA reconstruction is necessary to achieve sufficient length, and clinicians must decide whether to reconstruct ARSA. Zhou et al. (14) reported on 9 patients who had a covered ARSA, and there were no incidents of severe stroke or spinal cord ischemia after the surgery. Zhang et al. (15) combined the proximal landing zone with the side of the DVA to determine whether both subclavian arteries should be preserved. However, when the CAC is occluded, reconstruction of the DVA alone is insufficient to completely prevent stroke. As individuals age and atherosclerosis advances, it may result in stenosis or occlusion of the CAC. In our study, 2 patients with CAC occlusion, as indicated by CTA, underwent reconstruction of both ARSA and LSA without experiencing any neurological complications. With the advancement of endovascular reconstruction of supra-arch branch vessels, the LSA and ARSA should be reconstructed as much as possible in the future, given the experience and resources available.

To date, there is a lack of published literature that compares various methods of ARSA reconstruction. Parallel stents are commonly used for reconstruction of the LSA or ARSA (16). To our knowledge, published literatures about reconstruction of ARSA with periscope are mainly case reports (17, 18). In our study, 3 ARSA were reconstructed by periscope technique and no endoleak was observed. Fenestration, being a more recent technique compared to parallel stents, has had fewer reported cases in TBAD with ARSA. Gafoor et al. (19) reported a case involving a patient with a thoracic aortic aneurysm and ARSA, who underwent TEVAR with a customized, *in situ* fenestrated stent graft, based on CT image remodeling. Xu et al. (20) conducted a study on the endovascular repair of type B aortic intramural hematoma with ARSA. 8 patients received treatment using handmade fenestration stents, yielding positive outcomes. In our study, we performed *in vitro* fenestration for ARSA reconstruction in 1 patient, and during the follow-up period, no endoleak or neurological events were observed. Single-branched stents can be used for ARSA reconstruction as well. Zhang et al. (21) reported the application of an embedded modular single-

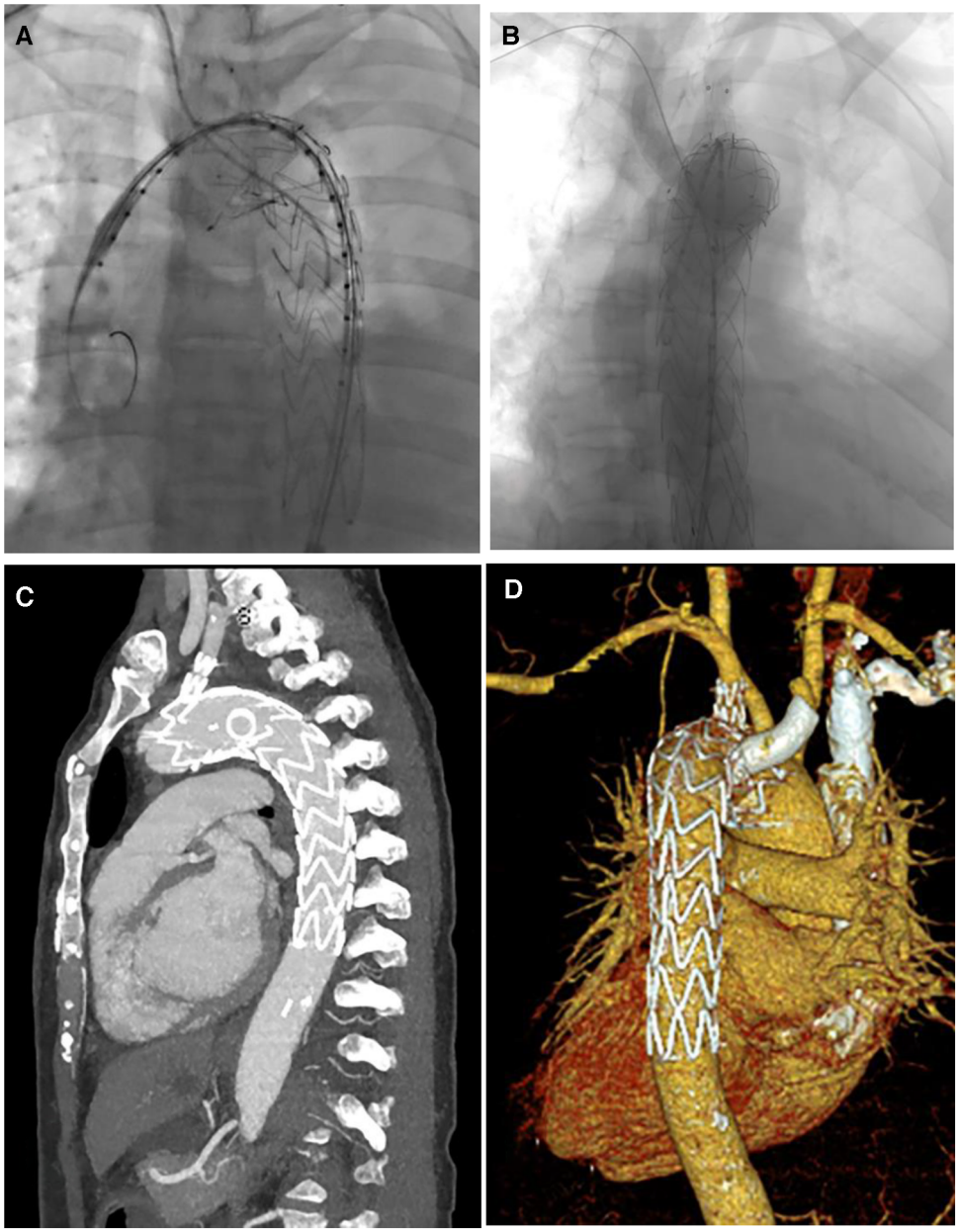

FIGURE 2
(A,B) Digital subtraction angiography in TEVAR of patient 4; (C,D) CT image remodeling 1 month after TEVAR.

branched stent for endovascular repair of TBAD with ARSA; however, this device has not seen widespread adoption. In recent years, a single-branched stent graft named "Castor", specifically designed for TBAD involving LSA, has been widely used and has achieved satisfactory results (22, 23). Pang et al. (24) reconstructed 5 ARSAs during TEVAR using Castor stents and the single branch was directly used to reconstruct the ARSA. However, this treatment option is limited by the anatomical condition of the lesion. We suggest that he periscope technique may be a suitable method for ARSA reconstruction due to three reasons. Firstly, unlike chimney technique that may result in type Ia endoleak, the periscope technique has minimal impact on the proximal part of the stent graft. Although the periscope technique may promote the occurrence of type Ib endoleak, its incidence and prognosis are better than those of type Ia endoleak. Secondly, The periscope technique's procedures are easy to perform, and the devices are also easy to obtain. Finally, compared to fenestration technique, the periscope technique has the advantages of maintaining stent stability. Furthermore, *in vitro* fenestration technique requires caution due to the risk of inaccurate fenestration positioning. With the increasing availability of fenestration methods, we consider that mechanical in-situ fenestration can be a promising reconstruction method. The single-branched stent such as Castor presents as a reliable option for reconstruction when the LSA is the DVA, effectively reducing the incidence of type I endoleaks. In addition, in cases

requiring reconstruction of the ARSA, the risk of severe endoleaks from the use of two parallel stents can be minimized by employing a single-branched stent.

The present study has several limitations. Firstly, the study is retrospective and based on a small sample size of only 9 cases, resulting in a low level of evidence. Hence, further prospective studies with larger samples are warranted. Secondly, due to the limited sample size, it was not feasible to compare the prognosis among different ARSA and LSA reconstruction modalities. Lastly, the study is lacking long-term follow-up results.

Conclusion

Our limited experience involving only 9 patients suggest that TEVAR is a feasible treatment option for TBAD with ARSA, demonstrating satisfactory early and mid-term outcomes. However, further researches with larger sample size are required.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Ethics Committee of Guizhou Provincial People's Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

YZ: Writing – original draft. PY: Writing – review & editing. QH: Data curation, Writing – original draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Expression of secreted frizzled-related proteins in acute aortic dissection patients and the effects on prognosis

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Background: Secreted frizzled-related proteins (SFRPs) were reported to be involved in cardiovascular diseases. This study aimed to observe plasma SFRP levels in acute aortic dissection (AD) patients and the effects of SFRP expression on AD prognosis.
Methods: Plasma levels of SFRP1, SFRP2, SFRP3, SFRP4, and SFRP5 were measured in AD patients and non-AD (NAD) patients. The end-point events information of AD patients, including all-cause death and various clinical complications due to aortic dissection, was collected during a 36-month follow-up.
Results: The SFRP1, SFRP2, SFRP3, and SFRP4 levels were increased in AD patients compared with those in NAD patients, while the SFRP5 concentrations were decreased. No differences in any of the SFRP levels were observed between the type A group and the type B group. The AD patients with end-point events exhibited higher SFRP1, SFRP2, SFRP3, and SFRP4 concentrations but lower SFRP5 levels than the patients without end-point events. In addition, the AD patients were divided into a high group and a low group based on the median SFRP levels, and Kaplan-Meier analysis revealed that the AD patients with high SFRP1, SFRP2, SFRP4, or SFRP5 levels had a better prognosis than those with low levels. However, the AD patients with high SFRP3 levels exhibited the opposite trends. The binary logistic regression analysis found that SFRP1, SFRP2, SFRP4, and SFRP5 were all negatively correlated with the occurrence of end-point events, while SFRP3 was positively correlated with its occurrence.
Conclusions: SFRP levels are all changed in acute AD, which may affect the prognosis of AD patients. SFRPs may be a target to improve the prognosis of AD.

KEYWORDS

acute aortic dissection, secreted frizzled-related proteins, follow-up, endpoint events, prognosis

Introduction

Aortic dissection (AD) is a complex clinical disease characterized by different degrees of aortic intimal tears, accompanied by the formation of a true lumen, a false lumen, and intermural hematoma. At present, aortic replacement and thoracic endovascular aortic repair (TEVAR) are the main treatments for AD (1, 2). However, both surgical

methods have certain limitations, postoperative complications such as acute renal failure, cardiac tamponade, recurrent AD and so on, which seriously affects the patient's prognosis and the overall prognosis is still poor (2, 3). Therefore, finding suitable methods to reduce the occurrence of complications is crucial for improving the prognosis of AD.

Secreted frizzled-related proteins (SFRPs) are an important class of adipokines. At present, a total of 5 members have been identified, and they are named SFRP1 to SFRP5. Both can competitively bind to SFRP receptors in the Wnt pathway and inhibit the function and activity of the Wnt pathway (4). Therefore, SFRPs are considered important residual inhibitors of the Wnt pathway. SFRPS can participate in a variety of biological activities by inhibiting the Wnt pathway, and these pathways include tissue and organ development, adipocyte differentiation, lipid metabolism, inflammatory response and oxidative stress (4–7).

Numerous studies have confirmed that all SFRP members are involved in the cardiovascular disease process (7). SFRP1 has been reported to promote angiogenesis and reduce myocardial infarction size and cardiac rupture in animal studies (8, 9). SFRP2 was found to induce endothelial tube formation, reduce myocardial infarction area and improve cardiac dysfunction (10, 11). Clinical studies have found that although SFRP3 can increase the survival rate of patients with chronic heart failure caused by ischemic cardiomyopathy; an elevated SFRP3 level means that the prognosis of patients with acute coronary syndrome is poor (12, 13). Animal studies suggest that SFRP4 inhibits the progression of atherosclerosis and alleviates ischemia-induced cardiomyocyte apoptosis and heart failure in ischemic cardiomyopathy (14, 15). SFRP5 expression is decreased in coronary heart disease patients, and a high SFRP5 level indicates a good prognosis (16). Nevertheless, the role of SFRPs in AD is unknown. The aims of this study were to examine SFRP expression in acute AD and to observe the effect of SFRP expression on prognosis.

Materials and methods

Study population, inclusion criteria and exclusion criteria

Consecutive patients with chest pain ($n = 352$) who were hospitalized in Beijing Anzhen Hospital from December 2019 to January 2020 were included in this study. Among them, patients ($n = 135$) who had a history of diseases that may affect the follow-up results were excluded from this study, similar to in our previous article (17), and these disease included coronary artery disease (CAD, $n = 35$), dilated cardiomyopathy (DCM, $n = 19$), valvular heart disease (VHD, $n = 9$), chronic heart failure (CHF, $n = 21$), cancers ($n = 11$), peripheral arterial disease (PAD, $n = 17$), chronic obstructive pulmonary disease (COPD, $n = 15$), and Marfan syndrome ($n = 8$). The remaining patients ($n = 217$) received aortic computed tomography angiography (CTA) and were divided into an AD group ($n = 157$) and a non-AD (NAD, $n = 60$) group according to their results. The AD group was further divided into a type A group and a type B group based on whether the tear site accumulated in the aortic arch. Most AD patients underwent aortic replacement ($n = 75$) or thoracic endovascular aortic repair (TEVAR, $n = 68$), and a small number of patients were not able to tolerate surgical treatment. A few patients (14) were not available or could not tolerate surgery. This study was approved by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University (approve No. 201912104C). All participants were informed of the basic procedure of the study and signed informed consent forms.

Information collection

Venous blood from each subject was collected in vacutainer tubes after the subjects were admitted, the samples were sent to the relevant testing center for further testing, and information on random glucose (Glu), total cholesterol (TC), high-density lipoprotein cholesterol (LDL-C), white blood cells (WBCs), creatinine (TC), D-dimer, cTnI, NT-proBNP, and C-reactive protein (CRP) was recorded. The admission records of the subjects were also required to be completed after admission, and information on sex, age, body mass index (BMI), hypertension, type 2 diabetes mellitus (T2DM), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were obtained. The aortic lesions and surgical information were obtained from the aortic CTA results and surgical records and are listed in **Table 1**.

Blood sample collection and SFRP detection

Blood samples from each subject were collected in vacutainer tubes containing sodium heparin. The plasma samples obtained were centrifuged at 4,000 × g for 20 min and then stored at −80°C until the beginning of the experiments. The plasma levels of SFRP1 (Yuanmu Biological Technology, China), SFRP2 (USCN Life Science Inc., USA), SFRP3 (Aviscera Bioscience, USA), SFRP4 (MyBioSource, San Diego, USA), and SFRP5 (USCN Life Science Inc., USA) were detected using enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions.

TABLE 1 Perioperative characteristics in aortic dissection patients.

Characteristic	Stanford A	Stanford B
Surgery		
Replacement of aorta (*n*, %)	71 (83.5)	4 (5.6)
TEVAR (*n*, %)	6 (7.1)	62 (86.1)
Do not underwent surgery (*n*, %)	8 (9.4)	6 (8.3)
Operation time (hours)		
Replacement of aorta	4.2 (2.9, 5.3)	4.1 (2.7, 5.2)
TEVAR	2.6 ± 1.4	2.3 ± 1.1
Time from attack to operation	7.2 (5.9, 11.3)	6.9 (5.5, 10.7)
Aortic tear information		
Tear length (mm)	139 ± 64	155 ± 77
Aorta coverage distance (mm)	150 ± 70	171 ± 89
Hospitalization time (days)	13.8 ± 4.7	7.9 ± 2.1

Follow-up and end-point events

All patients were asked to provide at least 2 commonly used telephone numbers at the time of admission to complete the admission chart and to ensure the smooth progress of follow-up. At the time of discharge, the local patients were required to be followed up monthly in the outpatient clinic, and the nonlocal patients were required to be followed up by telephone once a month. For patients who were not reviewed in time, we made inquiries and reminders by pre-leaving telephone numbers. The follow-up began after the patient was admitted, and the maximum duration did not exceed 36 months. The follow-up period for these patients was 30 ± 7.2 months. Information on end-point events, including all-cause death and various clinical complications due to aortic dissection, was collected during the follow-up. The occurrence and time of end-point events are shown in Table 2.

Statistical analyses

Data in this study were analyzed using GraphPad Prism 7 software. Continuous variables with normal distribution are expressed as the mean ± SD and were compared by Student's *t*-test, Continuous variables with abnormal distributions were expressed as the median (lower quartile to upper quartile) and compared by the nonparametric test. Categorical variables are presented as percentages and were analyzed by a chi-squared test. The Kaplan–Meier method and log-rank test were used to compute the outcome of AD patients. Binary logistic regression analysis was performed after the factors were adjusted to determine whether SFRPs were associated with the occurrence of end-point events. $p < 0.05$ was considered significant.

TABLE 2 Summary of endpoint events in aortic dissection patients.

Months	Numbers	Endpoint events
1	9	Death
	2	Acute left heart failure
	1	Acute renal failure
	1	Cardiac tamponade
	1	Acute abdominal pain
	1	Paraplegia
2	3	Death
	1	Acute left heart failure
	1	Acute renal failure
3	1	Death
4	1	Death
7	1	Ischemia and dysfunction of lower limbs
11	1	Recurrent aortic dissection
12	1	Death
15	1	Acute ischemic stroke
17	1	Recurrent aortic dissection
18	1	Ischemia and dysfunction of lower limbs
20	1	Death
22	1	Recurrent aortic dissection
26	1	Acute renal failure

Results

Comparison of clinical characteristics between NAD patients and AD patients

Compared with the NAD group, a higher incidence rate of smoking and hypertension and elevated values of SBP, WBC, D-dimer, NT-proBNP, and CRP were observed in the AD group. No differences in other characteristics, including sex, BMI, T2DM, DBP, Glu, TC, and LDL-C, were observed between these 2 groups. In addition, higher age and CREA, as well as lower hypertension incidence rate, WBC, D-dimer, cTnI, NT-proBNP and CRP were found in the type B group compared with the type A group. The characteristics for each group are listed in Table 3.

Expression levels of SFRPs in acute AD patients

The ELISA results showed that the acute AD patients exhibited higher plasma SFRP1, SFRP2, SFRP3, and SFRP4 levels and lower SFRP5 levels than the levels in the NAD group (Figures 1A–E). No differences in any SFRP were observed between the type A and type B groups (Figures 1A–E).

Plasma SFRP concentrations in AD patients with or without endpoint events

Compared with the AD patients without end-point events, the AD patients with end-point events exhibited higher SFRP1, SFRP2, SFRP3, and SFRP4 levels and lower SFRP5 concentrations (Figures 2A–E). The SFRP1, SFRP2, SFRP3, and SFRP4 levels in the AD patients with or without end-point events were increased compared with the NAD group, while the SFRP5 levels were reduced (Figures 2A–E).

Effects of SFRPs on prognosis in acute AD patients

To evaluate prognosis, the AD patients were divided into a high group and a low group based on the median SFRP levels, and the results showed that the group with high levels of SFRP1, SFRP2, SFRP4, or SFRP5 exhibited a better prognosis than the low group (Figures 3A,B,D,E). The high SFRP3 group had a worse prognosis (Figure 3C).

Effects of SFRPs on the occurrence of endpoint events in acute AD patients

To analyze the effect of SFRPs on the occurrence of endpoint events, binary logistic regression analysis was performed. The results showed that smoking and SFRP3 increased the occurrence of endpoint events, while SFRP1, SFRP2, SFRP4, and SFRP5 decreased the occurrence (Figure 4).

TABLE 3 Clinical characteristics of NAD patients and AD patients.

Characteristics	NAD	AD		
		Total	Type A	Type B
Male (*n*, %)	46 (76.7)	128 (81.5)	71 (83.5)	57 (79.2)
Age (years)	48.3 ± 8.0	52.5 ± 11.7*	46.8 ± 9.2	59.2 ± 10.4†
Smoking (*n*, %)	18 (30.0)	52 (61.2)*	29 (34.1)	23 (31.9)
BMI (kg/m^2)	24.4 ± 2.4	24.4 ± 2.5	24.2 ± 2.6	24.7 ± 2.2
Hypertension (*n*, %)	10 (17.0)	77 (77.3)*	77 (90.6)	46 (63.9)†
T2DM (*n*, %)	4 (6.7)	11 (7.0)	6 (7.1)	5 (6.9)
SBP (mmHg)	127 ± 15	141 ± 19*	141 ± 16	140 ± 22
DBP (mmHg)	82 ± 10	85 ± 11	84 ± 11	87 ± 11
Glu (mmol/L)	5.6 (5.0, 6.0)	6.0 (4.9, 6.4)	6.1 (5.0, 6.6)	5.9 (4.9, 6.3)
TC (mmol/L)	4.5 (4.0, 4.8)	4.5 (4.0, 4.9)	4.5 (4.2, 4.8)	4.5 (4.0, 5.0)
LDL-C (mmol/L)	2.4 (2.0, 2.7)	2.3 (1.9, 3.0)	2.1 (1.6, 2.8)	2.5 (2.2, 3.0)
WBC (×10^9/L)	5.6 (4.06 6.3)	7.2 (5.6, 9.4)*	7.5 (5.8, 11.9)	6.7 (5.4, 8.1)†
CREA (μmol/L)	57 (49, 63)	68 (57, 87)*	70 (59, 87)	67 (57, 88)†
D-dimer (ng/ml)	265 (217, 446)	1,652 (696, 3,127)*	1,972 (772, 4,892)	1,390 (624, 2,349)†
cTnI (ng/ml)	–	0.12 (0, 2.58)	2.35 (0.62, 6.73)	0.01 (0, 0.04)†
NT-pro BNP (pg/ml)	56 ± 25	244 ± 229*	316 ± 251	159 ± 164
CRP (mg/L)	2.0 (1.2, 2.7)	6.3 (3.6, 13.5)*	7.3 (3.7, 18.7)	5.2 (3.6, 9.0)†

*$p < 0.05$ vs. the NAD group.
†$p < 0.05$ vs. the type A AD group.

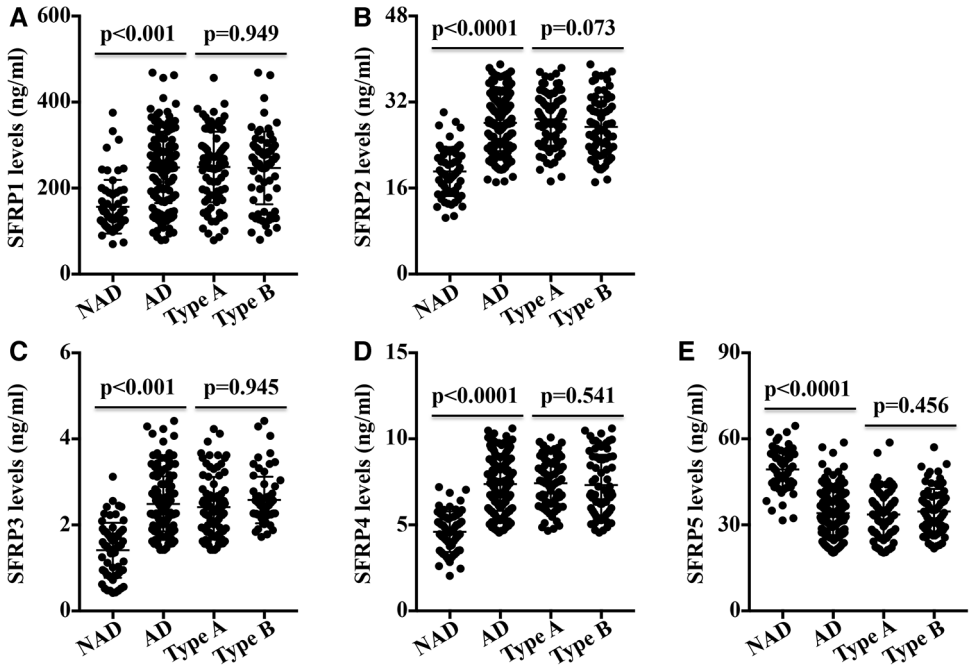

FIGURE 1
Circulating SFRP levels in NAD and AD patients were measured. (A) SFRP1, (B) SFRP2, (C) SFRP3, (D) SFRP4, and (E). The levels of SFRP5 in the NAD group, AD group, type A group, and type B group was measured.

Discussion

In this study, the expression levels of all SFRP members in acute AD patients were examined, and their effects on the prognosis of AD were analyzed. The results showed that the expression of SFRP1, SFRP2 and SFRP4 was increased in AD patients. The results showed that high levels were beneficial to the prognosis, despite decreased concentrations of SFRP5, and high levels of SFRP5 indicated a good prognosis. Although SFRP3 levels were increased, high levels indicated a poor prognosis. This study suggests that as members of the same adipokine family, the expression of SFRPs in AD and their effect on prognosis are not the same.

SFRP1 was the first SFRP family member discovered and is expressed in most tissues and organs. Previous studies found that

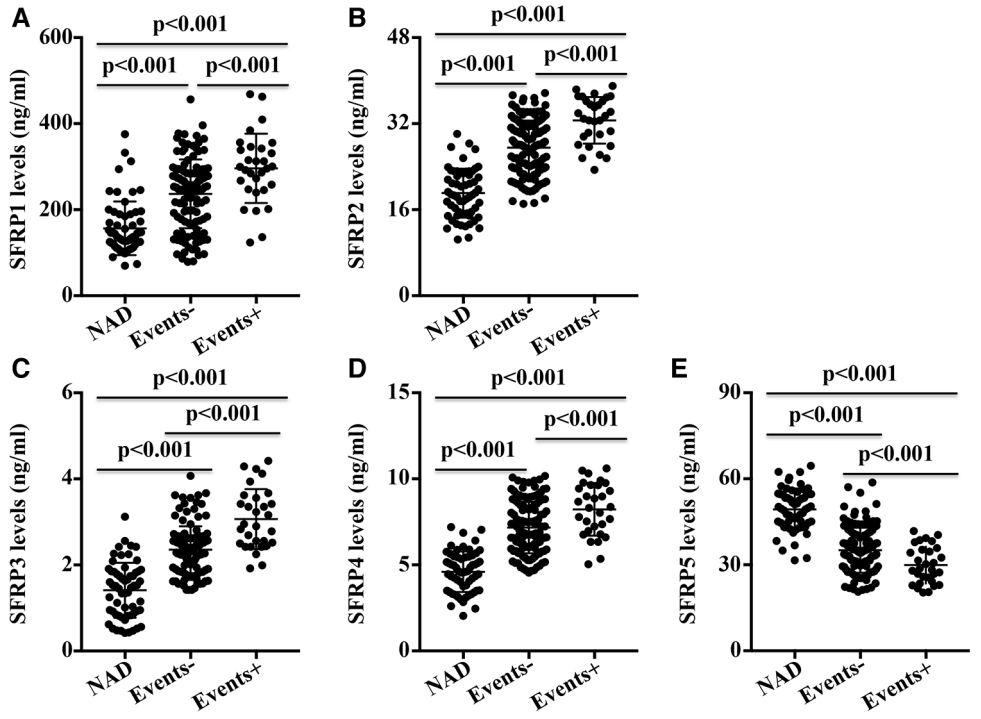

FIGURE 2
Plasma concentrations of SFRPs in AD patients with (events+) or without (events−) end-point events were detected. (**A**) SFRP1, (**B**) SFRP2, (**C**) SFRP3, (**D**) SFRP4, and (**E**). SFRP5 in the NAD group, events− group, and events+ group was analyzed.

SFRP1 is involved in downstream signal regulation by regulating the Wnt pathway, and Wnt3 is the main downstream signaling pathway (7). The regulatory effect of SFRP1 on downstream Wnt3 signaling depends on the microenvironment of the body. SFRP1 inhibits Wnt3a activity during the development of the dorsal ganglion neural tube while enhancing Wnt3a activity in L cells (17, 18). Previous studies have found that SFRP1 can significantly reduce cardiac fibrosis and delay the deterioration of cardiac function after acute myocardial infarction (8, 9). In addition, SFRP1 was found to significantly promote tubular formation and angiogenesis *in vitro* (8, 19). These beneficial effects make it possible to treat nonsurgical revascularization patients with angiotherapy, especially in patients with severe coronary artery stenosis who are not candidates for percutaneous coronary intervention (PCI). Our study found that SFRP1 was increased in AD patients, high SFRP1 indicated a better prognosis, and SFRP1 was negatively correlated with the occurrence of the end-point time. These studies suggest that SFRP1 plays a protective role in cardiovascular diseases associated with a variety of different microenvironments, which seems inconsistent with the previous conclusions. One possible reason is that Wnt3 does not mediate all the biological effects of SFRP1, and other pathways, such as P38 and Rac-1, may also play important roles.

SFRP2 is widely expressed and detected in the aorta, although it is not expressed in the heart. SFRP2 exerts its biological effects mainly through Wnt3: not only through wnt3a but also through Wnt3p (20). Similar to SFRP1, the regulatory role of SFRP2 on downstream Wnt3 signals also depends on the microenvironment. SFRP2 plays the same role as SFRP1 in the development of dorsal ganglion neural tubes and L cells (17, 18). In addition, SFRP2 enhances the nuclear translocation of the human embryonic kidney by enhancing the Wnt3p pathway (20). SFRP2 also has a strong protective effect on hypoxia-induced myocardial cell injury in acute myocardial infarction by activating the Wn3a pathway and increasing the expression of MMP2 and MMP9, and its mechanism is highly similar to that of SFRP1 (7, 10, 11). The difference is that SFRP1 mainly regulates angiogenesis by regulating both endothelial cells and vascular smooth muscle cells, while SFRP2 mainly acts on endothelial cells and promotes endothelial tube branching (10). In our current study, we found that the expression trends of SFRP2 were consistent with those of SFRP1 in acute AD patients, and the patients with high levels of SFRP2 showed fewer end-point events and a better prognosis. These results indicate that the role of SFRP2 in patients with AD is consistent with that of SFRP1, and they may have a special, undetermined connection in AD.

SFRP3 is also widely expressed, and the highest expression is in the spleen, suggesting that it may be related to the immune/inflammatory response (21). There are few studies on SFRP3 in cardiovascular diseases. Ueland et al. found that SFRP3 was elevated in patients with acute coronary syndrome, and high SFRP3 levels indicate poor prognosis (13). Askevold et al. reported a very interesting phenomenon in which CHF patients were divided into three groups according to the SFRP3 level, and

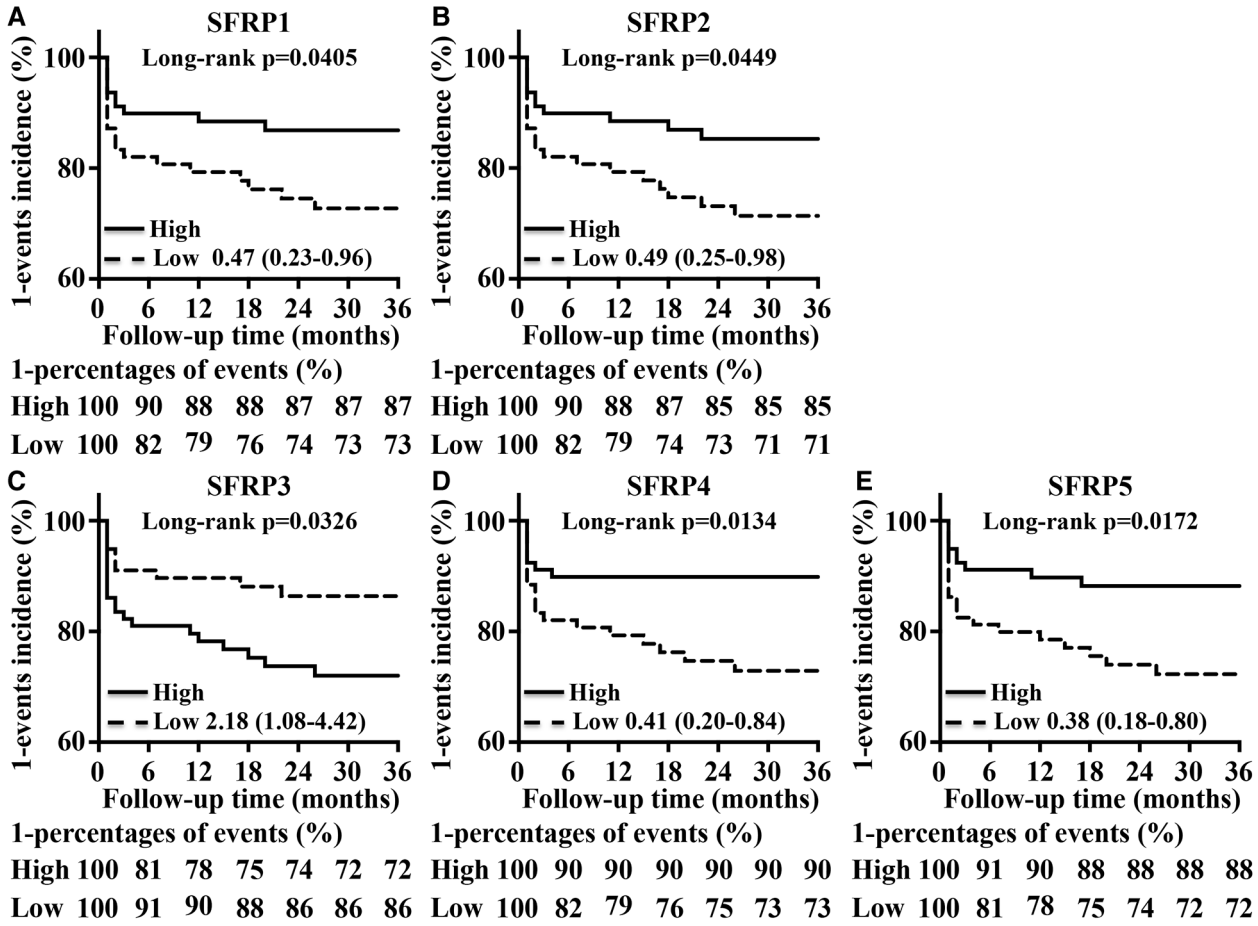

FIGURE 3
Effects of SFRPs on prognosis in AD patients. The incidence of end-point events in the high group and low group of (A) SFRP1, (B) SFRP2, (C) SFRP3, (D) SFRP4, and (E). SFRP5 in AD patients was analyzed by the Kaplan–Meier method and log-rank test.

the middle SFRP3 group showed a better prognosis than the low SFRP3 and high SFRP3 groups, suggesting that CHF patients who maintain SFRP3 at appropriate levels will benefit more than those who have high or low levels of SFRP3 (12). Our study found that acute AD patients had elevated levels of SFRP3, while high levels of SFRP3 suggested a poor prognosis and more end-point points. Unfortunately, the sample size was not large enough; therefore, we could not divide the patients into more groups to determine the optimal SFRP3 level of AD patients.

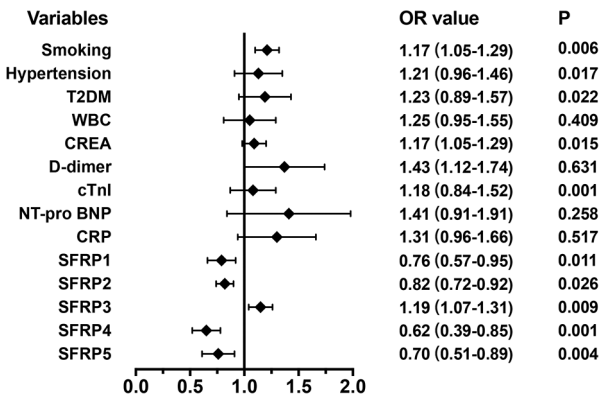

FIGURE 4
Effects of SFRPs on the occurrence of end-point events were analyzed using binary logistic regression analysis.

SFRP4 is moderately expressed in the cardiovascular system and plays an important role in atherosclerosis (AS)-related CAD (7). Our previous study found that SFRP4 played an antiatherogenic role via downstream Wnt1 signaling, while other researchers reported that it was involved in AS-related CAD through the Akt pathway (7, 15). Our previous studies confirmed that SFRP4 expression was increased in CAD and originated mainly from epicardial adipose tissue (EAT), which is a special type of perivascular adipose tissue that can secrete anti-inflammatory factors, inhibit the differentiation of proinflammatory immune cells, and maintain the normal function of blood vessels (8, 22, 23). Studies have found that the transplantation of healthy EAT inhibited the AS process, while the transplantation of diseased EAT played the opposite role (24–26). These seemingly contradictory results are confusing. With further study, researchers found that immune cell infiltration in the EAT of CAD patients was significantly increased and masked the protective effect of healthy EAT (10, 20, 21). In

this study, we found that SFRP4 was elevated in AD patients and had prognostic benefit. Combined with the previous studies above, we hypothesized that SFRP4 may be derived from the immune cells within the EAT and participate in the AD process by regulating the inflammatory response.

SFRP5 can also be expressed in the circulatory system. Similar to SFRP4, SFRP5 is secreted by the EAT and visceral fat, and its main downstream signal is Wnt5a (7, 27, 28). Studies have confirmed that SFRP5 is involved in the process of CAD, and both the Wnt5a pathway and JNK pathway are downstream signals. Studies have found that the expression of SFRP5 is decreased in CAD, and its levels are negatively correlated with the severity of CAD and multiple risk factors (28, 29). Our study found that SFRP5 was the only member with decreased expression in AD patients, and high SFRP5 levels suggested a better prognosis.

In conclusion, we examined the effects of SFRPs on the prognosis of AD patients in this study and found that high levels of SFRP1 and SFRP2 may reduce the occurrence of end-point events and have a beneficial effect on prognosis, while high SFRP3 levels may increase adverse events and lead to a poor prognosis. However, a large number of studies have demonstrated that the type of AD, whether undergo surgery, and the time from onset to surgery are the important factors affecting the prognosis of AD. In this study, due to the small sample size, AD patients were not divided into different groups base on these factors and observe the effects of SFRPs on prognosis, respectively. Therefore, whether the effects of SFRPs on prognosis of AD patients were affected by the above factors, although these factors do not differ in the patients with or without end-time points. This is a deficiency of our research that requires further confirmation from more research.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by This study was approved by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University (approve No. 201912104C). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

SN and HM designed the study; HM, XL and YL collected the blood samples and performed the follow-up; HT and ZS detected the SFRPs levels and analyzed the data; HM, YL and ZS wrote the manuscript; SN and HT revised the manuscript for intellectual content; SN is the guarantors of this work and are accountable for the integrity of the data and the accuracy of the data analysis. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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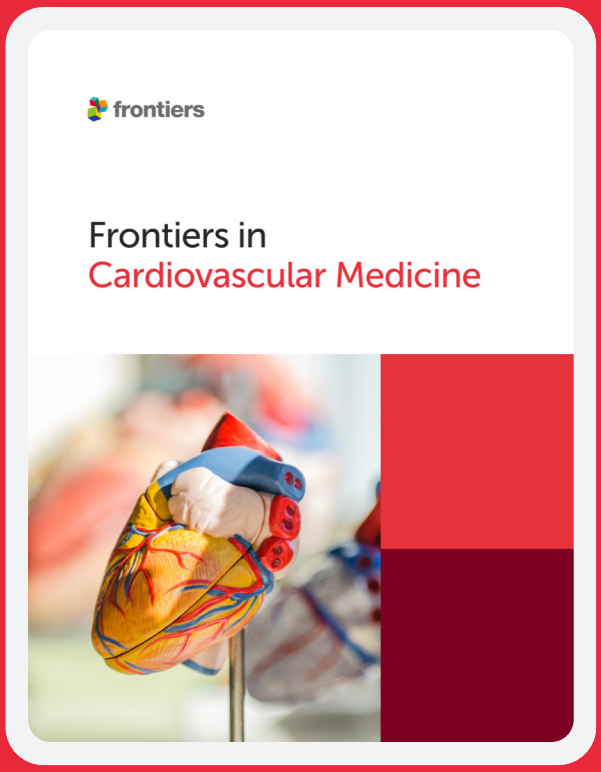

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