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Hybrid technique and total arch replacement combined with frozen elephant trunk in acute aortic dissection involving the aortic arch: a multi-center propensity-matched cohort study

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Abstract

Background The aim of this study was to investigate whether the hybrid technique yields superior outcomes in comparison with the total arch replacement combined with frozen elephant trunk (TAR + FET) for acute aortic dissection (AAD) involving the aortic arch.

Methods This retrospective cohort study using propensity-score matching included patients with AAD involving the aortic arch admitted to Nanjing First Hospital and Shanghai General Hospital from January 2015 to June 2020. The in-hospital and mid-term outcomes were compared between patients who received hybrid treatment ($n = 136$) and those who received TAR + FET ($n = 415$). Study end points included in-hospital mortality and morbidity, and mid-term rates of death from all causes, stroke, and aortic re-intervention.

Results A total of 121 pairs were formed after matching. In-hospital mortality did not differ between hybrid versus TAR + FET groups (5.8% vs. 7.9%, $P = .860$). Up to 6 years, patients treated with TAR + FET were associated with reduced rate of aortic re-intervention (HR 0.21, 95% CI 0.05–0.97; $P = .023$). There was no difference in death from all causes and stroke.

Conclusions Hybrid technique and TAR + FET showed comparable mid-term survival. Hybrid technique showed higher rate of aortic re-intervention and should therefore be applied with great caution in patients with AAD involving the aortic arch.

Keywords Acute aortic dissection, Aortic arch, Hybrid, Total arch replacement, Frozen elephant trunk

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Introduction

Despite advances in aortic surgery, acute aortic dissection (AAD) with aortic arch involvement remains a fatal and complicated condition that presents a great challenge for cardiac surgeons [1, 2]. The total arch replacement combined with frozen elephant trunk technique (TAR + FET) is life-saving for most patients and has been proposed as the standard procedure in treating AAD in China [3]. Efficient removal of arch lesions using TAR + FET can lower organ hypoperfusion and improve distal aortic remodeling. Nevertheless, the extensive aortic approach, long surgery duration, and deep hypothermic circulatory arrest (DHCA) have all contributed to remarkable mortality and morbidity, particularly in senior individuals suffering from multiple diseases. To ensure better early outcomes, more limited aortic procedures have been proposed to justify in selected patients [1, 4, 5].

Thoracic endovascular aortic repair (TEVAR) provides a surgical technique that is minimally invasive and has largely replaced open surgical procedures as the preferred therapy for acute complicated type B aortic dissection [6]. However, in AAD settings with aortic arch involvement, total TEVAR may not be accessible given the complexity of the aortic arch branches in anatomy and hemodynamics. Therefore, a strategy combining open surgery with endovascular techniques (performed under fluoroscopic guidance) was introduced to treat AAD patients with aortic arch involvement, namely, hybrid technique. Compared with TAR + FET, the hybrid requires less surgical time with no need of DHCA, making it more suitable for patients at high risk or patients who may not get through the extensive open surgical procedures. A few observational studies have consistently reported the potential advantages of the hybrid in reducing the rates of in-hospital morbidity, shortening the length of hospital and intensive care unit (ICU) stays [7–9]. However, whether the mid-term outcomes follow a similar pattern between the hybrid and TAR + FET remains a topic of debate. Herein, we created a two-arm retrospective, observational cohort study to assess the in-hospital and mid-term outcomes of patients who had received hybrid or TAR + FET.

Methods

Study design and participants

This is a retrospective cohort study. We enrolled consecutive adult patients (aged > 18 years) with AAD involving the aortic arch who were admitted to two centers from January 2015 to June 2020. The exclusion criteria are: (i) AAD involving the sinotubular junction (To minimize selection bias, we excluded patients with sinotubular junction involvement, as such cases may require combined valve surgery or coronary artery bypass grafting, making conventional open surgery a strong indication); (ii) combined with other major cardiac surgery (coronary artery bypass grafting, valve surgery, or congenital heart surgery); (iii) aortic root aneurysm or ascending aorta aneurysm; (iv) Marfan, Loyes-Dietz syndrome or other connective or hereditary conditions; (v) aortic ulcer; (vi) aortic hematoma; (vii) preoperative acute nerve damage (stroke and paraplegia) or renal failure requiring dialysis; (viii) preoperative death after admission. Finally, the study population were patients with AAD involving the aortic arch, with or without ascending or descending aorta involvement. Patients who received hybrid treatment comprised the hybrid group; patients who received TAR + FET treatment comprised the TAR + FET group(Figure 1). Before the procedure, the aortic anatomy was accurately assessed by review of aortic contrast-enhanced CTA (computed tomography angiography), including the extent, location of entry tear and aortic size. Through a thorough evaluation of patients' preoperative conditions and discussions within the Multidisciplinary Decision-making Team for Salvage or Emergency Surgery (conducted among the department director, the heads of the surgical treatment group and the endovascular treatment group), we tended to prefer hybrid surgery for older patients with more comorbidities, as they were less likely to tolerate prolonged and highly invasive procedures. For other patients, we opted for the TAR + FET procedure. This study was approved by the Ethics Committee of Nanjing First Hospital, Nanjing Medical University (Approval Number: KY20220425-05), and the Ethics Committee of Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine (Approval Number: 2018KY241) and complied with the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective design of this study. All data were obtained through the hospitals' electronic medical records and follow-up systems. This study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) standards for reporting [10].

Surgical procedures

TAR + FET group

According to patient's condition, we established arterial cannulation of cardio-pulmonary bypass (CPB) at specific sites (femoral artery, right axillary artery or the innominate artery) following median sternotomy, and we selected the right axillary artery for unilateral antegrade cerebral perfusion (ACP). As the nasopharyngeal temperature lowered to 18 °C to 22 °C, we conducted deep hypothermic circulatory arrest (DHCA) and performed ACP at 5-10mL/kg/min after cross-clamping brachiocephalic arteries and perfusion of the brain. Afterwards, we transected the aortic arch proximal to the left subclavian artery. With the FET stented graft

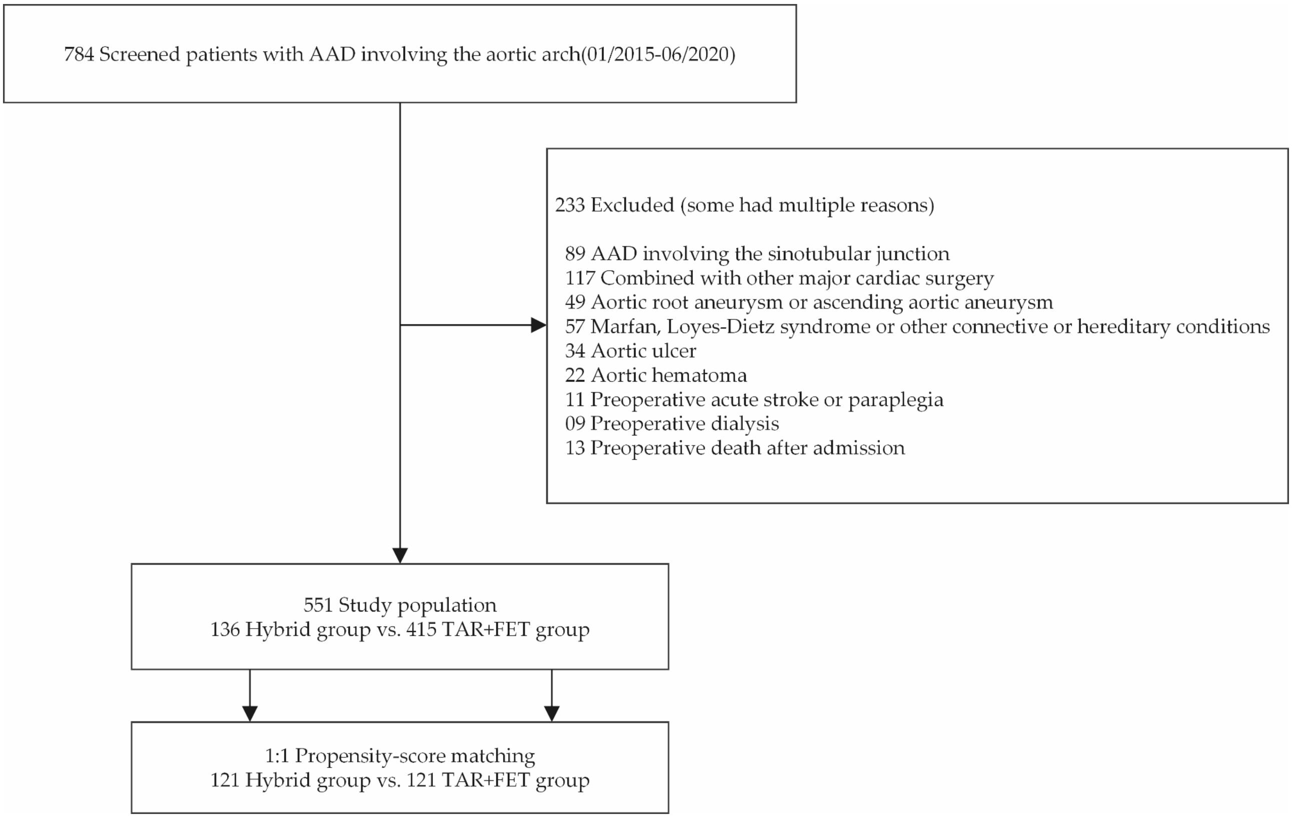

Fig. 1 Flow chart showing patients included in the analysis. AAD, acute aortic dissection; TAR + FET, total arch replacement combined with frozen elephant trunk

(MicroPort Medical Co Ltd, Shanghai, China) inserted into the descending aorta's true lumen, the stent graft was firmly attached with a four-branched prosthetic graft (Terumo, Vascutek Limited, Renfrewshire, Scotland, UK). After the anastomosis with the distal aortic arch, blood perfusion of the lower body was restarted through the branch for perfusion on the vascular graft. Then we sutured the left common carotid artery, proximal aortic stump, innominate artery and left subclavian artery in succession. Gradually, the body temperature returned to normal and we stopped CPB after ACP was discontinued.

Hybrid group (without DHCA)

In the hybrid operating room, the hybrid surgery was carried out with an angiography C-arm system. All patients underwent general anesthesia, tracheal intubation, and median sternotomy.

Firstly, we performed the open part of the hybrid surgery. With cannulation through the right femoral artery and right axillary artery, CPB was instituted. The nasopharyngeal temperature was maintained at 28 °C. Subsequently, we located one cross-clamp at the base of innominate artery for ACP, and a second cross-clamp between left common carotid artery and innominate artery. We resected the arch proximal to left common carotid artery to create a sufficient proximal anchoring zone. The ascending aorta was reconstructed with the four-branched prosthetic graft (Terumo, Vascutek Limited, Renfrewshire, Scotland, UK). Then we sutured the aortic arch with the distal end of the four-branched graft. The arch was unclamped to restore coronary perfusion. Afterwards, the branches were anastomosed with left common carotid artery, innominate artery and left subclavian artery in sequence. Then we restored the body temperature and terminated CPB.

Next, the endovascular part was performed. We applied the incision of the original cannulation on the femoral artery as the entry for endovascular treatment. CT contrast angiography was reviewed to determine the size and length of the stent graft. The diameter of the stent graft was oversized by 5–10%. Then we delivered the guide wire retrogradely into the ascending aorta and transported the stent graft along the wire, followed by release of the stent graft (MicroPort Medical Co Ltd, Shanghai, China). The proximal end of the stent, which partially crossed 2 cm of the artificial blood vessel's distal anastomosis, was securely anchored to the prosthetic graft. Subsequent contrast examination utilizing DSA revealed the closure of the break of dissection, with no remained contrast medium detected in the false lumen. If the first stent was inadequate for coverage of the lesions or surgeons discovered a secondary tear in the distal aorta, the second stent graft was employed.

Study end point

The primary outcome of this study was death from all causes. Secondary outcomes were stroke and aortic re-intervention. Stroke is defined as hemorrhagic or ischemic cerebrovascular event based on CT or MRI scanning; aortic re-intervention included any subsequent endovascular repair or open aortic surgery on aortic stump or supra-aortic branches. Tertiary outcomes were in-hospital mortality and morbidity. Additionally, we reported the event of endoleaks of Hybrid group, using the guideline of the SVS reporting standards [11]. All participants underwent aortic contrast-enhanced computed tomography angiography (CTA), chest X-ray and echocardiography prior to discharge. CT angiography scans of the aorta were re-examined during the patients' follow-up appointments. We primarily focus on the following aspects; stent migration, whether the proximal end of the interlayer was sealed with no leakage of the contrast agent, whether the false lumen near the stent was completely thrombosed and enlargement of the true lumen and reduction of the false lumen compared with the results of the pre-operative CT angiography scans. The aortic CTA and physical examination post-operation were firstly carried out one month after the operation, and every 6 to 12 months afterwards, depending on the patient's condition.

Follow-up data were collected through outpatient visits or direct telephone communication with the patients. The follow-up information mainly included the patient's survival status, death time, cause of death, adverse cardiovascular events and neurological function status. Patients were censored on 1st January 2021, and those who lost to follow-up were included in the study using the last data recorded in the systems.

Statistical analysis

Continuous variables are summarized as means ± standard deviations or medians (IQR) according to their distribution; categorical variables are expressed as numbers (percentage). Statistical differences between hybrid group and TAR + FET group were carried out using t-test, Mann-Whitney U test, chi-square test, or Fisher's exact probability method as appropriate.

Propensity-score matching

We assessed the effects of hybrid and TAR + FET on in-hospital and mid-term outcomes (death from all causes, stroke, and aortic re-intervention) after adjusting the potential confounding factors by using propensity-score matching (PSM) method. First, we generated the propensity score (PS) using a multivariable regression analysis model, with treatment group as the dependent variable (hybrid group vs. TAR + FET group) and all baseline characteristics as imputed variables. Patients who received hybrid were matched to patients who received TAR + FET in a 1:1 ratio using the nearest-neighbor matching method according to a caliper of 0.2 without replacement. This procedure was performed with the MatchIt package of R, version 4.0.1. Balance diagnostics among each pair of matched treatment cohorts were assessed by the standardized mean differences (SMD) and visually with the scatter diagram of the propensity score distributions. The SMD focuses on actual differences and presents more practical value than P-value in matching studies. A SMD ≤ 0.2 is deemed acceptable balance; a SMD ≤ 0.1 is deemed ideal balance [12].

Sensitivity analysis

As a sensitivity analysis, we created an inverse probability treatment weighting (IPTW) cohort, calculating stabilized inverse propensity score as weight in regression models for each observation. As an unbiased approach, IPTW uses the PS to obtain an estimate of average treatment effects [13]. Next, the treatment effect size in terms of in-hospital and long-term outcomes between hybrid and TAR + FET groups were evaluated in the IPTW cohorts, using the stabilized inverse PS as weight.

Between-group comparisons

Between-group comparisons of in-hospital outcomes were made using the log-binomial model (categorical variables) or linear mixed model (continuous variables). Relative risks (RR) with 95% confidence intervals (CIs) were calculated. Time to event is defined as the time from receiving treatment to the last follow-up or event occurrence. Comparisons of mid-term outcomes were done in the Cox or Fine and Gray models (by treating death as competing risk) [14]. Cumulative incidence curves were plotted to depict the 6-year rates of death from all causes, stroke, and aortic re-intervention. Cox proportional hazards models were generated to compare death from all causes, and Fine and Gray models were created to compare stroke and aortic reintervention. The Fine and Gray model was performed using the cmprsk package of R, version 2.2–10. Hazard ratios (HRs), subdistribution HRs (SHRs), and their 95% CIs were determined. Both PSM and IPTW cohorts were adjusted for center, by including center as random effect in log-binomial and linear mixed models, and as stratification factors in the Cox and Fine and Gray models. Because most of the baseline variables were obtained through manual review of the electronic health records, our dataset has extremely few missing data ranging 0-1.8%. We handled these missing values using multiple imputation methods. Data were analyzed using the R software (version 4.0.3, http://www.r-project.org/). Two-sided P values less than 0.05 were considered statistically significant.

Results

Demographics and clinical characteristics of the Study Population

From January 2015 to June 2020, a total of 551 patients were eligible for analysis, including 136 treated with hybrid and 415 treated with TAR + FET. The overall mean (SD) age was 55.0 ± 11.9 years; 432 (78.4%) of them were men. Prior to matching, most variables were already well balanced, except that patients treated with TAR + FET were younger, had a lower proportion of men and smokers, and fewer patients were with DM and COPD; patients treated with TAR had a higher index of LVEF and a higher proportion of CAD (all SMDs > 0.2). PSM successfully produced 121 matched pairs with SMDs ≤ 0.2 for all baseline variables (Table 1).

Intraoperative results

For intraoperative outcomes, patients treated with TAR were more likely to have received ascending aortic replacement procedures (14.0% vs. 33.9%, *P* < .001), and had longer surgical duration, CPB time, and ACC time (all *P* < .05) (Table 2).

In our cases of hybrid surgery, mean endovascular diameter was 33.2 ± 2.6 mm and mean coverage length was 191.6 ± 8.9 mm.

In-hospital outcomes

The in-hospital outcomes of hybrid and TAR + FET groups are presented in Table 3. In the PSM cohort, in-hospital death did not differ between hybrid and TAR + FET groups (5.8% vs. 7.4%, *P* = .86). Patients treated with TAR showed higher rates of delirium (2.5% vs. 13.2%, *P* = .005), pneumonia (13.2% vs. 25.6%, *P* = .016), RBC transfusion (36.4% vs. 93.4%, *P* < .001), and longer duration of mechanical ventilation (MV), ICU stay and hospital stay (all *P* < .001). The statistical differences of delirium (3.7% vs. 13.0%, *P* = .006), RBC transfusion (37.5% vs. 94.0%, *P* < .001) and longer duration of MV, ICU stay and hospital stay (all *P* < .001) were also observed in the IPTW cohort. Moreover, patients treated with TAR + FET in the IPTW cohort had higher

Table 1 Baseline characteristics according to hybrid or TAR + FET group before and after matching

Characteristics	Before matching			After matching		
	Hybrid	TAR + FET		Hybrid	TAR + FET	
	N = 136	*N* = 415	SMD	*N* = 121	*N* = 121	SMD
Age, years	59.7 ± 12.9	53.4 ± 11.1	0.52	58.5 ± 12.8	58.0 ± 10.8	0.04
Men	119 (87.5)	313 (75.4)	0.32	104 (86.0)	102 (84.3)	0.05
BMI, kg/m2	25.7 ± 3.5	26.1 ± 4.0	0.11	25.7 ± 3.6	25.9 ± 3.5	0.07
Smoker	82 (60.3)	186 (44.8)	0.31	70 (57.9)	66 (54.5)	0.07
Hypertension	121 (89.0)	354 (85.3)	0.11	107 (88.4)	109 (90.1)	0.05
DM	20 (14.7)	18 (4.3)	0.36	9 (7.4)	12 (9.9)	0.09
COPD	13 (9.6)	11 (2.7)	0.29	10 (8.3)	6 (5.0)	0.13
CVA	17 (12.5)	28 (6.7)	0.19	12 (9.9)	11 (9.1)	0.03
CAD	16 (11.8)	19 (4.6)	0.27	11 (9.1)	11 (9.1)	0
Previous MI	4 (2.9)	8 (1.9)	0.07	3 (2.5)	3 (2.5)	0
AF	9 (6.6)	14 (3.4)	0.15	3 (2.5)	6 (5.0)	0.12
LVEF	60.4 ± 3.3	61.5 ± 3.3	0.33	60.7 ± 3.3	60.7 ± 2.9	0.01
EuroSCORE II, %	9.4 ± 7.1	9.4 ± 6.0	0.01	8.6 ± 6.0	8.9 ± 4.6	0.06
Prior surgery	12 (8.8)	22 (5.3)	0.14	10 (8.3)	7 (5.8)	0.10
Malperfusion						
Periphery	24 (17.6)	64 (15.4)	0.06	22 (18.2)	16 (13.2)	0.13
Cerebral	8 (5.9)	25 (6.0)	0.01	7 (5.8)	10 (8.3)	0.10
Visceral	16 (11.8)	39 (9.4)	0.08	12 (9.9)	9 (7.4)	0.09
Cardiac	9 (6.6)	34 (8.2)	0.11	3 (2.5)	5 (4.1)	0.09
Syncope	7 (5.1)	23 (5.5)	0.06	7 (5.8)	9 (7.4)	0.08
Renal insufficiency	22 (16.2)	49 (11.8)	0.13	18 (14.9)	18 (14.9)	0
Hepatic inadequacy	9 (6.6)	26 (6.3)	0.02	8 (6.6)	9 (7.4)	0.03
Shock	3 (2.2)	17 (4.1)	0.11	3 (2.5)	4 (3.3)	0.05
Aortic size, mm	56.3 ± 12.6	57.2 ± 12.0	0.23	56.7 ± 12.3	57.0 ± 11.9	0.10

Data are presented as means ± standard deviation, median (IQR), or numbers (%). TAR + FET, total arch replacement combined with frozen elephant trunk; SMD, standardized mean difference; BMI, body mass index; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; CAD, coronary artery disease; MI, myocardial infarction; LVEF, left ventricular ejection fraction

Table 2 Intraoperative results according to hybrid or TAR + FET group before and after matching

Variables	Before matching			After matching		
	Hybrid	TAR + FET	P value	Hybrid	TAR + FET	P value
	***N* = 136**	***N* = 415**		***N* = 121**	***N* = 121**	
Ascending aortic replacement	19 (13.9)	147 (35.4)	< 0.001	17 (14.0)	41 (33.9)	< 0.001
Surgery duration, min	220.0 (165.0-265.0)	435.0 (375.0-500.0)	< 0.001	215.0 (165.0, 265.0)	438.0 (378.0, 500.0)	< 0.001
Surgery duration > 400 min	8 (5.9)	268 (64.6)	< 0.001	7 (5.8)	79 (65.3)	< 0.001
CPB time, min	155.0 (142.0-169.0)	167.0 (146.0-192.0)	0.010	158.0 (142.0, 169.0)	165.0 (145.0, 193.0)	0.037
CPB time > 200 min	5 (3.7)	61 (14.7)	< 0.001	5 (4.1)	19 (15.7)	< 0.001
ACC time, min	60.0 (55.0–69.0)	89.0 (73.5–107.0)	< 0.001	55.0 (55.0, 66.8)	85.0 (73.0, 104.0)	< 0.001
DHCA time, min	0	20.0 (18.0, 23.0)	NA	0	20.0 (18.0, 24.0)	NA

Data are presented as means ± standard deviation, median (IQR), or numbers (%). TAR + FET, total arch replacement combined with frozen elephant trunk; CPB, cardiopulmonary bypass; ACC, aortic cross-clamping; DHCA, deep hypothermic circulatory arrest; NA, not applicable

Table 3 In-hospital outcomes according to hybrid or TAR + FET group in the PSM and IPTW cohorts

Outcomes	Hybrid	TAR + FET	RR (95% CI)	*P* value
PSM Cohort	*N* = 121	*N* = 121		
Death	7 (5.8)	9 (7.4)	1.08 (0.48–2.78) †	0.860
Delirium	3 (2.5)	16 (13.2)	5.99 (1.93–26.28) †	0.005
Stroke	3 (2.5)	5 (4.1)	1.69 (0.39–7.26) †	0.477
Paraplegia	3 (2.5)	3 (2.5)	1	1
Dialysis	6 (5.0)	10 (8.3)	1.73 (0.62–5.22) †	0.306
Pneumonia	16 (13.2)	31 (25.6)	2.26 (1.17–4.48) †	0.016
Gastrointestinal hemorrhage	4 (3.3)	4 (3.3)	1	1
Mediastinal infection	3 (2.5)	4 (3.3)	1.34 (0.29–6.95) †	0.702
Liver dysfunction	12 (9.9)	15 (12.4)	1.28 (0.57–2.93) †	0.541
Heart failure	0 (0.0)	2 (1.7)	NA	NA
Re-operation for bleeding	5 (4.1)	6 (5.0)	1.21 (0.35–4.30) †	0.758
RBC transfusion	44 (36.4)	113 (93.4)	24.71 (11.62–59.42) †	< 0.001
MV, hr	12.0 (8.0, 23.0)	46.0 (27.0, 84.0)	1.68 (1.48–1.85) ‡	< 0.001
ICU stay, hr	24.0 (22.0, 48.0)	101 (61.0, 172)	1.58 (1.44–1.73) ‡	< 0.001
LOS, days	12.0 (10.0, 16.0)	20.5 (16.0, 25.0)	1.19 (1.14–1.26) ‡	< 0.001
IPTW Cohort	*N* = 136	*N* = 415		
Death	7 (5.1)	23 (5.5)	1.14 (0.93–3.54) †	0.190
Delirium	5 (3.7)	54 (13.0)	2.14 (1.28–3.91) †	0.006
Stroke	4 (2.9)	22 (5.3)	1.84 (0.63–5.45) †	0.267
Paraplegia	3 (2.2)	12 (2.9)	1.44 (0.60–4.63) †	0.465
Dialysis	8 (5.9)	38 (9.2)	1.41 (0.87–2.45) †	0.185
Pneumonia	23 (16.9)	104 (25.1)	1.22 (0.89–1.68) †	0.215
Gastrointestinal hemorrhage	5 (3.7)	16 (3.9)	1.48 (0.80–3.12) †	0.25
Mediastinal infection	3 (2.2)	30 (7.2)	4.65 (2.04–14.03) †	0.001
Liver dysfunction	14 (10.3)	39 (9.4)	0.92 (0.60–1.46) †	0.702
Heart failure	2 (1.5)	6 (1.4)	0.64 (0.28–1.81) †	0.338
Re-operation for bleeding	6 (4.4)	28 (6.7)	2.10 (1.15–4.31) †	0.026
RBC transfusion	51 (37.5)	390 (94.0)	31.77 (23.52–43.14) †	< 0.001
MV, hr	12.0 (8.0, 24.0)	44.0 (25.0, 80.0)	1.59 (1.46–1.70) ‡	< 0.001
ICU stay, hr	24.0 (22.0, 48.0)	100 (65.0, 168)	1.55 (1.45–1.66) ‡	< 0.001
LOS, days	12.0 (10.0, 16.0)	21.0 (16.0, 27.0)	1.18 (1.13–1.24) ‡	< 0.001

Data are presented as means ± standard deviation, median (IQR), or numbers (%). † Calculated using the linear mix model (on log-transformed data); ‡ Calculated using the log-binomial model. Results were adjusted for center (by including center as random effect). In the IPTW cohort, results were weighted by inverse probability of treatment using propensity score

TAR + FET, total arch replacement combined with frozen elephant trunk; RR, relative risk; CI, confidence intervals; PSM, propensity-score matching; RBC, red blood cell; MV, mechanical ventilation; ICU, intensive care unit; LOS, length of stay; IPTW, inverse probability of treatment weighting rates of mediastinal infection ($P = .001$) and re-operation ($P = .026$).

Mid-term survival analysis

In the matching cohort, there was no statistically significant difference in death from all causes between hybrid (20.2%) and TAR + FET (20.5%) groups up to 6-year follow-up (HR 1.09, 95% CI 0.48–1.74; $P = .78$) (Fig. 2A). A similar difference was found in the IPTW cohort (HR 0.59, 95% CI 0.32–1.12; $P = .11$) (Table 4) as well as in the unmatched patient cohort (HR 0.63, 95% CI 0.39–1.04; $P = .080$) (Figure S1A).

The median (IQR) follow-up time was 3.1 (1.6–4.8) years in the hybrid cohort and 2.9 (1.3–4.5) years in the TAR + FET cohort. Forty-five patients were lost to follow-up (3.9%), and no significant difference was found between two groups (7.1% vs. 5.7%, $P = .45$).

Calculated using a Cox or Fine and Gray model. Results were adjusted for center (by including center as stratification factors in the models). In the IPTW cohort, results were weighted by inverse probability of treatment using propensity score.

TAR + FET, total arch replacement combined with frozen elephant trunk; HR, hazard ratio; CI, confidence interval; PSM, propensity-score matching; IPTW, inverse probability treatment weighting.

Secondary outcomes

Competing risk analysis was performed in the Fine and Gray models to compare stroke and aortic reintervention after adjusting death as a competing risk. The incidence of stroke did not differ between hybrid and TAR + FET groups during the 6-year follow-up (HR 0.72, 95% CI 0.29–1.81; $P = .49$) (Table 4; Fig. 2B), corresponding to an unmatched-HR of 0.86 (95% CI 0.46–1.60; $P = .63$) (Figure S1B). However, patients treated with hybrid were associated with a higher rate of aortic re-intervention (HR 0.21, 95% CI 0.05–0.97; $P = .029$) (Table 4; Fig. 2C), corresponding to an unmatched-HR of 0.26 (95% CI 0.11–0.58; $P = .001$) (Figure S1C). Similar differences were found in the IPTW cohort, with an HR associated with TAR + FET group of 0.81 (95% CI 0.38–1.76; $P = .59$) for stroke and an HR of 0.12 (95% CI 0.05–0.29; $P < .001$) for aortic re-intervention (Table 4). The reasons for aortic re-interventions were summarized in Table S1.

Major adverse aortic events and CTA scanning

Major adverse aortic events included endoleak, distal aortic dilation, and aortic re-intervention. Computed tomography angiography (CTA) scans of patients with major aortic adverse events during follow-up were shown in Figure S3. In the entire hybrid cohort, 6 patients developed endoleaks during 6-year follow-up, corresponding to a cumulative incidence of 4.4% (Figure S2), whereas in the TAR + FET group, 28 patients encountered endoleaks over the same follow-up period, accounting for 6.7% of the cohort.

Discussion

The primary objective of this study was to compare the in-hospital and mid-term outcomes of conventional open surgery versus hybrid approach in patients with acute aortic dissection involving the aortic arch. Previous research explored postoperative outcomes after Total Arch Replacement with Frozen Elephant Trunk (TAR + FET) and hybrid procedure, but these have predominantly been limited to single-center studies. Our study enhanced this body of knowledge by employing a propensity-matched analysis that incorporates multicenter evidence.

In this investigation, we demonstrated that there was no statistically significant difference in in-hospital

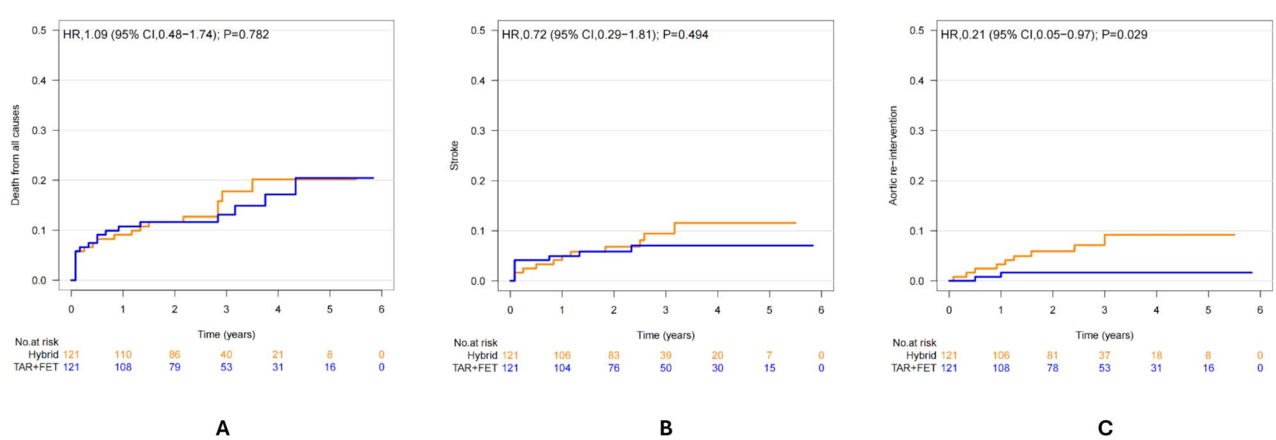

Fig. 2 Cumulative incidence curves for the rates of death from all causes **(A)**. HR, hazard ratio; CI, confidence interval; TAR + FET, total arch replacement combined with frozen elephant trunk. Cumulative incidence curves for the rates of stroke **(B)** and aortic re-intervention **(C)**. HR, hazard ratio; CI, confidence interval; TAR + FET, total arch replacement combined with frozen elephant trunk

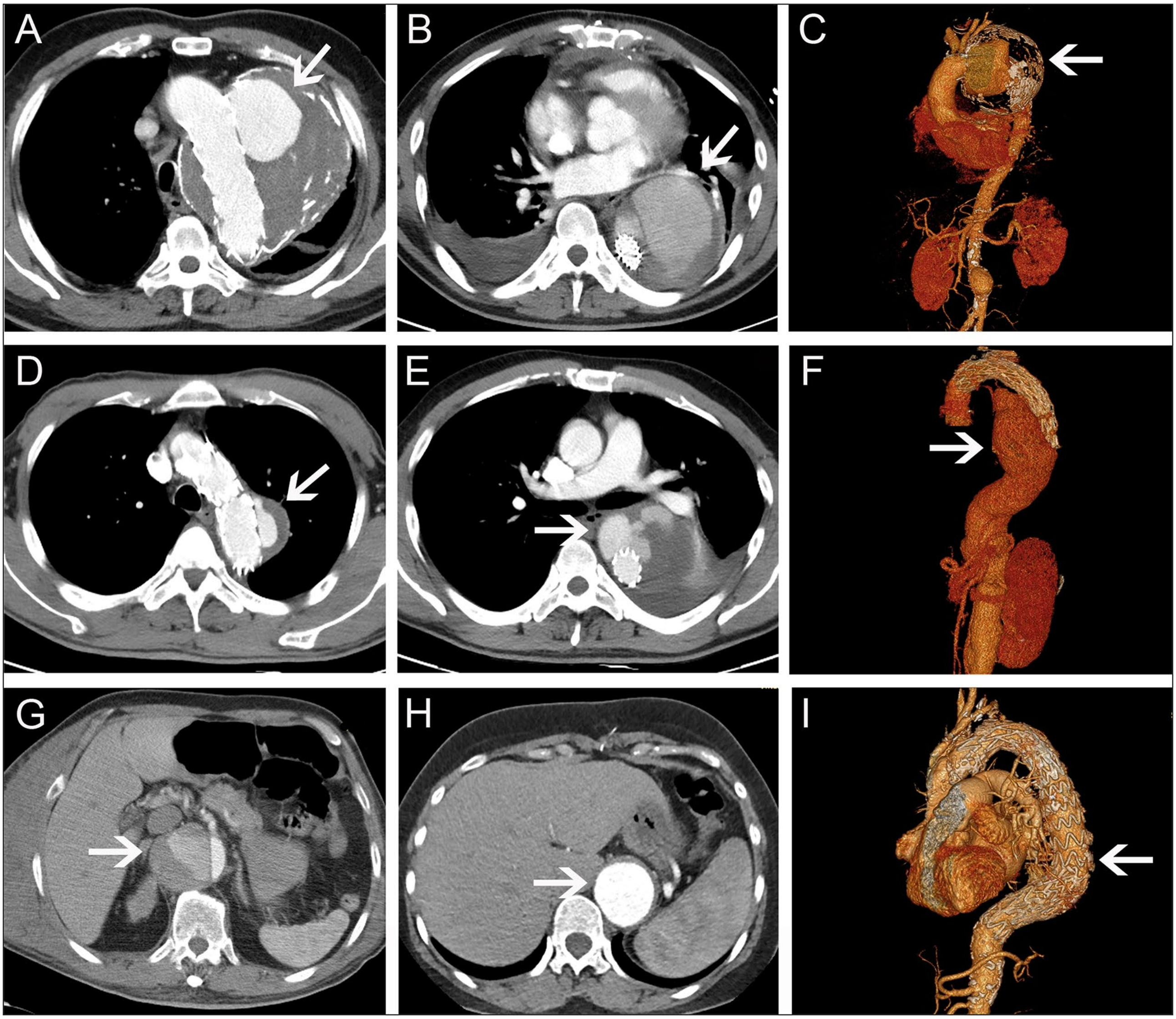

Fig. 3 Computed tomography angiography (CTA) scans of patients with major aortic adverse events during follow-up. The figures illustrate CTA scans of patients with endoleak (**A**-**F**), distal aortic dilation (**G**-**H**), or aortic re-intervention (**I**) after hybrid treatment (white arrows)

Table 4 Mid-term follow-up of hybrid or TAR + FET group in the PSM and IPTW cohorts

Outcomes	Hybrid	TAR + FET	HR (95% CI)	*P* value
PSM Cohort	*N* = 121	*N* = 121		
Death from all causes	20.2 (10.4–28.7)	20.5 (9.7–29.9)	1.09 (0.48–1.74)	0.782
Stroke	11.5 (5.8–19.5)	7.1 (3.3–12.9)	0.72 (0.29–1.81)	0.494
Aortic re-intervention	9.2 (4.2–16.6)	1.7 (0.3–5.4)	0.21 (0.05–0.97)	0.029
IPTW Cohort	*N* = 136	*N* = 415		
Death from all causes	21.5 (12.7–29.3)	20.4 (7.9–31.1)	0.59 (0.32–1.12)	0.108
Stroke	12.5 (5.4–19.1)	11.1 (6.8–15.2)	0.81 (0.38–1.76)	0.590
Aortic re-intervention	11.6 (4.7–17.9)	4.8 (0.1–8.5)	0.12 (0.05–0.29)	< 0.001

all-cause mortality between the hybrid group and the TAR + FET group in either the PSM cohort or the IPTW cohort, which warrants further discussion.

Our observations indicated that hybrid surgery was associated with less pulmonary infection, blood transfusion, mediastinal infection and re-operation for bleeding. These findings may result from the shorter surgery duration, reduced Cardiopulmonary Bypass (CPB) time and the less invasive nature of the hybrid procedure. This approach potentially decreased the risks associated with more aggressive surgical interventions, consequently leading to reduced mechanical ventilation (MV), length of stay (LOS), and Intensive Care Unit (ICU) stay. The diminished incidence of complications could contribute to a lower risk for in-hospital mortality, resonating with the findings of Jakob et al., who reported superior early outcomes with the hybrid technique [15].

One of the major differences between hybrid and TAR + FET procedure is the presence of Deep Hypothermic Circulatory Arrest (DHCA), which was speculated to associate with an elevated risk of coagulopathy, heightened inflammatory response, end-organ dysfunction and in-hospital neurological complications in the hybrid group [16]. Prior research have also identified the use of DHCA as a predictor of mortality following arch repair in patients with aortic arch pathology [17, 18].

While hybrid surgery without DHCA tended to reduce mortality and neurological complications [19], our observation revealed no statistical difference between the TAR + FET group and hybrid group. A recent investigation in aortic arch surgery found that the risk of permanent neurological dysfunction and mortality did not escalate until the DHCA duration exceed 38 min [20]. Consequently, the mean circulatory arrest time of 20.0 (18.0, 23.0) minutes in the TAR + FET group, which we suggest was adequately safe within acceptable limits, may explain our findings.

Prior studies with PSM reported similar results in in-hospital and mid-term mortality outcomes [21, 22]. In our study, PSM was used to ensure better comparability by reducing selection bias and confounding variables, however, its use was also liable to cause loss of sample size. Among the study participants, 136 in the hybrid group and 415 in the Total Arch Replacement (TAR) group, we identified 121 pairs suitable for propensity score matching. With a smaller sample size, the increased variability may lead to a less significant observed difference. To address this problem, we employed Inverse Probability of Treatment Weighting (IPTW) as a sensitivity analysis, validating the robustness of our findings.

Re-intervention on the aorta post-surgery not only diminishes the quality of life for patients but also heightens the risk of mortality and hospital readmission. In comparison with TAR + FET, hybrid technique was found to substantially promote thrombosis completeness of false lumen in thoracic aorta [21]. Nonetheless, it was well acknowledged that endovascular aortic repair made re-intervention more likely than open repair [23, 24]. In our study, the incidence of aortic re-intervention after hybrid surgery was higher than in TAR + FET. Absence of primary entry tear resection, new dissections, stent migration, graft infection, an initial aortic diameter > 40 mm and entry tears in descending thoracic aorta or aortic arch were among the causes cited in earlier studies [25, 26]. A prospective follow-up research conducted by Gaudry and his colleagues suggested that a short clamping time was one of the independent risk factors for re-intervention [26]. In our research, average ACC (Aortic cross-clamp) time in hybrid operation was lower than in TAR + FET, whether in the matched or unmatched cohort. Shorter ACC time brought about more restricted aortic resection, and more frequent occurrence of unresected tears or re-entry in the distal arch.

Re-intervention cases in hybrid group were mainly caused by subsequent proximal type I endoleak after initial operation (43%, 6/14) in our research, which was in line with earlier study [27]. Insufficient length of the proximal landing zone and arch lesions were known to increase the risk for type Ia endoleak [24]. Recent expert consensus did not recommend endovascular aortic repair for individuals whose lengths of proximal landing zone were less than 25 mm [28].

Technical problems remain to be solved regarding the rigid guide wire, endograft delivery system and the anchoring of stents. Despite the complicated anatomic basis of lesions in aortic arch, minimally invasive approaches for arch repairment should not be cast aside. Hybrid surgery holds superiority in improvement of in-hospital outcomes, such as lower incidence of delirium, less blood transfusion and fewer infections. Thus, the hybrid technique is an available alternative for patients who are not able to get through conventional open repair. However, regular follow-up with imaging examination and prompt re-intervention are crucial to prevention of severe complications.

The rapid advancements in hybrid and total endovascular procedures highlight the need for specialized training paradigms and multidisciplinary aortic teams [29]. Given the steep learning curves for complex techniques, we recommend standardized training pathways, including simulation-based education and exposure to high-volume centers. Aortic teams, integrating aortic surgeons, vascular surgeons, interventional radiologists, and cardiologists, are essential for managing complex cases [30]. To expand the use of hybrid procedures, we advocate for their incorporation into structured training programs and the development of clear clinical guidelines to prepare the next generation of thoracic aortic surgeons.

Limitations

Limitations of this study are as follows. (1) The intrinsic selection bias of the retrospective design is the main limitation of this research. We applied the propensity score matching to minimize selection bias and performed sensitivity analysis to validate the robustness of the results. (2) PSM is associated with a reduction in sample size after matching, making the conclusion of no mortality difference very cautious. Although we conducted sensitivity analysis with IPTW, which preserves the entire sample, to address the bias caused by PSM, a larger sample size after PSM would still be necessary. (3) The follow-up time was inadequate to verify long-term outcomes. The follow-up work is currently ongoing, and we will conduct further research in the future.

Conclusions

Our study suggested that hybrid technique was associated with a higher mid-term rate of aortic re-intervention in comparison with TAR + FET and should be cautiously taken into account as a procedure of choice for patients with acute aortic dissection involving the aortic arch. More adequately powered studies from different centers are required to further evaluate the long-term outcomes of patients who had received the hybrid treatment.

Abbreviations

>AAD	Acute aortic dissection
ACC	Aortic cross-clamping
ACP	Anterograde cerebral perfusion
BMI	Diabetes mellitus
CAD	Coronary artery disease
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CPB	Cardiopulmonary bypass
CT	Computed tomography
CTA	Computed tomography angiography
CVA	Cerebrovascular accident
DHCA	Deep hypothermic circulatory arrest
DM	Diabetes mellitus
FET	Frozen elephant trunk
HR	Hazard ratio
ICU	Intensive care unit
IPTW	Inverse probability of treatment weighting
IQR	Interquartile range
LOS	Length of stay
LVEF	Left ventricular ejection fraction
MDT	Multi-disciplinary treatment
MI	Myocardial infarction
MRI	Magnetic resonance imaging
MV	Mechanical ventilation
PS	Propensity score
PSM	Propensity-score matching
RBC	Red blood cell
RR	Relative risk
SD	Standard deviation
SMD	Standardized mean difference
TAR	Total arch replacement
TEVAR	Thoracic endovascular aortic repair

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

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Author contributions

HZ and XW designed the study. HZ and RZ analyzed the data and wrote the manuscript. RZ completed the visualization. ZY, MY and DQ collected data from Shanghai General Hospital for this article. FH and XW collected data from Nanjing First Hospital for this article. WC reviewed and edited the manuscript. XC supervised the study. XC, XW and MY provided fundings for this research. HZ and RZ have contributed equally. All authors contributed to the article and have approved the submitted version.

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Data availability

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

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Nanjing First Hospital, Nanjing Medical University (protocol code KY20220425-05), and the Ethics Committee of Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine (protocol code 2018KY241) and conducted in accordance with the Declaration of Helsinki. Due to the retrospective study design, the written informed consent was waived by the Ethics Committee of Nanjing First Hospital, Nanjing Medical University and the Ethics Committee of Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine. The data in the research was de-identified to protect patients' privacy.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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