

Pre-Loaded Fenestrated Thoracic Endografts for Distal Aortic Arch Pathologies: Multicentre Retrospective Analysis of Short and Mid Term Outcomes

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WHAT THIS PAPER ADDS

To avoid the risk of overestimating mortality and stroke rates associated with low volume reporting, this study reports outcomes with the pre-loaded fenestrated thoracic endograft from six experienced endovascular centres. A total of 108 patients were included. The 30 day mortality, major stroke, and spinal cord ischaemia rates were 3.7%, 5.6%, and 3.7%, respectively. Median follow up was 12 months, with estimated one, two, and three year freedom from re-intervention rates of 86.3%, 84.4%, and 73%, respectively. Patients with post-dissection type B aneurysms without prior ascending substitution appeared to be more susceptible to intra-operative retrograde aortic dissection (16%).

Objective: To determine short and midterm outcomes of a pre-loaded fenestrated thoracic endograft (f-TEVAR) for exclusion of distal aortic arch pathologies.

Methods: This was a multicentre, retrospective study including consecutive patients from six experienced European vascular centres undergoing f-TEVAR for distal arch pathologies. Primary endpoints included peri-operative mortality and peri-operative stroke and/or spinal cord ischaemia rates. Secondary outcomes were technical success and mid to late events, including death and re-interventions. Statistical analysis was performed with SPSS 26. Mid to late term events were calculated using Kaplan–Meier survival analysis.

Results: One hundred and eight patients were included (mean age 68 ± 11 years, 70% men). A total of 38% ($n = 42$) had a prior history of aortic dissection, and 24% ($n = 26$) prior aortic surgery. The mean aneurysm diameter was 59 ± 12 mm and the most frequent indication for treatment was post-dissection aneurysms ($n = 42$, 39%). Technical success was 99% ($n = 107$) despite intra-operative wire entanglement occurring in 29% ($n = 31$). The 30 day mortality rate was 3.7% ($n = 4$), with a 5.6% major stroke incidence ($n = 6$) and 3.7% ($n = 4$) spinal cord ischaemia rate. Three cases of retrograde dissection occurred (two of which were fatal), all in post-type B dissecting aneurysm patients without prior aortic surgery (three of 19, 15.8%). Median follow up was 12 months (range, 1 – 26). Endoleaks were documented during follow up, with 3.5% type Ia (4/104) and 2.9% type Ib (3/104) as a result of persistent false lumen perfusion. The one, two, and three year survivals and freedom from re-intervention rates were 93.2% and 92.1%, 89.1% and 86.3%, and 84.4% and 73%, respectively.

Conclusion: This multicentre study shows that treatment of the distal aortic arch by f-TEVAR is feasible, with promising 30 day mortality, stroke, and spinal cord ischaemia rates.

Keywords: Aneurysm, Aorta, Arch repair, Endovascular, Fenestrated, Post-dissecting

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INTRODUCTION

The aortic arch has been referred to as “the last frontier” for total endovascular aortic repair.¹ The proximal landing zone is often wide, angulated, and limited in length by the supra-aortic vessels, mobile, with an extremely high volume flow and three dimensional pulsation.¹ Open surgery with cardiopulmonary bypass and hypothermic circulatory arrest still represents one of the best strategies in fit patients with pathology involving the ascending aorta or aortic arch, with 4% – 10% 30 day mortality rates.^{2,3} However, in unfit patients (i.e., age, comorbidities, extensive aortic disease, or prior open cardiothoracic procedures), peri-operative mortality and stroke rates have been reported to be as high as 2% – 16.5% and 2% – 18%, respectively.^{2,3} The frozen elephant trunk (FET) technique, combining both open arch surgery and endovascular descending thoracic repair, is a potential treatment alternative for most of the pathologies involving the aortic arch, broadening the armamentarium of surgeons and simplifying the treatment of complex thoracic arch pathologies.^{2–4} However, this procedure may be performed at the cost of a significantly higher rate of spinal cord ischaemia (0 – 21%), acute kidney injury (4% – 35%), and a still significant in hospital mortality (1.8% – 17.2%).^{3,4}

For pathology involving Ishimaru zones 1 – 3 (the distal aortic arch), hybrid repair with a combination of supra-aortic vessel bypass/re-routing for creation of a sufficient landing zone, and thoracic endovascular aortic repair (TEVAR) has often been used.² Extra-anatomic bypass/re-routing of the supra-aortic vessels (i.e., debranching by carotid-carotid-subclavian bypass or ascending-carotid-carotid-subclavian bypass) has less morbidity than open arch repair, but remains associated with a significant stroke risk as well other local surgical complications (phrenic nerve palsy, lymph leak, infection).² Additionally, for those aortic pathologies requiring sealing in Ishimaru zone 2, the latest Society for Vascular

Surgery 2020 guidelines for the management of descending thoracic aneurysms strongly recommend pre-operative or concomitant LSA revascularisation (with a moderate degree of evidence), a stronger recommendation than was given in the 2017 ESVS Management of Descending Thoracic Aorta Diseases guidelines.^{5,6}

Technological advances have enabled complete endovascular exclusion of aortic pathologies involving the visceral vessels, with excellent results in this segment paving the way for the extension of these procedures into the arch.⁷ As in thoraco-abdominal endovascular repair, two main configurations exist: 1) branched endografts, incorporating one to three branches and typically used for proximal arch pathologies; and 2) fenestrated endografts, more frequently used in mid to distal arch diseases.^{2,7} There are five aortic arch endografts commercially available in Europe: two branched designs, Zenith (Cook Medical, Bloomington, IN, USA) and Relay (Terumo Aortic, Inchinnan, UK); and three fenestrated devices, Zenith (Cook Medical), Relay (Vascutek), and Najuta stent graft (Kawasumi Laboratories, Inc. Kanagawa, Japan).²

Although recent large single centre and multicentre collaborations have reported outcomes after branched arch endografts, only smaller case series are currently available with the Zenith pre-loaded fenestrated thoracic endograft (f-TEVAR).^{8,10–12} The aim of this study was therefore to evaluate short and midterm outcomes of f-TEVAR from an international group of experienced aortic centres.

METHODS

Stent graft design

The Zenith f-TEVAR (Figs 1 and 2) is a custom made device with one pre-loaded fenestration and the possibility of a proximal scallop. Potential target vessels of the fenestration

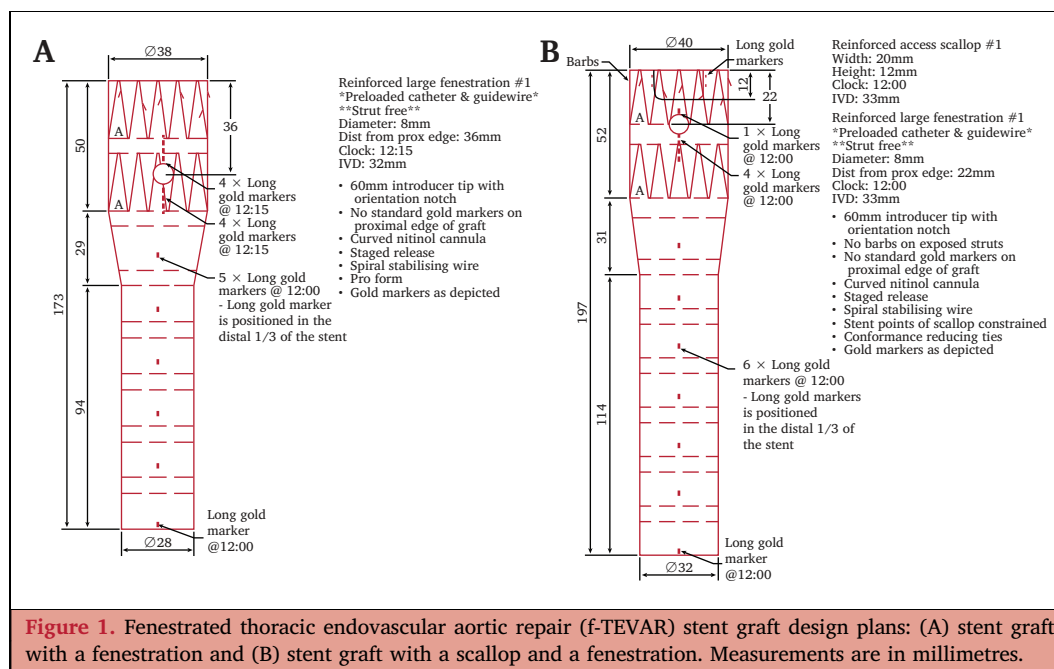
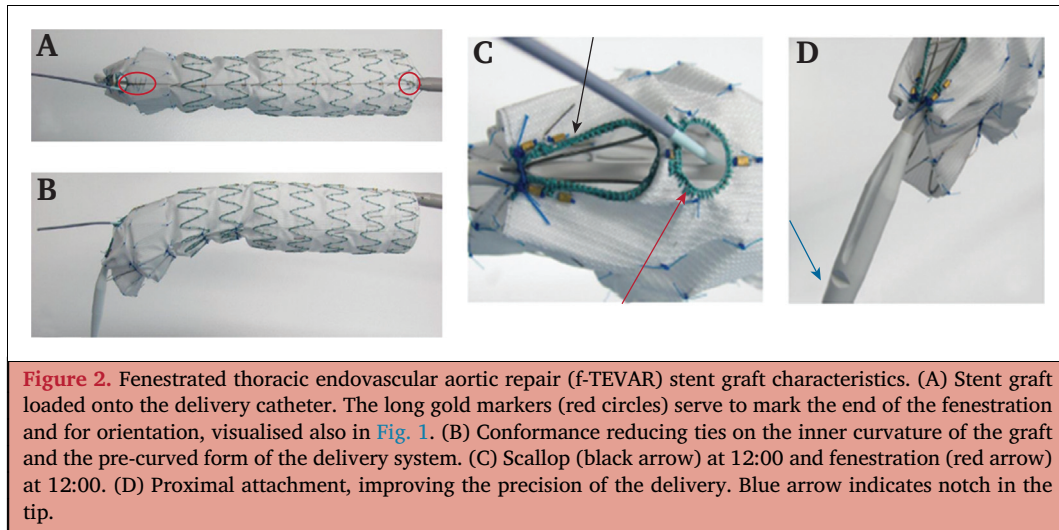


Figure 1. Fenestrated thoracic endovascular aortic repair (f-TEVAR) stent graft design plans: (A) stent graft with a fenestration and (B) stent graft with a scallop and a fenestration. Measurements are in millimetres.



± scallop are the LSA and the LCCA, or the LCCA and the brachiocephalic trunk (after a carotid-subclavian bypass, [CSB]), respectively, enabling sealing in zones 1 or 2. The Zenith f-TEVAR requires between four and six weeks of manufacturing time, limiting its applicability in urgent and emergency cases. It is mounted on a Z-Track Plus introducer sheath and attached with a spiral wire, allowing for correct orientation in the arch. The pre-loaded fenestration serves as an additional adjunct. It exits the graft at the level of the fenestration and should be snared from the target vessel, with positioning of a through and through wire from the main femoral access to the main upper access; aiding with stability and orientation correction. The scallop does not have stents across it and does not require target vessel cannulation. The step by step treatment technique and potential problem solving during implantation have been described previously and extend the scope of this manuscript.^{13,14}

Population

Consecutive patients undergoing f-TEVAR in six high volume European centres were analysed in this study, including all cases since the beginning of their experience up to January 2020. Participating centres included Ludwig Maximilians University Hospital, Klinikum Frankfurt Höchst, University Hospitals Birmingham NHS Foundation Trust, Malmö Vascular Centre, German Aortic Centre Hamburg, and Uppsala University. Indications for treatment included arch pathologies requiring sealing in distal zone 0, 1, or 2. All centres had significant experience (> 100 each) with thoraco-abdominal branched and fenestrated repair and had performed over five f-TEVAR procedures. Patients undergoing repair with endografts with either a single fenestration or with a fenestration and a scallop were included. Endografts with only a scallop were not included in this study. Fenestrations used for the innominate artery were also excluded, as they are rare and could potentially confound outcomes. Approval by the ethics committee was acquired from each centre separately according to local

guidelines on whether retrospective anonymous data collection required approval or not.

Data collection and statistical analysis

Retrospective data were collected at each centre and gathered in a single electronic anonymised database. Early events were defined as occurring within 30 days of the procedure, and late events thereafter. Technical success, defined as successful implantation of the device and cannulation of the fenestrations, without the presence of type I or III endoleaks, and intra- and post-operative morbidity and mortality were documented according to TEVAR reporting standards.¹⁵ Primary outcomes were 30 day death, stroke, and or spinal cord ischaemia (SCI) rates. Secondary outcomes were technical success and mid to late events, including death and re-interventions. To evaluate whether centre experience could be a confounder and mitigate the effects of the potential “learning curve”, two variables were created: Cases performed before and after 2017 (48 vs. 60) and cases performed after $n = 5$ at each centre (30 vs. 78). The “Strengthening the Reporting of Observational Studies in Epidemiology” (STROBE) statement guidelines were used in assessment of collected data.

Statistical analysis was performed with SPSS version 26 (IBM Statistics, Chicago, IL, USA) and Stata 14.2 (StataCorp LLC). Normality was assessed statistically with the Kolmogorov-Smirnov test. Normally distributed variables were expressed as mean ± standard deviation, while variables that did not follow a normal distribution were expressed with median and range or interquartile range (IQR). Categorical variables were analysed with Pearson’s chi-square test or Fisher’s exact test, while quantitative variables were analysed with the Student *t* test or Mann–Whitney *U* test. A *p* value < .050 was considered to be significant for all calculations. Comorbidities, anatomical factors, endograft characteristics, and procedural data were analysed on univariable analysis for 30 day mortality. Survival estimates were calculated with Kaplan–Meier curves.

RESULTS

Demographics and pre-operative data

One hundred and eight patients were included (mean age of 68.2 ± 11.1 years, 69.4% men). The most frequent comorbidities were hypertension (85.7%), dyslipidaemia (40%), and coronary heart disease (28.6%). The full range of comorbidities is shown in Table 1. Of the cohort, 38% had a prior history of aortic dissection and 24% prior aortic surgery, with the most frequent indications for repair being post-dissection

Table 1. Demographic characteristics of 108 patients treated by fenestrated thoracic endovascular aortic repair stent grafts for distal aortic arch pathology

| | Patients (n = 108) | P value* |
|---|-----------------------|-------------|
| Age – y | 68.2 ± 11.1 | .87 |
| Men | 75 (69.4) | .39 |
| BMI ≥ 30 kg/m ² | 23 (25.6) | .23 |
| Hypertension | 90 (85.7) | .53 |
| Dyslipidaemia | 42 (40) | .53 |
| Coronary artery disease | 30 (28.6) | .20 |
| Prior CABG | 7 (6.7) | .58 |
| Prior PTCA/stenting | 12 (11.5) | .46 |
| COPD | 19 (18.1) | .72 |
| Chronic renal insufficiency | 15 (14.3) | .81 |
| Dialysis | 1 (.09) | .84 |
| Peripheral artery disease | 15 (14.3) | .41 |
| Chronic heart failure | 14 (13.3) | .48 |
| Diabetes | 11 (10.5) | .48 |
| Stroke / TIA history | 10.2 | .32 |
| ASA | | .31 |
| II | 7 (6.8) | |
| III | 89 (82.4) | |
| IV | 7 (6.5) | |
| Prior medication | | |
| Acetylsalicylic acid | 67 (63.8) | .13 |
| Clopidogrel | 11 (10.5) | .77 |
| NOAC | 18 (16.7) | .35 |
| Anti-cholesterol medication | 51 (47.2) | .95 |
| Nitrates | 6 (5.6) | .092 |
| Calcium channel blockers | 35 (32.4) | .72 |
| ACE inhibitors | 59 (54.6) | .80 |
| Beta blockers | 70 (64.8) | .074 |
| Prior aortic dissection | 42 (38.9) | .83 |
| Stanford A | 19 (17.4) | |
| Stanford B | 23 (21.3) | |
| Prior aortic surgery | 26 (24.1) | .25 |
| Prior ascending repair | 16 (14.8) | .39 |
| Prior abdominal aortic repair | 10 (9.2) | .51 |
| Prior descending thoracic repair | 6 (5.6) | .61 |
| Genetic aortic pathology | 7 (6.5) | .58 |
| Family history of aortic disease | 4 (3.8) | .68 |
| Total procedures performed after case number five | 78 (76.9) | .26 |
| Procedures performed after 2017 | 60 (55.6) | .076 |

Data are presented as n (%) or mean \pm standard deviation. BMI = body mass index; CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angiography; COPD = chronic obstructive pulmonary disease; TIA = transitory ischaemic attack; ASA = American Society of Anesthesiologists; NOAC = novel oral anticoagulant; ACE = angiotensin converting enzyme.

* p values represent the association with 30 day mortality on univariable analysis.

(38.9%) and degenerative aneurysms (36.1%). The maximum aortic diameter was 59.2 ± 12.2 mm (degenerative aneurysms 62 ± 1.6 mm, post-dissecting aneurysms 62 ± 1.5 mm, penetrating aortic ulcers (PAUs) 48 ± 3.8 mm, and other 56 ± 3.7 mm). Overall, 85.2% of the cases were asymptomatic and 14.8% were non-ruptured symptomatic, with no frank ruptures. Pre-operative computed tomography angiography (CTA) details are shown in Table 2.

Procedural data

One hundred and eight patients and 172 target vessels were included. Of the target vessels, 108 were fenestrations (87 for the LSA with a 98.8% success rate and 21 for the LCA, with 100% success rate) and 64 were scallops (43 for LCA, 18 IA and three in bovine arches). The proximal landing was zone 0 in 19.4%, zone 1 in 41.7%, and zone 2 in 38.9%. Specific endograft and bridging stent characteristics used are shown in Table 2.

Technical success was 99.1% (107 of 108 patients), with inability to cannulate one LSA because of wire entanglement (a low profile device with an LSA fenestration and LCA scallop) and patient instability during the intervention (the patient required cardiac resuscitation). Entanglement of the pre-loaded catheter and subsequent wire (around the graft edge or the struts of the scallop) was reported in 28.7% of patients ($n = 31$). A subanalysis evaluating its relationship to surgeon experience found no differences between before or after case #5 or cases performed before or after 2017. Median surgical time was 140 minutes (interquartile range, IQR, 116, 174 minutes), 160 minutes in patients undergoing simultaneous CSB vs. 137 minutes in patients without CSB. Concomitant procedures were performed in 44 patients (Table 2), among which there was a concomitant CSB in 23 patients, distal extension to the coeliac trunk with a TEVAR in 11, and five patients underwent false lumen occlusion.

Three cases of retrograde aortic dissection occurred (two of which were fatal), all in patients with post-type B dissecting aneurysms without prior aortic surgery (maximum aortic diameters of 62, 66, and 73 mm). The patient who survived underwent thoracotomy and an ascending aortic graft. The two others were conservatively managed and died during the hospital stay. All three underwent exclusion with the proximal seal in zone 1 (LSA fenestration and a scallop for the LCA), with wire entanglement being documented in one. Overall, 23 patients had post-type B aortic dissection, 19 without prior intervention. In this specific group of patients, the incidence of retrograde aortic dissection was 15.8% (three of 19).

Four other patients had intra-operative complications: two access bleeding, one cardiac arrest requiring resuscitation, one intra-operative stroke, and one common femoral artery dissection.

Thirty day outcomes

The 30 day mortality was 3.7% ($n = 4$) (Table 3). Two patients died following retrograde type A dissection (one on post-operative day 2, one on post-operative day 14), one

Table 2. Pre-operative computed tomography angiography and endograft characteristics and procedural data on 108 patients treated with fenestrated thoracic endovascular aortic repair (f-TEVAR) stent grafts for distal aortic arch pathology

| | Patients (n = 108) | p value* |
|---|-------------------------|----------|
| Aortic diameter – mm | 59.2 ± 12.2 | .23 |
| Symptomatic | 16 (14.8) | .56 |
| Type of aortic pathology | | .46 |
| Degenerative aneurysm | 39 (36.1) | |
| Post-dissecting aneurysm | 42 (38.9) | |
| PAU / pseudoaneurysm | 17 (15.7) | |
| Other | 10 (9.3) | |
| Endograft design | | .087 |
| Fenestration only | 44 (40.7) | |
| Fenestration + scallop | 64 (59.3) | |
| Scallop target vessel | | .092 |
| LCA | 43 (67.2) | |
| IA | 18 (28.1) | |
| Bovine arch | 3 (4.7) | |
| Fenestration target vessel | | .32 |
| LSA | 87 (80.6) | |
| LCA | 21 (19.4) | |
| Proximal landing zone | | .048 |
| Zone 0 | 21 (19.4) | |
| Zone 1 | 45 (41.7) | |
| Zone 2 | 42 (38.9) | |
| LCA stent graft | | .28 |
| Advanta V12 | 21 (100) | |
| Diameter – mm | 8.7 ± 1 | |
| Length (range) – mm | 38.5 ± 5.4 (32 – 59) | |
| LSA stent graft | | .67 |
| Advanta V12 | 68 (77.3) | |
| BeGraft | 3 (3.4) | |
| VBX | 5 (5.7) | |
| Other | 6 (9) | |
| Diameter – mm | 9.15 ± 1.1 | |
| Length (range) – mm | 39.6 ± 8.4 (22 – 59) | |
| Low profile device | 8 (7.8) | .55 |
| Technical success | 107 (99.1) | <.001 |
| Percutaneous access for the main endograft device | 67 (62) | .69 |
| Carotid access | 13 (12) | .74 |
| Right | 2 (1.8) | |
| Left | 11 (10.1) | |
| Brachial access | 98 (90.7) | .32 |
| Right | 1 (0.9) | |
| Left | 97 (89.8) | |
| Wire entanglement | 31 (28.7) | .81 |
| Spinal drainage | 14 (13) | .44 |
| Carotid subclavian bypass | 26 (24.1) | .51 |
| Simultaneous | 23 (21.3) | |
| Staged | 3 (2.8) | |
| Concomitant procedures | 44 (40.7) | <.001 |
| Simultaneous CSB | 23 (21.3) | |
| Distal extension with TEVAR | 11 (10.2) | |
| False lumen occlusion | 5 (4.6) | |
| Iliac conduit | 4 (3.7) | |
| Iliac PTA | 1 (0.9) | |
| Intra-operative complications | 7 (6.5) | <.001 |
| Total surgical time – min | 140 (116, 174) | .83 |
| Total contrast used – mL | 73 (50, 109) | .85 |

Continued

Table 2-continued

| | Patients (n = 108) | p value* |
|------------------------------|-----------------------|----------|
| Total fluoroscopy time – min | 26.5 (22, 35.7) | .13 |
| Estimated blood loss – mL | 150 (100, 200) | .61 |
| >1 L – % | 2.7 | |

Data are presented as n (%), mean ± standard deviation or median (interquartile range), unless stated otherwise. LCA = left carotid artery; IA = innominate artery; LSA = left subclavian artery.

* p values represent the association with 30 day mortality on univariable analysis.

Table 3. Thirty day and midterm outcomes of 108 patients treated with fenestrated thoracic endovascular aortic repair (f-TEVAR) stent graft for distal aortic arch pathology

| | Patients (n = 108) |
|---|--------------------|
| 30 day mortality | 3.7 |
| 30 day post-operative complications | |
| Stroke | 7.5 |
| Major | 5.6 |
| Minor | 1.9 |
| Pneumonia | 5.6 |
| Chronic heart failure | 5.6 |
| Acute kidney injury | 4.6 |
| Temporary dialysis | 3.7 |
| Permanent dialysis | .9 |
| Spinal cord injury | 3.7 |
| Retrograde Type A dissection | 2.8 |
| SIRS | 2.8 |
| Myocardial infarctions | 1.9 |
| Vascular access complication | 22.4 |
| Intensive care unit stay – d | 2 (1, 3) |
| Early re-intervention rate | 9.4 |
| Post-operative stay – d | 6 (5, 9) |
| Discharge location | |
| Home | 85.6 |
| Another hospital | 3.8 |
| Rehabilitation centre | 7.7 |
| Median follow up – mo | 12.8 (1, 96) |
| Late re-intervention rate | 23.1 |
| Late aortic related complications | |
| Aortic rupture | 2.8 |
| Conversion to open repair | 1.9 |
| Graft infection | .9 |
| Rate of late endoleaks | |
| Type Ia | 3.8 |
| Type Ib | 2.9 |
| Type II | 4.8 |
| Type III | 2.9 |
| Changes in the aneurysm sac on last CTA | |
| Unchanged | 48.1 |
| > 5 mm enlargement | 6.5 |
| > 5 mm decrease | 34.3 |
| Primary target vessel patency | |
| IA | 100 |
| LCA | 98.1 |
| LSA | 89.3 |

Data are presented as % or median (interquartile range). CHF = chronic heart failure; SIRS = systemic inflammatory response syndrome; LCA = left carotid artery; IA = innominate artery; LSA = left subclavian artery.

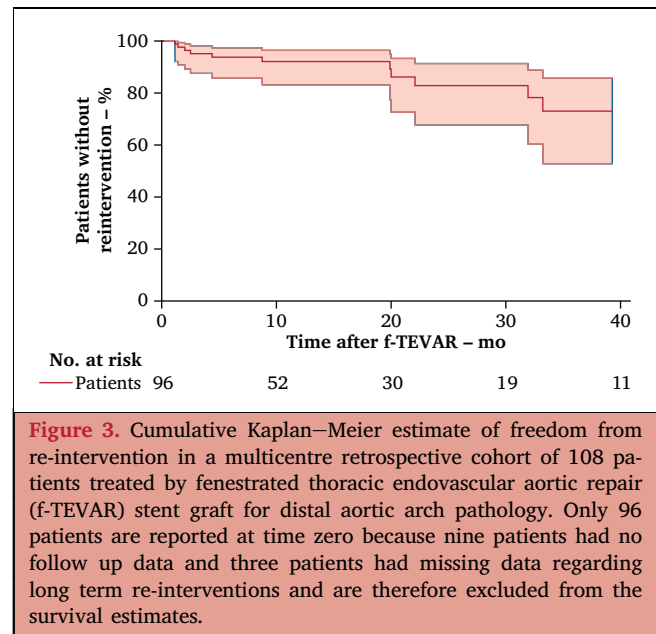
patient died on post-operative day one from intraoperative cardiac arrest with multiple post-operative complications (acute kidney injury, myocardial infarction, access complications), and one patient died from unknown causes on day 8.

The 30 day stroke rate was 7.5% ($n = 8$), including six major and two minor strokes. One was anterior, four posterior, and three were both, and all were ischaemic. Wire entanglement was reported in five of the eight cases. Four patients had undergone f-TEVAR with a single LSA fenestration, one patient had a prior CSB and f-TEVAR with a single LCA fenestration, and three patients had received a fenestration for the LSA and a scallop for the LCA. The 30 day spinal cord ischaemia (SCI) rate was 3.7% ($n = 4$). One patient had a concomitant stroke, one suffered post-operative bleeding requiring re-intervention, and one a retrograde aortic dissection. Regarding the symptomatology, only one patient had a complete motor deficit, with the rest making a significant recovery. Thus, permanent SCI deficit was observed in only one (< 1%).

The median ICU stay was two days (IQR 1, 3 days). The short term re-intervention rate was 9.2% ($n = 10$): four wound revisions for bleeding, two embolectomies, one femoral stenting, one stenting of the scallop, one fasciotomy, and one sternotomy and ascending aortic repair. All patients were discharged with either single (82 patients 78.8%) or dual antiplatelet therapy (12 patients, 11.5%), or anticoagulant treatment (10 patients, 9.6%). Post-operative CTA within the first 30 days was performed in 74 patients (71.8%), with a total of 21 endoleaks documented: one type Ia (1.4%), 13 type Ib/persistent false lumen perfusions (17.6%) of which six were pre-planned for second stage repair, four type II endoleaks (5.4%), and one type III endoleak (2.7%). In two patients, an endoleak was documented but not specified. The median post-operative length of stay was six days (IQR 5, 9 days).

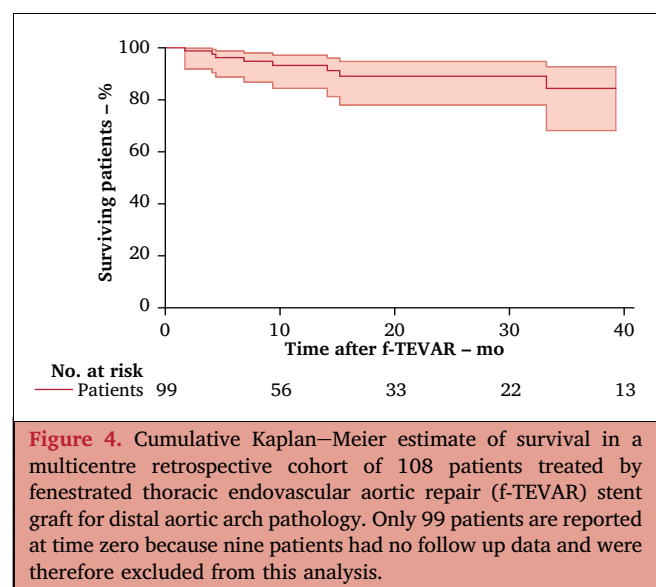
Mid and long term follow up

Median follow up was 12.4 months (1 – 96 months) (Table 3). The global re-intervention rate was 12.9% and included five cases of unplanned distal extension with TEVAR, two LSA relining, one femoral aneurysm repair, one false lumen embolisation, one EVAR, one iliac stenting, and one homograft substitution of the arch and descending aorta in a patient with an aortic infection, which ultimately lead to death. The estimated freedom from re-intervention was 92.1%, 82.9% and 73.0% at one, two and three years, respectively (Fig. 3). There were two aortic ruptures during follow up: one AAA rupture and one endograft infection requiring substitution. Nine of the 104 patients discharged died during follow up, four from aortic related events: the two cases of aortic rupture previously mentioned (at 1.7 months and at 32.3 months, respectively), one patient a from right iliac artery aneurysm rupture and one from haemorrhagic shock and bowel ischaemia. The cause of death was unknown in one patient. The one, two, and three year survival rates were 93.2%, 89.1%, and 84.4%, respectively, with long term survival Kaplan–Meier curves shown in Figure 4. The one, two, and three year survivals free from



aortic related death were 94.7%, 94.7% and 89.7%, respectively.

Of the 64 patients whose target vessel for the f-TEVAR was the LSA, only two patients required relining during follow up (3%). Two patients underwent a subsequent carotid intervention because of stenosis, one of which had a scallop for the LCA (the fenestration was used for the LSA) and the other patient had a stent graft design with a fenestration only for the LSA. The freedom from fenestration target vessel re-intervention because of stenosis or occlusion was 100% and 93.8% for the LSA at 12 and 24 months of follow up, while the primary patency of the LCA was 100% and 100% at 12 and 24 months, respectively. In the last available CTA, 6.4% type I endoleaks were detected (3.5% type Ia and 2.9% type Ib endoleaks resulting from



persistent false lumen perfusion), 4.8% type II endoleaks, and 2.9% type III endoleaks. The presence of type Ia endoleaks was not correlated with the stent graft design nor the proximal landing zone on univariable analysis. Nearly 50% of patients did not present changes in the aneurysm size during the follow up, 35% had sac decrease and 6.5% had sac enlargement. No separations or fractures of the bridging stents were reported, nor were any cases of graft migration documented.

Variables that were statistically significantly associated with 30 day mortality on univariable analysis were included in a multivariable analysis; however, no variables were found to be statistically significant in the multivariable analysis, possibly a result of the low number of 30 day deaths. Univariable analysis for peri-operative death, stroke, and SCI ($p = .071$, $p = .47$, $p = .11$ for patients before and after 2017; $p = .26$, $p = .058$, $p = .74$ for patients after case #5) showed no significant statistical differences.

DISCUSSION

Early results of total endovascular arch repairs were associated with high stroke rates.² However, with increasing physician experience and the development of adjuncts (specific delivery systems, pre-loaded fenestrations, inner branches, etc.), post-operative stroke and mortality rates have decreased from 15% to 7% and from 20% to 0–10%, respectively.^{2,8–10} In the present study, the 30 day mortality and major stroke rates were 3.7% and 5.5%, considerably lower than in previous series.^{10,16} SCI rates were also low (3.7%), with only one case of major motor loss.^{10,16} When compared with outcomes of high risk or prior published f-TEVAR patients, these results are promising, reflecting an improvement.^{3,10,16} Flushing with CO₂, increased operator experience, and better patient selection may have played a role in these results, alongside stent graft technological developments.

Despite this, high rates of wire entanglement were observed, occurring in nearly 30% of the cases, without differences before and after case #5 and or 2017. This finding suggests that wire entanglement is not associated with physician/centre experience, but rather with the characteristics and design of the endograft. Methods of avoiding this problem have been described previously, for example, rotation of the endograft delivery system in the descending aorta after the target vessel has been correctly cannulated to disentangle the wire; however, there is not always a simple solution.^{13,14} Furthermore, wire entanglement can lead to longer operating times, increased manipulation in the arch, and may condition the conformability of the graft. In this study, it occurred in five of eight strokes, although there was no statistically significant association. This could be because this was a *post hoc* analysis, and the design of the study was not specifically tailored to address this question. Notwithstanding the potential complications of wire entanglement, the present authors believe that the tension on the through and through brachiofemoral wire during deployment allows for correction

of the endograft and fenestration orientation, and should be maintained in the fenestrated endograft design.

The 30 day stroke rate was 7.5% ($n = 8$). Procedures were routinely performed with a target intraprocedural activated clotting time > 250 s, standard for complex aortic repairs requiring vessel cannulation. Unfortunately, data on CO₂ flushing were not collected in this study, nor on the use of other additional stroke prevention techniques. However, strokes were not associated with identifiable intra-operative technical problems, such as maldeployment of the stent graft or vertebral artery coverage. Of course, in terms of manipulation, there is a difference between patients with the LSA as the fenestration target vessel vs. those in which the LCA was the fenestration target vessel, as these require the establishment of a through and through wire. However, after performing a subanalysis of stroke risk according to fenestration target vessel, no differences were observed. Finally, there were three cases of retrograde type A dissection, all in patients with post-type B dissecting aneurysms and without prior ascending aortic substitution. Given the small numbers of patients, it is not known whether these patients were particularly susceptible, or whether this was coincidental. Additional reports are warranted specifically considering patients with post-dissecting type B aneurysms without prior ascending substitution.

Besides open surgery, other “endovascular” techniques for distal arch repair are available, including other fenestrated designs (large fenestrations that do not require bridging stents, custom made and *in situ* fenestrations), branched endografts with retrograde branches, “chimney” grafts, hybrid repairs with partial debranching of the supra-aortic vessels, and TEVAR with coverage of the LSA without revascularisation.^{2,10}

The Najuta endograft (Kawasumi Laboratories) has large fenestrations that do not requiring bridging. Iwakoshi *et al.* have reported outcomes of 32 patients (28 degenerative and four post-dissecting aneurysms), with a mean follow up of 2.5 years. Technical success was 91%, with a 9% intra-operative type Ia endoleak rate. Five patients (15.6%) presented intra-operative complications (two retrograde type A dissections, one stroke, one coeliac artery occlusion, and one case of SCI), with two early branch occlusions (LCA and LSA) secondary to endograft infolding.¹⁷ Fukushima *et al.* report outcomes of 24 type B aortic dissection patients, with a technical success rate of 92.3%, although without retrograde type A dissections. One patient had an early type Ia endoleak, one a post-operative stroke, and two required secondary re-interventions for stent graft induced distal new entry tears.¹⁸ Although the patient cohort is not directly comparable, the technical success in the present study is higher, almost reaching 100%, with a lower rate of type Ia endoleaks.

Physician made fenestrations are another possibility. Canaud *et al.* report on 35 patients (51% emergency), with post-surgical arch aneurysms (24%) and type B aortic dissection (TBAD) (7%).^{19–21} Technical success was 100% in grafts with single fenestrations and zone 2 sealing; however, in 10 double fenestration grafts used for sealing in

zone 0, they could not cannulate the LSA in two cases and required adjunctive stenting of the LCA because of inadvertent coverage in three. Although they did not report any retrograde dissections, peri-operative mortality was 6%, with 3% and 6% rates of type I and III endoleaks in the peri-operative period. Although this could be explained by the large number of acute type B dissections, the risk of type Ia and III endoleaks was considerable and could be substantially higher in patients with aneurysms.¹⁹ Finally, although short term results appear promising, both “on the table” modification and *in situ* fenestrations are off label techniques with unknown long term durability. This is a crucial aspect, as the grafts have not been designed to resist the high pulsatile forces and angulations of the aortic arch, there is a potentially increased risk of late stent fractures and endograft displacement.^{20–23} Chimney grafts have been associated with high mortality (range, 0 – 29%) and endoleak rates (28%), as well as poor stent patency rates (69% for the LSA and 73% for LCA).^{2,24–26} Furthermore, stent grafts were not designed for chimneys or periscopes, thus the radial force, elasticity, shape, and even length of the currently used stents are not optimal, and with worse haemodynamic parameters when compared with specifically designed grafts.²⁷ Until more long term information is available, these techniques should be limited to urgent cases.

Finally, cervical debranching occurring with endovascular aortic repair has been associated with an increased risk of bleeding complications, re-interventions, peripheral neurological damage, and infection, as well as increased short term mortality compared with endovascular aortic repair alone, especially in those cases in which both procedures were performed simultaneously.²⁸ Similarly, another study comparing f-TEVAR vs. CBS plus TEVAR reported higher rates of local complications (29.4% in patients undergoing CBS debranching) and a higher re-intervention rate for patients undergoing CBS plus TEVAR vs. f-TEVAR (35.3% vs. 10.5%).²⁹ Although still necessary in some cases, f-TEVAR can obviate the need for cervical debranching, thereby reducing the overall rate of complications and re-interventions in complex endovascular arch repair.

Although this is a multicentre collaboration, this study does pose some limitations. On one hand, the specific reason why a f-TEVAR device (as opposed to a hybrid approach or a branched TEVAR) was selected is unknown, perhaps creating selection bias and potential confounding by indication. Given its retrospective nature, some variables could not be adequately evaluated, and some specific procedural characteristics were not recorded (i.e., CO₂ flushing, fusion guidance, other specific stroke prevention strategies, etc.) Pre-procedural studies, intra-hospital management, and follow up protocols differed from centre to centre, with each centre having their own peri- and post-operative regimens. Device selection and design according to physician preference may also differ, which may potentially play a role in branch vessel patency, durability, and post-operative complications, and each surgeon may have their own specific techniques and adjuvant procedures,

potentially causing a difference in outcomes. Furthermore, only experienced high volume centres in complex endovascular aortic surgery participated, which may affect the external validity of the outcomes. Additionally, as a multicentre retrospective collaboration, each participating centre has included less than 40 patients over a seven year period. Not all included patients had the same pathology (type B aortic dissection, aneurysms, etc.), nor did they all require sealing in the same proximal landing zone. Therefore, this study is composed of a heterogeneous group of patients. Lastly, correction for multiple testing during the statistical analysis was not performed. Notwithstanding these limitations, to the present authors’ knowledge, this is the largest series of f-TEVAR reported to date.

This multicentre study shows that treatment of the distal aortic arch by f-TEVAR is feasible, with a high technical success and promising 30 day mortality, stroke, and spinal cord ischaemia rates.

CONFLICT OF INTEREST

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