Featured Article

Total aortic arch replacement with frozen elephant trunk in patients with Marfan syndrome

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Background: Marfan syndrome (MFS) is a connective tissue disease which can lead to aortic aneurysm and dissection. The performance outcomes of total aortic arch replacement with frozen elephant trunk (FET) are not well known in these patients. This study summarizes our experience with FET in MFS.

Methods: Between August 2001 and December 2021, 435 patients underwent FET at Hannover Medical School. Of these, 34 patients had MFS. The mean age was 43.3±11.9 years and 27 (79%) were male. The indication for surgery was aortic aneurysm in 1 (3%), acute aortic dissection in 12 (35%), and chronic aortic dissection in 21 (62%) patients.

Results: All patients underwent total aortic arch replacement with FET. In addition, the following procedures were performed: conventional aortic root replacement (Bentall operation, n=8), valve-sparing aortic root replacement (David procedure, n=8), coronary artery bypass grafting (n=3), mitral valve surgery (n=2), and tricuspid valve surgery (n=1). Cardiopulmonary bypass (CPB) and aortic cross clamp times were 270±87 and 139±69 minutes, respectively. Postoperatively, there were 2 (6%) disabling strokes, and 0 (0%) patients required permanent dialysis or suffered from permanent paraplegia, respectively. In-hospital mortality was 12% (n=4). The mean follow-up time was 8.4±5.9 years. The 1-, 5-, 10, and 15-year survival rates were 82%, 70%, 70% and 65, respectively. There were 18 (53%) re-interventions on the distal aorta. Mean time to re-intervention was 2.7±3.1 years. The majority of patients underwent open surgical repair (n=14, 77%), while only 4 (22%) had endovascular therapy. The freedom from distal aortic re-intervention at 1-, 5-, 10- and 15 years was 86%, 61%, 55% and 44%, respectively.

Conclusions: The main indication for FET surgery in MFS is acute or chronic aortic dissection. Despite multiple concomitant procedures, early mortality was relatively low, suggesting that FET is feasible and effective to treat complex aortic pathology in MFS. However, our study showed a high incidence of distal aortic re-interventions, underscoring the progressive nature of the disease and the need for tailored long-term management strategies.

Keywords: Marfan syndrome (MFS); total aortic arch replacement; frozen elephant trunk (FET)

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Introduction

Marfan syndrome (MFS) is a connective tissue disorder characterized by systemic manifestations, with cardiovascular involvement being the primary determinant of morbidity and mortality (1). Aortic root aneurysm and dissection are the most life-threatening complications in these patients, often necessitating complex surgical intervention. Surgical management of MFS patients remains a challenging situation. Repair of the aortic root and ascending aorta has shown excellent outcome in MFS (2-4), however, surgical management of the aortic arch remains more complex. The frozen elephant trunk (FET) procedure has emerged as an excellent hybrid approach to treat complex aortic disease, and numerous studies have documented this (5-8). However, the application of FET in MFS remains a subject of ongoing debate (9-12). Concerns regard the durability of stent grafts, the potential for endo-leaks and distal stent-induced new entry (DSINE). However, the number of published studies on the usage of FET in MFS is very limited. This study aims to evaluate the indications, surgical outcomes, and long-term implications of the FET procedure in MFS patients, contributing to the growing body of evidence regarding its efficacy and safety in this high-risk population.

Methods

Ethical statement

This is a retrospective analysis with prospective follow-up. The study was approved by the Institutional Review Board of Hannover Medical School, Germany (# 10162_BO_K_2022).

Study design

This is a single-center retrospective study with follow-up. We searched our hospital's database to identify patients who underwent total aortic arch replacement with the FET technique. Between 08/2001 and 12/2021, a total of 435 patients underwent FET at Hannover Medical School, Germany. Of these, 34 patients had MFS.

Surgical technique

Full sternotomy is performed, and heparin is given. CPB is established via cannulation of the right atrium and aortic cannulation via echocardiography guidance. A left ventricular vent is placed via the right superior pulmonary vein. The aorta is cross-clamped, and the ascending aorta is opened. Cold blood cardioplegia is applied directly into both coronary ostia. Cardioplegia is reapplied every 30 minutes. Proximal aortic repair of the ascending aorta and/or aortic root is performed while cooling the patient. Concomitant procedures are performed during cooling if necessary. Once proximal aortic repair and concomitant procedures are completed, aortic arch surgery is performed.

During arch surgery, we prefer to use the continuous myocardial perfusion (13). The heart is perfused antegrade via a cannula inserted proximal to the aortic clamp in the ascending aortic prosthetic graft. The cardiac perfusion pressure and coronary flow are monitored continuously. Systemic perfusion is stopped, and the aortic arch is replaced while the heart is continuously perfused. Cerebral protection is established via bilateral selective antegrade cerebral perfusion. The distal anastomosis is performed either between the left common carotid artery and the left subclavian artery (zone 2) or distal to the left subclavian artery (zone 3). The FET is deployed in the proximal descending aorta. Perfusion of the lower body is restarted via the fourth branch of the graft. Next, the supra-aortic vessels are anastomosed to the respective side branches of the FET prosthesis. After rewarming, CPB is discontinued and the patient is closed in a standard fashion.

Statistical analysis

Data analysis was performed using SPSS 27 Statistics software (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp.). Normal distribution of variables was analyzed with the Shapiro-Wilk test. Normally distributed continuous variables are stated as mean ± standard deviation, while continuous variables without normal distribution are stated as median and interquartile range. Categorical variables are stated as absolute numbers and proportions. Kaplan-Meier analysis was used for evaluation of survival, and the log-rank test was used to test for differences.

Results

Patient demographics

The preoperative patient demographics are shown in *Table 1*. The mean age of MFS patients was 43.3±11.9 years and 27 (79%) were male. The indication for surgery was aortic aneurysm in 1 (3%), acute aortic dissection in 12 (35%), and chronic aortic dissection in 21 (62%) patients. Eight (24%) had pre-operative malperfusion. Twenty-three (68%) patients had previous cardiac surgery and required redo-sternotomy.

Intraoperative data

The detailed intraoperative data are shown in *Table 2*. All patients underwent total aortic arch replacement with FET.

Table 1 Pre-operative data

Variables	Value (n=34)
Gender: male	27 [79]
Age (years)	43.3±11.9
Indication for surgery	
Aortic aneurysm	1 [3]
Acute aortic dissection	12 [35]
Chronic aortic dissection	21 [62]
Preoperative neurological deficit	2 6]
Preoperative malperfusion	8 [24]
Previous cardiac surgery	23 [68]
Right-sided descending aorta	1 [3]

Data are presented as mean ± standard deviation or n [%].

Table 2 Intra-operative data

Variables	Value (n=34)
Aortic cross-clamp time (minutes)	139±69
CPB time (minutes)	270±87
HCA time (minutes)	589±22
SACP time (minutes)	85±41
Operation time (minutes)	429±97
Beating heart arch surgery	14 [41]
Length of endograft	
≤100 mm	22 [65]
>100 mm	12 [35]
Concomitant procedures:	
Bentall operation	8 [24]
Valve-sparing root (David)	8 [24]
CABG	3 [9]
Mitral valve surgery	2 [6]
Tricuspid valve surgery	1 [3]

Data are presented as mean ± standard deviation or n [%]. CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; HCA, hypothermic circulatory arrest; SACP, selective antegrade cerebral perfusion.

In addition, the following procedures were performed: conventional aortic root replacement (Bentall operation, n=8), valve-sparing aortic root replacement (n=8), coronary artery bypass grafting (n=3), mitral valve surgery (n=2), and tricuspid valve surgery (n=1). The 'beating heart arch surgery' technique was used in 14 (41%) of patients. CPB and aortic cross-clamp times were 270±87 and 139±69 minutes, respectively.

Postoperative results

The early postoperative results are shown in *Table 3*. Postoperatively, there were 2 (9%) disabling strokes. and 0 (0%) patients required permanent dialysis. There were no (0%) patients who had permanent paraplegia. The in-hospital mortality rate was 12% (n=4).

Table 3 Post-operative data

Variables	Value (n=34)
Mechanical ventilation >96 h	6 [18]
ICU stay (days)	10.7±13.2
Rethoracotomy for bleeding	12 [35]
Disability stroke	2 [6]
Tracheostomy	7 [21]
Paraplegia	
Temporary	3 [9]
Permanent	0
Dialysis	
Temporary	8 [24]
Permanent	0
In-hospital mortality	4 [12]
30-day-mortality	3 [9]

Data are presented as mean ± standard deviation or n [%]. ICU, intensive care unit.

Late outcome

Detailed information on late outcome is shown in *Table 4*. The follow-up was completed for all 34 patients (100%). The mean follow-up time was 8.4±5.9 years. The Kaplan Meier curve for survival is shown in *Figure 1*. The 1-, 5-, 10, and 15-year survival rates were 82%, 70%, 70% and 65, respectively. The Kaplan Meier curve for freedom from distal aortic re-intervention is shown in *Figure 2*. There were 18 (53%) re-interventions on the distal aorta. The mean time to re-intervention was 2.7±3.1 years. The majority of patients underwent open surgical repair (n=14,

Table 4 Follow-up data

Variables	Value (n=34)
Re-intervention in distal aorta	18 [53]
Surgical re-intervention	14 [41]
Thoraco-abdominal aortic repair	8 [24]
Descending aortic repair	4 [12]
Infrarenal aorto-biiliac repair	2 [6]
Endovascular re-intervention	4 [12]
Time to re-intervention (days)	960±1,116
Follow-up time (months)	95±68

Data are presented as mean ± standard deviation or n [%].

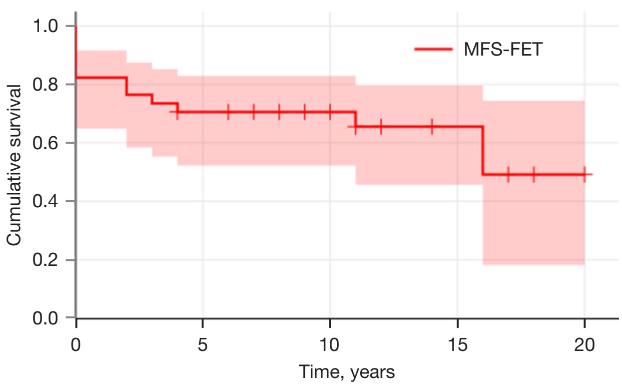

Figure 1 Survival curve. FET, frozen elephant trunk; MFS, Marfan syndrome.

77%), while only 4 (22%) had endovascular therapy. The freedom from distal aortic re-intervention at 1-, 5-, 10- and 15 years was 86%, 61%, 55% and 44%, respectively.

Discussion

This retrospective analysis of MFS patients who underwent total aortic arch replacement with FET over a 20-year period provides valuable insights into the surgical outcomes, long-term survival, and re-intervention rates in this high-risk population. Our findings suggest total arch repair with FET has a relatively low perioperative risk and therefore seems to be a viable surgical strategy in MFS patients with complex aortic pathology. However, MFS patients have a high incidence of distal aortic re-interventions, thereby rendering the long-term management of the distal aorta a

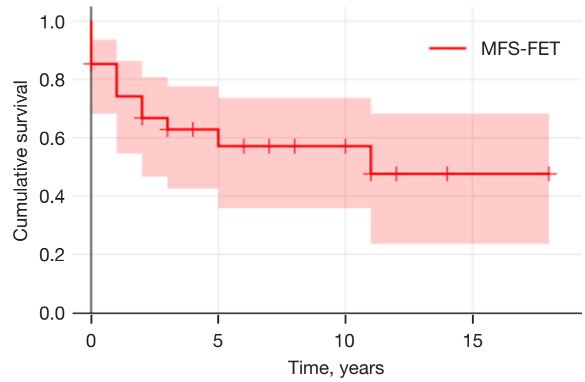

Figure 2 Freedom from distal aortic re-intervention. FET, frozen elephant trunk; MFS, Marfan syndrome.

surgical challenge.

The preoperative baseline characteristics of our patient group reflect the typical demographic distribution of MFS, with a predominance of male patients (79%) and a relatively young mean age (43 years), consistent with prior literature on aortic disease in MFS (12). The majority of patients presented with chronic (62%) or acute (35%) aortic dissection. This demonstrates that only the minority of patients with MFS develop aortic arch aneurysm. The fact that majority of patients presented with chronic aortic dissection shows the progressive nature of aortic dissection, and the importance of life-long surveillance to ensure timely surgical intervention.

In addition to total arch replacement with FET many patients required concomitant procedures such as aortic root replacement (Bentall or valve-sparing David operation), coronary artery bypass grafting, or valve surgery. The operative complexity is mirrored in the prolonged CPB and cross-clamp times. Despite this, perioperative morbidity was acceptable, with a disabling stroke rate of 6% and no cases of permanent dialysis. The in-hospital mortality rate was 12%, reflecting the high-risk nature of this surgical population. However, this number is comparable to previously published rates for FET (6,7).

The long-term analysis of our patient cohort showed that more than half of the patients (53%) required re-interventions on the distal aorta, with a mean time to re-intervention of just under three years. This high re-intervention rate aligns with other studies (14), indicating that MFS patients are predisposed to progressive distal aortic disease even after successful proximal repair. The long-term survival analysis showed that MFS have a reduced life expectancy. Despite the patients' young age, only 70%

were alive at 10 years and 65% at 15 years. These figures are noteworthy given the extensive aortic disease burden and underscore the progressive nature of residual aortic dissection. The majority of re-interventions were open procedures (77%), highlighting both the severity of distal pathology and the limitations of endovascular strategies in this population due to connective tissue fragility and anatomical considerations. The freedom from distal aortic re-intervention declined steadily over time, dropping to 44% at 15 years, underscoring the need for lifelong surveillance and a comprehensive aortic treatment strategy.

Our findings support the notion that while the FET technique provides excellent proximal aortic reconstruction, it does not obviate the need for close follow-up and potential future surgeries on the distal aorta in MFS patients. These results further advocate for a multidisciplinary approach involving geneticists, cardiologists, and cardiovascular surgeons to optimize long-term outcomes.

Limitations

This study is limited by its retrospective, single-center design and relatively small sample size. Selection bias and evolving surgical techniques over the 20-year study period may have influenced outcomes.

Conclusions

In conclusion, FET is a feasible and effective approach for complex aortic pathology in MFS. However, the high incidence of distal aortic re-interventions underscores the progressive nature of the disease and the need for tailored long-term management strategies. Future studies should aim to refine patient selection and explore adjunctive therapies to improve distal aortic outcomes in this unique patient population.

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Footnote

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Conflicts of Interest: The authors have no conflicts of interest to declare.

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