Single-center experience with thoracoabdominal aortic replacement in patients with Marfan syndrome

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ABSTRACT

Objectives: Patients with Marfan syndrome are usually not suitable for endovascular repair of the thoracoabdominal aorta. This study was designed to analyze our center's experience with open surgical thoracoabdominal aortic replacement in Marfan patients.

Methods: This was a retrospective study with prospective follow-up. Between January 1995 and September 2021, a total of 648 patients underwent thoracoabdominal aortic replacement at our center. Of these, 60 had Marfan syndrome and were included in this study.

Results: The mean age was 39.5 ± 10.7 years, and 36 (60%) were male. Ten (17%) had aortic aneurysm, 4 (7%) acute/subacute dissection, and 46 (77%) chronic dissection. Patients presented with the following extent of aortic disease according to the Crawford classification: I-17 (28%), II-18 (30%), III-22 (37%), IV-2 (3%), and V-1 (2%). The mean cardiopulmonary bypass time was 173.9 ± 84.7 minutes. Four (7%) patients required stent graft extraction. Postoperatively, 5 (8%) patients required rethoracotomy and 6 (10%) tracheostomy. One (1.7%) patient had permanent paraplegia and 2 (3%) permanent paraparesis. Two (3%) patients had stroke. One (1.7%) patient was discharged with dialysis. The 30-day mortality was 3% (n = 2). Median follow-up time was 21.5 (range, 9.4–33.6) years. The 1-, 5-, and 10-year survival rate was 87%, 80%, and 68%, respectively. There were 16 aortic reinterventions in 9 patients during follow-up.

Conclusions: Thoracoabdominal aortic replacement remains a complex procedure but can be done extremely safely in Marfan patients. Perioperative mortality rates are very low, and the long-term outcomes are enduring. Because endovascular aortic repair is not recommended for patients with connective tissue disease, open surgery remains an important cornerstone of therapy. (JTCVS Open 2022;12:13-9)

CENTRAL MESSAGE

Open surgical thoracoabdominal aortic replacement in Marfan patients can be performed with very low perioperative risk and provides enduring outcome.

PERSPECTIVE

Open surgical aortic replacement remains the gold standard for Marfan patients with thoracoabdominal aortic disease, even in the age of endovascular therapy. Thoracoabdominal aortic replacement can be performed with acceptable risk and enduring long-term outcome.
reintervention. Open thoracoabdominal aortic replacement remains the gold standard treatment for aneurysms and chronic dilatations after aortic dissection in Marfan syndrome patients.1

However, open surgical replacement of the thoracoabdominal aorta is a complex procedure and carries some risk for morbidity and mortality. Previously published studies report perioperative mortality rates ranging from 1.3% to 17%.10-12 Perioperative complications, including paraplegia, stroke, renal failure, and vocal cord paralysis, remain also a matter of concern.13,14 The aim of this study was to present our short- and long-term results and clinical outcome of open thoracoabdominal aortic replacement in patients with Marfan syndrome.

**METHODS**

**Study Design**

We set up a single-center retrospective clinical study with follow-up. The main findings of this study are summarized in Figure 1 and in Video 1. The study was approved by our institution’s ethics committee (10425_BO_K_2022). Patients were asked to give informed consent. We retrospectively analyzed our center database to identify patients with Marfan syndrome, who received thoracoabdominal aortic replacement.

From January 1995 to September 2021, a total of 648 patients underwent open thoracoabdominal aortic replacement at our center. Of these, 60 patients had Marfan syndrome. The Crawford classification and the DeBakey classifications were used to specify aortic pathology.

**Study Definitions and Follow-up**

We examined data related to patient characteristics, surgical procedures, postoperative outcome, and survival. Operative mortality was defined as death occurring within 30 days of the operation.

Operative complications were considered temporary if present at the time of hospital stay and re-treated at the discharge or within follow-up. Stroke was defined as a new-onset clinically and/or radiographically evident permanent brain injury. Paraplegia was defined as a complete loss of motor strength of the lower extremity, and paraparesis as a partial motor lower extremity deficit. Renal failure was defined as an increase of the serum creatinine >2.5 mg/dL.

Follow-up was done according to the common guidelines.15 Patients were contacted via telephone, and seen in our clinic. Primary care physicians were contacted to obtain examination results.

**Surgical Technique**

This section describes the current protocol at our institution. Patients at high risk for spinal cord injury underwent preoperative placement of a cerebrospinal fluid drainage. In this study, 13 patients received an intrathecal catheter the day before the operation and cerebrospinal fluid was drained if pressure increased to >10 mm Hg intra- and postoperatively. To enable the collapse of the left lung, intubation was performed with a double-lumen endotracheal tube. Patients were placed in the left helical position on a vacuum beanbag. A left lateral thoracolaparotomy with diaphragmatic detachment and retroperitoneal dissection was used to obtain access. After systemic heparinization, extracorporeal circulation was established via femoro–femoral access, and the patient was cooled to 32°C. The descending aorta was reconstructed from proximal to distal with a Dacron graft prosthesis (Unigraft; Braun). During the early years of our experience, the thoracoabdominal aorta was replaced using a straight Dacron prosthesis and the visceral arteries were reimplanted as an island. More recently, we prefer a 4-branched Dacron prosthesis to reconnect the visceral arteries.
individually. Intercostal arteries were reimplanted depending on the size and backflow. After the operation, patients were transferred to the intensive care unit. Patients underwent early wake-up trial for neurological assessment. If low-risk patients who did not undergo preoperative cerebrospinal fluid drainage placement showed symptoms of spinal cord injury, they received emergent cerebrospinal fluid drainage.

**Statistical Analysis**

Data analysis was done using SPSS 26 Statistics software (IBM Corp). Normal distribution of variables was analyzed via the Kolmogorov–Smirnov test. Normally distributed continuous variables are stated as mean ± standard deviation, whereas continuous variables without normal distribution are stated as median and interquartile range. Kaplan–Meier analysis was used for evaluating survival and aortic reoperation.

**RESULTS**

**Preoperative Patient Demographic Characteristics**

The preoperative patient characteristics are presented in Table 1. The mean age of patients at the time of surgery was 39.5 ± 10.7 years. Most of our cohort was male (n = 36; 60%). Of our cohort, 49 patients (82%) had previously undergone cardiac surgery and 3 (5%) patients presented with endoleak after previous thoracic EVAR (TEVAR) or EVAR. Aortic dissection was present in 50 (83%) patients, and aortic aneurysm in 10 (17%). Fifty-seven procedures (95%) were scheduled electively and 3 patients (5%) underwent an emergency surgery. The extent of aortic repair is summarized in Table 2.

**Intraoperative Data**

Intraoperative data are summarized in Table 2. The mean operation time was 374.1 ± 126.8 minutes. Of all cases, 2 (3%) involved left heart bypass and 10 (17%) involved hypothermic circulatory arrest. Cerebrospinal fluid drainage was used in 13 patients (22%) and selective renal artery perfusion in 22 cases (36.7%). Lumbal artery reinsertion was performed in 32 patients (53%) and visceral artery bypass was used in 9 patients (15%). Extraction of previous stent graft was performed in 4 (7%) patients (2 TEVAR, 2 EVAR) and completed with aortic replacement.

**Early Postoperative Outcome**

The postoperative outcome is shown in Table 3. Prolonged mechanical ventilation (>96 hours) was necessary in 10 patients (16.7%), and 6 (10%) patients required tracheostomy. Postoperative bleeding complications requiring surgical revision occurred in 5 patients (8.3%). Permanent paraplegia was present in 1 (1.7%) patient, and permanent paraparesis in 2 (3.3%). Two patients suffered from stroke (3%). Six patients (10%) developed acute renal failure necessitating temporary dialysis in 3 patients (5%). At discharge, only 1 (2%) patient required dialysis. The 30-day mortality rate was 3% (n = 2). The first patient who died was a 40-year-old woman with mega-aortic syndrome. She underwent composite aortic root replacement and total aortic arch replacement with elephant trunk as a cardiac redo operation initially in our hospital, and had acute rupture of the descending aorta on the sixth postoperative day. She was brought emergently to the operating room with cardiopulmonary reanimation and thoracoabdominal aortic replacement was carried out. However, the patient died on the same day due to myocardial failure. The second patient was a 32-year-old woman with severe obesity (body mass index of 44) and status postaortic valve-sparing root replacement (David) at our center at the age of 20 years.

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**TABLE 1. Preoperative patient demographic characteristics (N = 60)**

| Characteristic | Value |
|---------------|-------|
| Male sex      | 36 (60) |
| Age, y        | 39.5 ± 10.7 |
| Height, cm    | 186 (180-190) |
| Weight, kg    | 87.7 ± 22.6 |
| Endoleak      | 3 (5) |
| Stent dislocation | 0 (0) |
| Previous cardiac surgery | 49 (82) |

**Extent of disease**

| Extent of disease | Value |
|-------------------|-------|
| Crawford I        | 17 (28) |
| Crawford II       | 18 (30) |
| Crawford III      | 22 (37) |
| Crawford IV       | 2 (3) |
| Crawford V        | 1 (2) |

**Aortic pathology**

| Aneurysm | 10 (17) |
| Acute dissection | 2 (3) |
| Subacute dissection | 2 (3) |
| Chronic dissection | 46 (77) |

**Type of dissection**

| DeBakey I | 26 (43) |
| DeBakey II | 16 (27) |

**Status of operation**

| Elective | 57 (95) |
| Emergent | 3 (5) |

Data are presented as n (%), median (interquartile range), or mean ± SD.
She underwent thoracoabdominal aortic replacement and infrarenal aorto–bi-iliac replacement. She suffered from intracranial hemorrhage due to cerebral aneurysm rupture and died on postoperative day 3.

Late Outcome

The follow-up was complete for 95% of all patients and comprised a total of 512 patient-years. The Kaplan–Meier survival curve is shown in Figure 2. The 1-, 5-, and 10-year survival rates were 87%, 80%, and 68%, respectively. The causes of late deaths were: 1 patient underwent redo mitral valve surgery 357 days after descending aortic replacement and died postoperatively due to cardiac failure. One patient died because of hemorrhagic shock due to gastrointestinal bleeding 337 days after descending aortic replacement, and 1 patient died from multiorgan failure 635 days after the index surgery. The causes of death in all other patients are unknown.

During a median follow-up time of 21.5 (range, 9.4-33.6) years, a total of 16 aortic reinterventions were performed in 9 patients. The Kaplan–Meier survival curve for freedom from reintervention is shown in Figure 3. The freedom from aortic reintervention at 1, 5, and 10 years was 96%, 70%, and 68%, respectively. The aortic reinterventions were: 1 ascending aortic replacement combined with aortic valve replacement, mitral valve surgery and left internal mammary artery bypass, 1 conventional total aortic arch replacement, 4 total aortic arch replacements with the frozen elephant trunk procedure, 3 descending aortic replacements, 2 TEVAR, 1 infrarenal aortic replacement, 2 abdominal EVAR, 1 renal bypass due to insufficiency of the anastomosis, and 1 aorta–subclavian bypass.

**DISCUSSION**

Thoracoabdominal aortic replacement remains a complex procedure but this study showed that this operation can be done extremely safely in Marfan patients. Our study showed very low perioperative mortality rates, and enduring long-term outcomes. Many Marfan patients require aorta-related reinterventions, however. Because EVAR is not recommended for patients with connective tissue disease, open surgery remains an important cornerstone of therapy.

Marfan patients have an increased risks for morbidity and mortality if history of complex aortic disease is present.³ Open thoracoabdominal aortic repair remains the treatment of choice with good outcomes and associated with a low reintervention.¹⁶

Coselli and colleagues¹⁰ reported 4% mortality in 127 patients with Marfan syndrome who underwent thoracoabdominal aortic repair. Similarly, Omura and colleagues¹⁷ reported no in-hospital mortality in their experience of thoracoabdominal aortic repair in 20 patients with Marfan syndrome. Ghanta and colleagues¹⁸ reported no deaths with in 30 days of operations. With an early mortality rate

**TABLE 2. Intraoperative data (N = 60)**

| Characteristic                        | Value             |
|---------------------------------------|-------------------|
| Operation time, min                   | 374.1 ± 126.8     |
| CPB time, min                         | 173.9 ± 84.7      |
| Crossclamps time, min                 | 111.7 ± 66.6      |
| **Extent of repair**                  |                   |
| I                                     | 19 (32)           |
| II                                    | 14 (23)           |
| III                                   | 21 (35)           |
| IV                                    | 4 (7)             |
| V                                     | 2 (3)             |
| Reversed elephant trunk               | 2 (3)             |
| (Frozen) elephant trunk completion    | 9 (15)            |
| Lumbar artery reinsertion             | 32 (53)           |
| Visceral artery bypass                | 9 (15)            |
| Cerebrospinal fluid drainage          | 13 (22)           |
| Left heart bypass                     | 2 (3)             |
| Hypothermic circulatory arrest        | 10 (17)           |
| Extraction thoracic stent graft       | 2 (3)             |
| Extraction abdominal stent graft      | 2 (3)             |

Data are presented as n (%) or mean ± SD. CPB, Cardiopulmonary bypass.

**TABLE 3. Early postoperative outcome**

| Characteristic                        | Value             |
|---------------------------------------|-------------------|
| Intensive care unit stay, d           | 3 (2-7)           |
| Mechanical ventilation time, d        | 0.8 (0.5-2.0)     |
| Tracheostomy                          | 6 (10)            |
| Stroke                                | 2 (3)             |
| Paraparesia                           |                   |
| Temporary                             | 1 (1.7)           |
| Permanent                             | 1 (1.7)           |
| Paraparesia                           |                   |
| Temporary                             | 0 (0.0)           |
| Permanent                             | 2 (3.3)           |
| Chylothorax                           | 0 (0)             |
| Left vocal cord paralysis             | 3 (5)             |
| Bleeding                              | 5 (8)             |
| Acute kidney failure                  | 6 (10)            |
| Dialysis                              |                   |
| Temporary                             | 3 (5)             |
| Permanent                             | 1 (1.7)           |
| Myocardial infarction                 | 0 (0)             |
| Extracorporeal membrane oxygenation   | 1 (1.7)           |
| 30-Day mortality                      | 2 (3)             |

Data are presented as n (%) or median (interquartile range).
of 3%, our study showed comparable results. We believe that the relatively young age at the time of the operation contributed to the low mortality rate. It has been previously shown that younger patients have a lower perioperative risk when undergoing thoracoabdominal aortic repair.11

Although neurological complications including stroke, paraplegia, and paraparesis represent catastrophic events, most studies show that the incidence of these complications is relatively low after thoracoabdominal aortic repair in Marfan syndrome patients.5,17,19,20 Our study showed a very low incidence of permanent paraplegia (n = 1; 1.7%) and permanent paraparesis (n = 2; 3.3%) due to spinal cord ischemia. These results seem to be acceptable, especially against the background that some studies report spinal cord ischemia of up to 14% after descending aortic/thoracoabdominal aortic replacement.21 The incidence of stroke (n = 2; 3%) was low as well in our study. Neurological complications can be an issue, because previous studies reported stroke rates of up to 5%.22

Acute renal failure is not uncommon after complex thoracoabdominal aortic repair. Six patients in our study (10%) developed acute renal failure postoperatively. Four patients required dialysis (6.6%) and 1 patient (1.7%) required permanent dialysis. These results are comparable with other studies published previously.10 We think that renal protection is of great importance to minimize the risk of renal failure.

Our study investigated the long-term survival, too. The 1-, 5-, and 10-year survival rates were 87%, 80%, and 68%, respectively. Although our patient cohort had a relatively young age at the time of initial surgery, Marfan patients have a reduced life expectancy. This might explain the acceptable but reduced survival rates. The causes of death are known in 3 patients, but are unknown in the remaining patients. This is because of the retrospective character of this study and represents another minor limitation.

In our study, 16 aortic reinterventions were necessary during follow-up. This underlines that patients with connective tissue disease are not cured after aortic replacement, but have a lifelong elevated risk for vascular (re-)operation with associated periprocedural risks. One might have expected an even higher number for aortic reoperation at other aortic segments. With regard to this, we mention that most of our patient cohort had already undergone a cardio (vascular) procedure in the past, mostly for acute aortic type A dissection. In these patients, the aortic root/ascending aorta had already been addressed. Also, some of the patients in the present study might have had an enlarged distal aorta, but died before reaching a diameter necessitating aortic repair.

EVAR in patients with Marfan syndrome is still controversial with little experience and lack of mid- and long-term follow-up studies. Kölbl and colleagues4 presented a series of 24 Marfan patients who underwent endovascular repair or hybrid procedures with a follow-up time of
42 months. The early mortality was 4%, and the survival was 87% at 24 months. The freedom from reintervention at 12 months was 77%. On the contrary, a small study with 6 patients and a follow-up time of 51 months showed that open surgical repair was necessary in 2 patients, and a third patient was considered for surgery. Further, 1 patient died 12 months after endovascular repair. These data show that endovascular therapy is not an enduring solution for Marfan patients. As endovascular therapies improve, it might be an option in the future but not at present. However, it can be a bailout strategy in emergent situations. For instance, our group has published a study on the surgical management of patients with native and prosthetic graft infection of the thoracic aorta. In this study, some patients underwent emergent endovascular stent graft placement because of aortic rupture or fistula formation as a bridge to open surgical repair. Similarly, we think that endovascular therapy could be an option in urgent situations for patients with connective tissue disorders. For these reasons, we think that open surgical replacement remains the preferred choice of therapy for Marfan patients with thoracoabdominal pathologies.

CONCLUSIONS
We believe that open surgical repair remains the gold standard of treatment for the thoracic and thoracoabdominal aorta in patients with Marfan syndrome. This study showed that open surgical repair in modern times can be performed with extremely low perioperative risks. We think that endovascular repair in connective tissue disease can be considered for emergent bailout situations, for instance, as bridge to open repair. However, endovascular repair still remains to show enduring long-term outcome in Marfan patients.

Conflict of Interest Statement
The authors reported no conflicts of interest.

The Journal policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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**Key Words:** thoracoabdominal aortic repair, descending aortic repair, Marfan syndrome