

# Stent Grafting of Dissected Descending Aorta in Patients With Marfan's Syndrome

## Mid-Term Results

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**Objectives** This study sought to assess the safety and the effectiveness of endovascular stent grafting of chronic aortic dissection (AD) in Marfan patients.

**Background** The management of chronic AD of the descending thoracic aorta (DTA) is challenging. This is especially true in Marfan patients, who tend to exhibit poor short- and long-term results after conventional surgery.

**Methods** Fifteen patients with Marfan's syndrome and chronic AD of the DTA were identified among the 457 patients of the European Talent Registry. All patients underwent endovascular treatment.

**Results** No major adverse event was encountered during the procedure. Five patients experienced a primary endoleak (type 1, n = 4; type 2, n = 1). Three of them died, and 1 underwent successful conversion to open surgery. Five other patients experienced secondary endoleak (type 1, n = 4; type 3, n = 1). Four of them underwent successful conversion to either open or endovascular reintervention. Two other patients underwent successful conversion to open repair because of secondary aortic enlargement below the stent graft. After a mean follow-up of  $2.1 \pm 1.4$  years, 12 patients are alive. Of these 12, conversion to open repair was successfully performed in 5 patients. In the remaining 7 patients, complete thrombosis of the false lumen was achieved in 6 patients, with partial thrombosis in 1 patient.

**Conclusions** Endovascular stent grafting of the dissected DTA is feasible in selected Marfan patients with low mortality and morbidity rates. Nevertheless, the rate of primary and secondary endoleak is high. Close imaging surveillance is crucial to detect secondary aortic complications and to assess long-term results. (*J Am Coll Cardiol Intv* 2008;1:673–80) © 2008 by the American College of Cardiology Foundation

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The aim of this work was to assess the safety and the effectiveness of thoracic aortic endovascular stent grafting in Marfan patients. Fifteen patients with chronic aortic dissection (AD) underwent endovascular treatment. After a mean follow-up of  $2.1 \pm 1.4$  years, 12 patients are alive. Five of these underwent successful conversion to open repair. In the remaining 7 patients, complete thrombosis of the false lumen was achieved in 6 patients and partial thrombosis in 1 patient. Endovascular stent grafting of the dissected descending thoracic aorta (DTA) is feasible in Marfan patients with low mortality and morbidity rates. Nevertheless, the rate of primary and secondary endoleak is high.

Marfan's syndrome is an autosomal dominant pathology of the connective tissues caused by mutations of the fibrillin gene located in chromosome 15q. Mutant fibrillin is synthesized with the inability to bind calcium and weakening of the elastic layers of connective tissue (1). In Marfan patients, aortic disease is characterized by progressive dilatation of the aortic root and annulus, aortic valve incompetence, and increased risk of proximal AD or rupture (1-3).

Unlike aortic root surgery in Marfan patients, which is well codified and may be routinely performed electively or emergently, the management of the dissected DTA is still challenging (4). In cases of uncomplicated AD of the DTA, medical treatment remains the best therapeutic option. However, aneurysmal dilatation of the descending aorta is a frequent critical late complication responsible for poor long-term outcomes (1,2). To prevent aortic rupture, lifelong close clinical and imaging follow-up is essential to determine the best timing for intervention (5-8).

Endovascular stent grafting has recently been reported as a safe and effective therapeutic option for patients with dissection of the DTA, with favorable results when compared with conventional open surgery results. This is especially true in the case of chronic AD (8,9). Stent grafting in Marfan patients has been reported in small series or case reports, providing controversial results (10-12). The aim of this study was to assess the mid-term results of aortic stent grafting in patients with Marfan's syndrome. Patients were retrospectively pulled from the cohort of 457 patients who underwent stent graft repair in 7 European centers.

## Methods

**Population.** The entire cohort study consisted of 457 consecutive patients who underwent endovascular thoracic aortic repair with the Talent Thoracic Stent Graft (Medtronic, Minneapolis, Minnesota). Seven European referral centers

(Bologna, Italy; Toulouse, Lille, and Marseille, France; Rostock, Germany; Vienna, Austria; Nieuwegein, the Netherlands) provided data from patients consecutively treated with the Talent Thoracic Stent Graft between November 1996 and March 2004 (13). The ethical committee of each institute approved the study. Data were prospectively collected on case report forms and entered in databases. Case report forms were all reviewed and checked for inconsistencies. In cases of discrepancies, the participating investigator at each site was asked to ensure appropriate interpretations of events.

**Patient characteristics and imaging evaluation.** Of the entire cohort, patients with Marfan's syndrome and chronic dissection of the DTA were retrospectively extracted for this study. All the patients presented with an aneurysmal dilatation of the DTA (defined as a diameter over 40 mm and rapid aortic enlargement of more than 0.5 cm within a period of 6 months). These patients were considered high risk, thus favoring intervention. All were treated with stent grafts.

Before treatment, all patients were examined by computed tomography or magnetic resonance imaging, in addition to angiography or transesophageal echocardiography (Fig. 1). Morphological data on maximum aortic diameter, proximal and distal anatomic extension of the lesion, and distance from the entry of the AD to the ostium of the left subclavian artery were recorded. Information on the procedure (number of stent grafts used, aortic covered length, and immediate angiographic results) was also recorded.

Follow-up analysis was performed on clinical and imaging findings until the last visit date and included all adverse events. Clinical and imaging follow-up was performed in each center according to accepted guidelines. Follow-up consisted of a standard chest X-ray and contrast-enhanced spiral-computed tomography or magnetic resonance imaging before discharge and at 3, 6, and 12 months after the intervention. The same imaging, as well as clinical follow-up, was performed annually thereafter. In case of rapid aortic enlargement of more than 0.3 cm within a 1-year period, subsequent imaging and clinical follow-up was performed at 3-month intervals.

**Device description and endovascular procedures.** The endovascular Talent device was used as previously described (13). Stent grafts were 5% to 10% oversized in comparison to the diameter of the normal aorta and were at least 30 to 40 mm longer than the lesion.

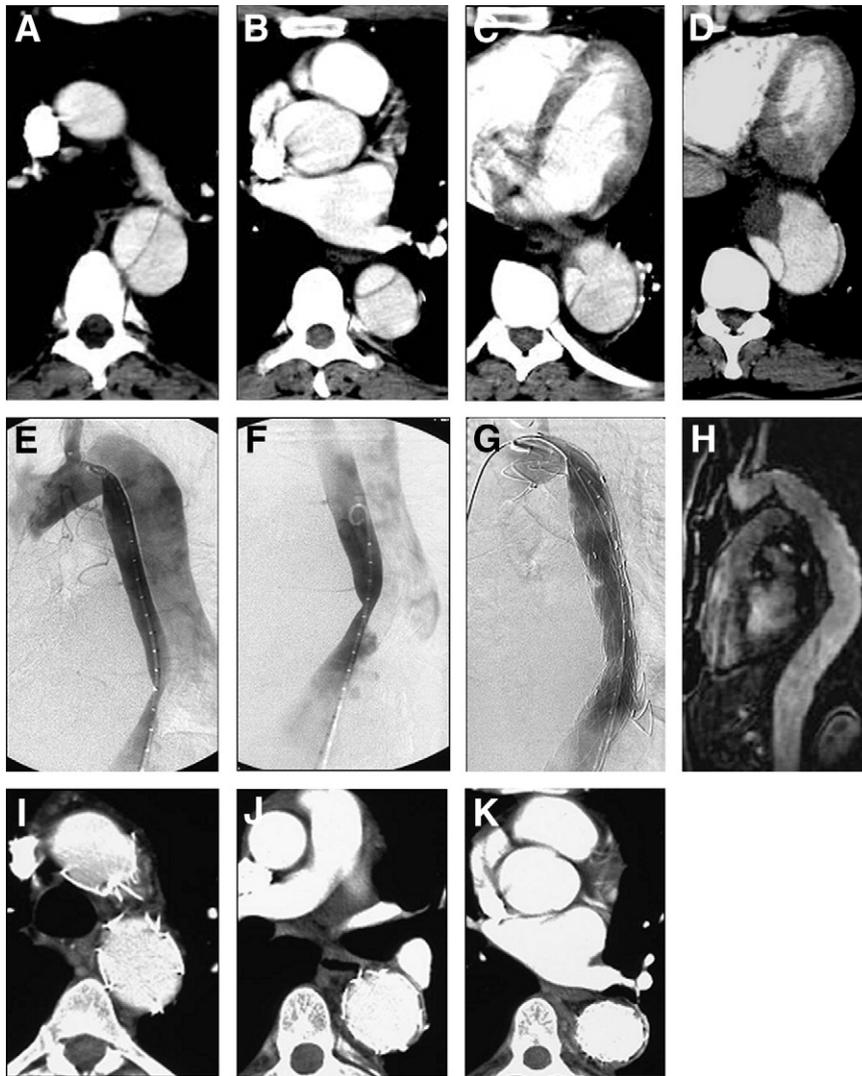
**Statistical analysis.** Incidence rates of events are reported by the number of patients experiencing the event, followed by the corresponding percentage. Continuous data are reported by giving the mean  $\pm$  SD and/or median (minimal and maximal values). Several factors were specifically analyzed: age, gender, pre-operative American Association of Anesthesiologists (ASA) score, history

### Abbreviations and Acronyms

AD = aortic dissection

ASA = American Association of Anesthesiologists

DTA = descending thoracic aorta



**Figure 1.** Imaging of Chronic Aortic Dissection of the Descending Thoracic Aorta

(A to D) Spiral computed tomography shows a chronic aortic dissection of the descending thoracic aorta in a patient with Marfan's syndrome. (E to G) Perioperative angiographic images show the proximal edge of the device distal to the left carotid artery ostium, with complete exclusion of the entry tear and the false lumen. (H) Magnetic resonance imaging demonstrates the exclusion of the false lumen 1 year after the procedure. (I to K) Spiral computed tomography demonstrates the exclusion of the entry tear and the false lumen 2 years after the procedure.

of aortic root surgery, maximal aortic diameter, extension of the AD below the diaphragm, number of deployed stent grafts, coverage of the left subclavian artery, emergency setting, and covered aortic length. These factors were analyzed to assess their potential influence on outcomes, including endoleak, reintervention (endovascular or open), conversion to open surgery, and death. The bilateral Fisher exact test was used to assess qualitative variables, and the nonparametric Wilcoxon test was used to assess quantitative variables. Statistical analyses were carried out with SAS software, version 9.1 (SAS Institute, Cary, North Carolina).

## Results

From November 1996 through March 2004, 15 patients (11 males) with Marfan's syndrome were identified as part of the European Multicenter Talent Thoracic Registry.

**Pre-operative data.** All the patients presented with a chronic dissection of the DTA. Two patients were treated urgently because of an impending rupture of the dissected DTA (hemodynamically stable). The remaining 13 patients presented with a progressive dilatation and were treated electively (Table 1).

**Table 1. Pre-operative Characteristics of the Patients**

<b>Patients</b>	
Age mean $\pm$ SD, yrs	38.7 $\pm$ 12.8
Male/female ratio	9:3
Pre-operative ASA score, mean $\pm$ SD	2.9 $\pm$ 2.5
<b>Comorbidities, n</b>	
Diabetes	1
Hypertension	7
Chronic renal failure	5
Chronic obstructive pulmonary disease	6
<b>Aortic disease, n</b>	
Chronic aortic dissection of the thoracic descending aorta	12
Progressive aortic enlargement	13
Impending rupture	2
Mean aortic diameter, mm	57.5 $\pm$ 26.8
<b>Past history of surgery of the aortic root, n</b>	
Bentall	9
Aortic valve sparing surgery	2
ASA = American Association of Anesthesiologists; SD = standard deviation.	

Mean age was  $40 \pm 12$  years (range 22 to 61 years). Mean ASA score was  $2.9 \pm 0.2$ . The main comorbidities were hypertension (n = 7), chronic pulmonary obstructive disease (n = 6), chronic renal failure (n = 5), and diabetes mellitus (n = 1).

Eleven patients had previously undergone aortic root surgery (Bentall procedure: n = 9; Tyrone-David procedure: n = 2). For those patients, the mean time between surgery of the ascending aorta and stent grafting of the DTA was  $5.7 \pm 2.9$  years (range 1.5 to 10.7 years).

The pre-operative morphologic assessment showed a mean aortic diameter of  $61.3 \pm 24.7$  mm. The 2 patients

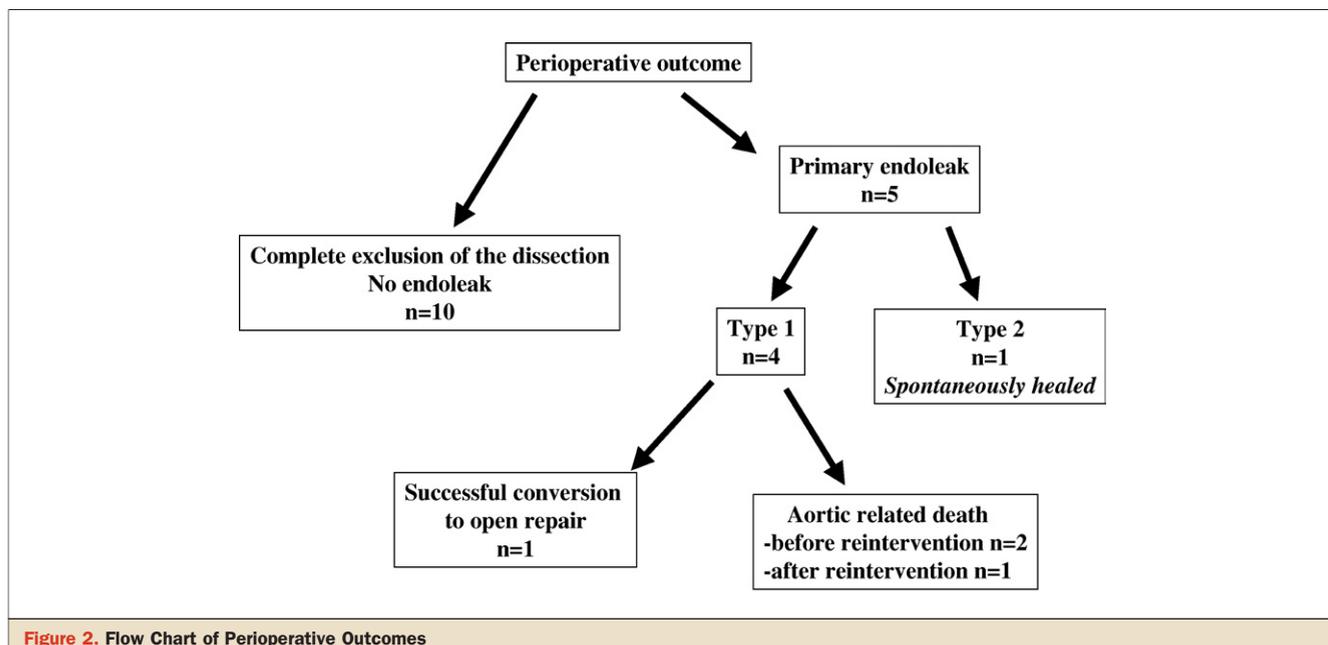
with impending aortic rupture had respective aortic diameters of 33 and 46 mm. Mean pre-operative aortic diameter of the other 13 patients was  $64.6 \pm 25.7$  mm.

The mean distance between the entry tear and the ostium of the left subclavian artery was  $47.7 \pm 30.8$  mm (range 0 to 100 mm). The AD was limited to the DTA in only 2 patients, and the dissection extended below the diaphragm in the remaining 12 patients. One patient had involvement of the aortic arch and the DTA.

**Perioperative data.** Transfemoral stent graft deployment was uneventful and technically successful in all the patients. An average of  $1.5 \pm 0.7$  stent grafts was used (range 1 to 3 stent grafts). The ostium of the left subclavian artery had to be covered in 2 patients. No deaths occurred, and no conversion to open surgical intervention was required during the procedures. No patient sustained paraplegia, and 1 patient presented with a transient hemispheric stroke. The mean duration of hospital stay was  $14.4 \pm 13$  days (Fig. 2).

Post-deployment angiography demonstrated the exclusion of the false aneurysms without endoleak in 10 patients.

Primary endoleaks were seen in 5 patients (type 1, n = 4; type 2, n = 1). Two patients with type 1 primary endoleaks died of rupture of the descending aorta (n = 1, post-operative day 274) or of the abdominal aorta (n = 1, post-operative day 335) before reintervention. Another patient with a type 1 primary endoleak died after endovascular reintervention (n = 1, 2.8 years after the initial procedure). One patient with a type 1 primary endoleak underwent successful secondary conversion to open surgery (n = 1, 1 month after the endovascular procedure). The primary type 2 endoleak (from an intercostal artery) spontaneously healed.



**Figure 2. Flow Chart of Perioperative Outcomes**

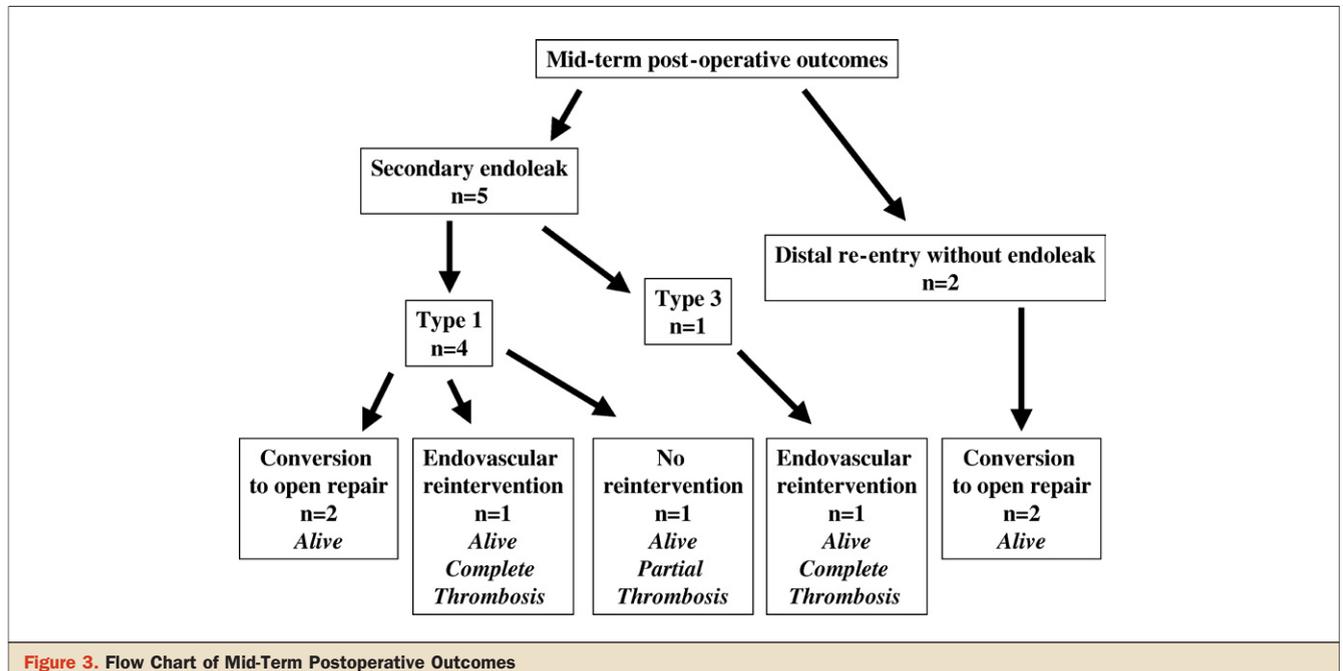


Figure 3. Flow Chart of Mid-Term Postoperative Outcomes

**Mid-term post-operative data.** Five other patients presented with secondary endoleaks (type 1, n = 4; type 3, n = 1). Two patients with secondary type 1 endoleaks underwent successful secondary conversion to open repair (n = 2, 3.7 and 5.2 years after the endovascular procedure). One patient with a secondary type 1 endoleak underwent successful endovascular reintervention (n = 1, 1 month after the endovascular procedure). One mild secondary type 1 endoleak was observed with partial thrombosis of the false lumen. The patient with a secondary type 3 endoleak underwent successful secondary endovascular reintervention (n = 1, post-operative month 9). Two other patients presented with secondary aortic enlargement below the stent graft because of a persistent celiac entry. Both underwent successful conversion to open thoracic aortic replacement (n = 2, 0.2 and 3.1 years after the endovascular procedure) (Fig. 3).

Table 2 presents the peri- and post-operative patient characteristics and outcomes. Patients with primary endoleaks had significantly longer covered aortic segments (p = 0.05). Also, large aortic diameter was found to be a borderline predictive factor for reintervention (p = 0.06). The other statistical tests did not achieve significance.

Follow-up (before discharge; at 3, 6, and 12 months; and every subsequent year) was performed in all the patients. After the first yearly visit, the imaging and clinical follow-up periods for 2 patients were reduced to 3-month intervals because of rapid enlargement of the dissected DTA (between 0.3 and 0.5 mm over 12 months). Overall, mean time interval between the last visit and the outcome event was 1.7 ± 1 months.

Mean follow-up for the cohort was 2.1 ± 1.4 years (range 0.8 to 4.9 years). Twelve patients are still alive. Conversion to open repair was required and was successful in 5 patients. In the remaining 7 patients, complete thrombosis of the false lumen was achieved in 6 patients and partial thrombosis with stable aortic diameter was achieved in 1 patient.

In summary, for the cohort of 15 patients, 7 are alive with partial or complete false lumen thrombosis, 5 are alive after a conversion to open surgery, and 3 are dead.

Seven living patients underwent a secondary procedure (open or endovascular).

## Discussion

In patients with Marfan's syndrome, AD with rupture has long been the main cause of death, even in younger patients. Modern surgical techniques of ascending aortic repair have been essential for improving patient prognoses. Bentall procedures or aortic root reconstruction are currently electively performed with acceptable morbidity and mortality rates.

Unlike in aortic root surgery, which is well codified and may be routinely performed on patients with Marfan's syndrome, management of the dissected DTA is still challenging. This is especially true in cases involving aneurysmal dilatation (1,4,14). In contrast with the excellent surgical results of elective root replacement, both early and long-term results of repeat surgery for the descending aorta remain poor (15). De Olivera et al. (16) reported on 6 surgical repairs of the DTA after previous valve-sparing operations. In this series, 3 patients died after surgical repair

**Table 2. Peri- and Post-operative Characteristics of the Patients and Outcomes**

	Primary Endoleak		Secondary Endoleak		Reintervention		Open Conversion		Death	
	Yes (n = 5)	No (n = 10)	Yes (n = 5)	No (n = 10)	Yes (n = 4)	No (n = 11)	Yes (n = 5)	No (n = 10)	Yes (n = 3)	No (n = 12)
Age, yrs*	35 [22–52]	43 [24–61]	44 [24–61]	33 [22–52]	46 [22–52]	32 [22–61]	32 [22–61]	43 [27–52]	35 [27–47]	43 [22–61]
Female, n (%)	1 (20)	3 (30)	1 (20)	3 (30)	1 (25)	3 (27)	0 (0)	4 (40)	1 (33)	3 (25)
ASA score*	3 [3–3]	3 [2–3]	3 [3–3]	3 [2–3]	3 [3–3]	3 [2–3]	3 [3–3]	3 [2–3]	3 [3–3]	3 [2–3]
Prior aortic root surgery, n (%)	3 (60)	8 (80)	4 (80)	7 (70)	4 (100)	7 (64)	4 (80)	9 (90)	2 (67)	9 (75)
Aortic diameter, mm*	46 [39–92]	56 [33–136]	55 [40–70]	56 [33–136]	68 [58–92]†	54 [33–136]†	55 [40–60]	62 [33–136]	70 [39–92]	55 [33–136]
Extension below the diaphragm, n (%)	4 (80)	9 (90)	5 (100)	8 (80)	4 (100)	9 (82)	5 (100)	8 (80)	3 (100)	10 (83)
Number of stent grafts <1, n (%)	4 (80)	1 (10)	0 (0)	5 (50)	1 (25)	4 (36)	2 (40)	3 (30)	2 (67)	3 (25)
Coverage of the left subclavian artery, n (%)	1 (20)	1 (10)	0 (0)	2 (20)	0 (0)	2 (18)	1 (20)	1 (10)	0 (0)	2 (17)
Emergency setting, n (%)	1 (20)	1 (10)	0 (0)	2 (20)	0 (0)	2 (18)	1 (20)	1 (10)	0 (0)	2 (17)
Aortic length covered, mm*‡	180 [150–200]§	125 [60–200]§	100 [60–134]	165 [130–200]	117 [100–134]	135 [60–200]	130 [60–200]	134 [100–180]	150 [150–150]	132 [60–200]

\*Median (minimal and maximal value); †p = 0.06; ‡data for aortic length covered were available for 11 patients; §p = 0.05. Percentages are given to describe the population. These should be interpreted with caution because of the small number of patients. Only significant tests are shown in the table; other test results did not achieve significance.  
Abbreviation as in Table 1.

of the descending aorta, 1 sustained post-operative paraplegia, and 2 survived to surgery without complication (16). Further, Alexiou et al. (17) reported a mortality rate of 33% in Marfan patients undergoing secondary surgery of the DTA. Gott et al. (18) reported 30.8% mortality among 26 patients subjected to a secondary surgical procedure for progressive disease or dissection. In a larger study focusing on long-term data, 63 of 653 Marfan patients with previous aortic root replacement required late surgery, and only 46 patients were still alive at the last follow-up (5).

Endovascular stent grafting has recently been reported as a valuable alternative therapeutic option to conventional open surgery for patients with dissection of the DTA (8,19,20). The results appear promising, especially in comparison with the poor results of conventional open surgery. This is also true in cases involving chronic AD (9,15). Nevertheless, the English literature concerning stent grafting in Marfan patients is scarce (10–12).

Our study represents the largest literature-reported series that assessed early and mid-term results of stent grafting in Marfan patients, specifically those with an aneurysmal enlargement in the setting of a chronic thoracic descending AD.

This series demonstrates the technical feasibility of stent graft repair in Marfan patients with chronic dissection of the DTA compared with patients with similar thoracic disease but without Marfan's syndrome (13). The

endovascular devices were successfully deployed in all the patients; no patient died perioperatively; there were no perioperative conversions to open repair; and limited complications were observed. In particular, no patients presented with paraplegia, demonstrating the ability of endovascular procedures to preserve the integrity of the aorta.

Our series also points out the limitations of endovascular procedures in Marfan patients. The rate of primary endoleak (33%) was higher in Marfan patients than in patients without Marfan's syndrome (21.4%) (13). In longer covered aortic segments, the potential risk for primary endoleak was higher. In addition, large aortic diameter was a borderline predictive factor for reintervention. Because of the limited number of patients included in this analysis, other statistical tests were not significant. For the same reason, these results should be interpreted with caution, and definitive conclusions regarding good or bad candidates for endovascular repair may be premature. The high rate of primary and secondary endoleaks may constitute a major problem in these patients. This higher rate is probably related to the fragility of the tissues in Marfan's syndrome. However, it is important to consider that these cases were treated several years ago, at the beginning of the dissection endovascular experience, using a first-generation thoracic device. It is possible that more experience, improved imaging assessment, and better device conformability could mitigate the negative long-term outcomes of endovascular treatment.

These primary endoleaks, especially primary type 1 endoleaks, appear to be more severe in Marfan patients, with 3 aortic-related deaths before reintervention (of 5 primary endoleaks). The poor outcomes in cases of primary type 1 endoleaks underline the necessity for quick and aggressive management of such endoleaks in Marfan patients. This also supports the necessity for closer imaging and monitoring.

The secondary endoleaks were also more frequent in Marfan patients than in the non-Marfan's population, with a 3-fold higher rate of such events (33% vs. 10.4%) (13). Secondary type 1 endoleaks were encountered in 4 patients. Two patients underwent successful conversion to open repair because of aortic enlargement, and 2 secondary type I endoleaks spontaneously healed. No aortic-related complications occurred in these patients with secondary type 1 endoleaks.

As in the non-Marfan's population, another problem in repair of AD of the DTA was encountered. Two patients presented with aortic enlargement below the stent grafts without evidence of endoleak. These aortic enlargements were due to the presence of a re-entry tear at the level of the celiac artery. Both required secondary conversion to open repair.

Despite these limitations of aortic endovascular treatment in Marfan patients, 12 patients were alive after a mean follow-up of  $2.1 \pm 1.4$  years. Conversion to open repair was required and successful in 5 patients. Like the findings of Ince et al. (12), this point suggests that stent grafting could be considered as a safe therapeutic option as a bridge to surgery in case of acute aortic syndrome complicating a chronic AD. All the secondary conversions to open repair were successfully performed, and the open procedure was not made more difficult by the presence of an intra-aortic device. In the remaining 7 patients, complete thrombosis of the false lumen was achieved in 6 patients, and partial thrombosis with stable aortic diameter was achieved in 1 patient. These encouraging outcomes in 7 patients highlight the potential applicability of endovascular therapy in Marfan patients, especially in emergency cases. Longer follow-up is still mandatory to assess the effectiveness of aortic stent grafting in such patients.

**Study limitations.** This study has several limitations: 1) data were prospectively collected but retrospectively analyzed, 2) the depth of the statistical analysis was limited because of the relatively small number of patients included in this study, 3) the comparison with conventional surgery is limited, as results could only be compared with historical studies of open repair, and 4) this study only included patients treated exclusively with the Medtronic Talent Thoracic Stent Graft, and it is not possible to evaluate the performance of other devices in this cohort.

## Conclusions

Although the cohort size was limited, this study demonstrates the feasibility of stent grafting in Marfan patients with chronic dissection of the DTA. Immediate outcomes were favorable, without increased perioperative mortality rates. However, the rate of primary and secondary endoleaks is high compared with the rate of endoleaks in patients who do not have Marfan's syndrome. This is probably due to the fragility of the aortic tissues in Marfan patients. Closer imaging surveillance is crucial to detect secondary aortic complications to enable aggressive treatment of endoleaks. Stent grafting can also be considered a therapeutic option as a bridge to conventional open surgery in situations involving acute aortic syndrome or expansion of the false lumen in chronic AD.

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**Key Words:** aorta ■ stent graft ■ endovascular ■ Marfan's ■ aortic dissection ■ acute aortic syndrome.