

Endovascular management of chronic aortic dissection in patients with Marfan syndrome

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Introduction: Marfan syndrome patients are prone to aortic dilatation, dissection, and rupture. Success of aortic root replacement has generated a cohort of patients surviving longer and presenting with distal aortic dissection and enlargement. Thoracic endovascular stent-graft repair (TEVR) is being increasingly utilized to exclude aneurysms resulting from chronic aortic dissection. This report explores the role of TEVR in Marfan patients with this pathology.

Methods: Review of a prospectively maintained database identified seven patients with Marfan syndrome offered endovascular repair of aneurysmal chronic aortic dissection. All patients had previous aortic root repair. Talent or Valiant (Medtronic Vascular, Santa Rosa, Calif) aortic stent-grafts were used to occlude the dissection entry tear and cover the thoracic aorta. Electronic data, case notes, and radiological surveillance were analyzed.

Results: Seven consecutive patients (six male; mean age, 45.9 ± 10 years, range, 29 to 63) underwent successful thoracic stent-graft deployment. Mean aortic aneurysmal diameter was 63.4mm (± 11.2) with six of seven dissections extending to the aortic bifurcation. No perioperative neurological events occurred. Thirty-day mortality was 1/7 (14%) due to congestive cardiac failure. At median 16 month follow-up, two of six cases (33%) required intervention for endoleak. Aortic false lumen thrombosis (FLT) occurred in 5/6 (83%) cases and partial FLT occurred in 1/6 (17%). All thoracic aortas continued to dilate during follow-up. Crude median aortic growth rate was 7.2 mm/year (range, 3.5 to 19 mm).

Conclusion: TEVR in Marfan syndrome patients with chronic aortic dissection is technically feasible. However, post intervention surveillance confirms that the aorta continues to dilate despite graft deployment and false lumen thrombosis. Endovascular repair may offer a viable option in patients who have contraindications to open surgery, but longer follow up of more patients is required to define the place of this therapy. (J Vasc Surg 2009;50:987-91.)

Marfan syndrome is a systemic disorder of connective tissue caused by mutations in the extracellular matrix protein fibrillin 1. Aortic aneurysm and dissection remain the most life-threatening manifestations of this syndrome;¹ without intervention, death occurs in early adulthood. The success of current medical and surgical treatment of Marfan syndrome has substantially improved the life expectancy in this patient population.

Aortic root dilatation is a typical vascular lesion in patients with Marfan syndrome.² Open surgical therapy for proximal aortic disease is well established with excellent long-term results.³ Marfan syndrome is a disease of the whole aorta. Prolonged survival after aortic root surgery has led to a cohort of patients experiencing complications in the aorta beyond their primary surgical repairs.

Endovascular treatment of type B aortic dissections and descending thoracic aneurysms has been utilized in non-Marfan patients. Reports confirm high rates of primary procedural success with limited morbidity and mortality.^{4,5} The IRAD (International Registry of Aortic Dissection) database has reported that 5% of patients undergoing stent graft deployment for thoracic dissection have Marfan syndrome.⁶ However, the utility of endovascular stent grafting

in this relatively young population with complex evolving aortic pathology remains unclear.

Current consensus is that stent grafts should be used with great caution, if at all, to repair aortic dissection in patients with Marfan syndrome or other connective tissue disorders.⁷ The aorta is prone to further dilation making any endovascular solution of limited durability.^{8,9}

PATIENTS AND METHODS

We retrospectively reviewed our institutional aortic database to identify Marfan patients treated at this centre for aneurysmal dilatation of the thoracic aorta. During a five year period, seven consecutive patients (six male; mean age 45.9 ± 10 years, range, 29 to 63 years) presented with aneurysmal degeneration of the thoracic aorta consequent to chronic dissection (Table I). A diagnosis of Marfan syndrome had previously been established in each patient according to the revised Ghent criteria.¹⁰ Patients were not genotyped for specific variants of Marfan syndrome.

All patients had relative contra-indications to open thoracic aortic surgery. These included chronic type II respiratory failure¹¹ secondary to emphysematous changes and diaphragmatic weakness, pleurodesis for recurrent spontaneous pneumothoraces, cerebrovascular disease, and renovascular disease. Five of seven patients were taking warfarin following prosthetic aortic root/valve replacement. They were appropriately counseled and consented for endovascular management.

Prospectively gathered data, including demographic, clinical, and serial imaging of this patient cohort were analyzed. Morphological characteristics of aneurysms with

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Competition of interest: none.

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Table I. Patient details

	<i>Age</i>	<i>Gender</i>	<i>Previous aortic root revision</i>	<i>Time between root and stent (yrs)</i>	<i>Origin of dissection</i>	<i>Extent of dissection (level)</i>	<i>Current situation</i>
1	44	M	Yes	10	LCCA	Aortic bifurcation	Alive
2	48	F	Yes	9	LCCA	Aortic bifurcation	Alive
3	63	M	Yes	4	Mid thoracic aorta	Aortic bifurcation	Alive
4	41	M	Yes	8	LSA	Right common iliac artery	RIP – Congestive cardiac failure
5	55	M	Yes	9	Root anastomosis	Aortic bifurcation	Alive
6	29	M	Yes	3	Root anastomosis	Bronchial carina	Alive
7	41	M	Yes	14	Root anastomosis	Right common iliac artery	RIP* – Congestive cardiac failure

LCCA, Left common carotid artery; LSA, left subclavian artery; RIP, dead.

*Death within 30 days of procedure.

Table II. Procedural detail

	<i>Preceding adjunctive bypass surgery</i>	<i>Graft</i>	<i>Number of stents</i>	<i>Stent deployed into revised aortic root</i>	<i>Ishimaru proximal landing zone¹⁸</i>	<i>Stent coverage (distal landing)</i>	<i>Endoleak warranting treatment within one year</i>
1	C-C-S*	Valiant	3	No	1	Coeliac axis**	No
2	C-C-S*	Talent	3	No	1	Coeliac axis**	No
3	—	Talent	6	No	4	Coeliac axis**	Type 1b
4	3 vessel aortic de-branching	Valiant	4	No	2	Mid-abdomen	No
5	Ascending aorta to selective arch vessels	Valiant	3	Yes	0	Mid-thoracic	Type 3
6	Ascending aorta to selective arch vessels + 2 vessel visceral de-branching	Valiant	3	Yes	0	Mid-abdomen	No
7	Ascending aorta to selective arch vessels + LCCA to LSA bypass	Valiant	5	Yes	0	Coeliac axis**	—

LCCA, Left common carotid artery; LSA, left subclavian artery.

*C-C-S: Right-left carotid-carotid bypass and left carotid-subclavian artery bypass.

**Distal landing proximal just proximal to celiac axis; the vessel was not covered or incorporated.

regard to maximal diameter as well as suitability for thoracic endovascular repair (TEVR) were based on preoperative contrast-enhanced spiral computed tomography (CT). Measurements in this report are based on 3mensio (3mensio Medical Imaging, Bilthoven, The Netherlands) 3-dimensional reconstructions generated from the coronal CT images.

Procedures were performed in the operating room with portable C-arm fluoroscopy (Siemens, Munich, Germany) or in the angiography suite. Follow-up protocol included pre-discharge CT scan then serial review in the outpatient clinic with interval CT angiograms at six weeks, three months, six months, 12 months, and annually thereafter.

All patients had previously had reconstructive aortic root surgery and had stable blood pressure with beta-blockade and/or angiotensin-converting enzyme (ACE) inhibition. Once appropriately consented, all patients were managed by TEVR. Patients underwent endovascular exclusion of the aneurysmal aorta utilizing either Talent or Valiant thoracic aortic stent grafts (Medtronic Vascular, Santa Rosa, Calif). Six of seven patients required additional bypass procedures, including carotid-subclavian, carotid-

carotid bypasses, and aortic de-branching, to allow appropriate stent-graft deployment (Table II).

It is our policy to consider surgery in patients presenting with thoracic aortic dilatation of the arch or descending thoracic aorta of greater than 55 mm, and/or symptomatic. Covered stent-grafts are deployed to occlude the entry tear in dissections; grafts are routinely used to obtain coverage of the entire thoracic aorta to the level of the coeliac axis. Bare stents are not used. Stent-grafts are oversized by 10% to 20% at the proximal landing zone. The sizing of the distal landing zone is more controversial; it remains our policy in these cases to match the distal landing size to the true luminal diameter. We believe that preservation of the left subclavian artery (LSA) is valuable if the morphology of the dissection allows.¹² Additional to this in the perioperative period, mean arterial pressure (MAP) is maintained at >90 mm Hg (using inotropes if required) and spinal drains are sited for 48 hours. Spinal drains are maintained with maximal CSF (cerebrospinal fluid) drainage of 30 mL/hr and clamped if drainage exceeds that rate.

All hybrid aortic de-branching was performed prior to stent deployment in elective cases.

Table III. Changes in aortic morphology and false lumen thrombosis

	<i>Length of follow-up (months) (If > 3/12)</i>	<i>Original aortic diameter (cm)</i>	<i>Aorta at recent follow-up (mm)</i>	<i>FLT at graft</i>	<i>Infra-diaphragmatic FLT</i>
1	28	76	92	Yes	No
2	54	57	73	Yes	No
3	3	48	53	Partial*	Yes**
4	—	52	—	—	—
5	11	60	67	Yes	No
6	16	58	66	Yes	Yes**
7	—	66	—	Yes	—

FLT, False lumen thrombosis.

Measurements taken at maximal external aneurysmal aortic diameter.

*Partial FLT- thrombus visible in false lumen, but also persistent flow.

**AAA stent graft in-situ.

RESULTS

Seven cases have been treated to date; three urgent cases for symptomatic aneurysms with increasing back pain, and four elective for large aneurysms. Mean aortic aneurysmal diameter was 64.4 mm (± 11.2) and mean proximal landing zone diameter was 36.3 mm (± 3.3). In all cases, stent-graft deployment was completed successfully (Table II). No perioperative neurological complications were encountered. A median three (range, two to six) grafts were deployed. Procedures lasted a mean 160 ± 55 minutes (range, 120 to 300 minutes). One patient required reoperation for a groin hematoma at the femoral access vessel. Thirty-day mortality was 1/7 (14%). The peri-operative mortality occurred following discharge. The patient was readmitted to his local hospital where he presented with pneumonia and severe, irreversible cardiac failure. CT scanning revealed an intact stent-graft with no endoleak or coarctation.

All patients were enrolled in a graft surveillance program on discharge. Median follow-up was 16 months (range, 3 to 54 months) in the five patients surviving ≥ 3 months following primary treatment. Two of six (33%) patients developed endoleaks requiring treatment within the first year. One type 1 endoleak and one type 3 endoleak were managed by additional stent graft deployment without complication (Table II). In neither case, at the primary surgery, were manufacturers' recommendations for length of landing zone or graft overlap compromised.

False lumen thrombosis (FLT) was assessed at each surveillance CT scan. Five of six patients showed complete FLT at the level of the stent-grafts during follow-up. One of six patients demonstrated partial FLT. Only patients with additional AAA stent grafts thrombosed their false lumen below the thoracic stents, in the infra-diaphragmatic aorta (Table III).

All patients demonstrated continued thoracic aortic dilatation despite stent graft deployment. Crude median aortic growth rate after graft deployment was 7.2 mm/year (range, 3.5 to 19 mm/year).

Five of seven of the cohort remain alive and under close surveillance. One patient died three months following treatment from congestive cardiac failure.

DISCUSSION

The incidence of Marfan syndrome is around one in 10 000 live births. Progressive aortic dilatation associated with aortic dissection and rupture is the principal cause of mortality. The excellent surgical results of elective aortic root replacement are generating an increasing cohort of patients who present later with an expanding false lumen of the descending aorta. All patients in this series had undergone previous aortic root replacement. The median time from aortic root replacement to presentation with grossly aneurysmal thoracic aorta was nine years (range, 3 to 14 years) in this series.

After successful aortic root replacement, the dissected descending aorta remains a source of late complications in Marfan syndrome.¹³ Elective aortic root replacement^{14,15} and thoracoabdominal aneurysm repair^{16,17} have reported excellent results in Marfan syndrome patients. In contrast, open surgical treatment of proximal descending aortic dissection is associated with significant morbidity. Early mortality can be up to 20% without absolute protection from the requirement for further surgery.¹⁸ These risks escalate if aortic arch replacement is required with increasing risks of stroke.¹⁹ Endovascular stent-graft repair would appear an attractive alternative to open surgery because it is associated with a reduction in morbidity (particularly stroke and spinal cord ischemia) and mortality.²⁰

The experience of endovascular management of the descending thoracic aorta in patients with Marfan syndrome remains limited. Small observational studies have confirmed it to be feasible and relatively safe.²⁰⁻²² This series is the largest to date and corroborates these conclusions. It confirms 100% primary technical success and a 30-day mortality of 1/7 (14%). It is not appropriate to compare the cohort we present with the other three series. In this series, six of seven cases required stent graft deployment into the aortic arch (Ishimaru zones 0-2²³). No cases in the series reported by Ince et al required coverage of the left subclavian artery,²⁰ and the series by Baril et al only included two thoracic aneurysms in Marfan patients.²¹ Treating the more challenging cases involving the aortic arch may be an explanation of our relative greater morbidity and mortality.

Long-term outcome of management of chronic dissections in the general population has been shown to be related to false lumen thrombosis. Continued false lumen patency is associated with increased rupture risk²⁴ and partial FLT has been reported as an independent predictor of mortality.²⁵ FLT occurred in five of six patients and partial FLT in one of six patients. Despite thrombosing the false lumen, the aortas continued to dilate. This highlights the difficulty of managing aortic dissection in patients with connective tissue disorders. This study confirms that patients appear to continue to dilate their aorta despite coverage of the primary entry tear and false lumen thrombosis.

The significance of this finding is unclear yet does not appear to be associated with graft type. Successful exclusion of the false lumen and associated thrombosis should confer protection against rupture. How and why the aorta continues to dilate and the clinical relevance of this finding is yet to be elucidated.

It has been proposed that once aortic dissection occurs in patients with Marfan syndrome, an unfavorable “natural” history begins.²⁶ This proceeds through surgery, revision surgery, and eventual premature death. A significantly better outcome is observed if aortic dissection can be prevented by elective aortic root surgery on the non-dissected aorta.

It is our philosophy, when possible, to target stent deployment into a replaced aortic segment; as was possible in three of seven cases in this series. This provides a stable platform that should reduce proximal type I endoleaks. A key challenge of endovascular treatment of thoracic aneurysms is the variable morphology of the aortic arch. This challenge is reduced when deploying into a prosthetic proximal landing zone, such as an elephant trunk. In Marfan patients there will be continued dilatation of the distal thoracic and abdominal aorta. Supplemental stent-grafting can be performed, and where necessary hybrid extra-anatomical bypass or branch/fenestrated stent-graft technology to maintain aortic branch perfusion may be considered.

Aortic disease in Marfan syndrome will often require repeated interventions and multiple surgeries, regardless of the modality utilized for repair.²⁷ Geisbusch et al reported three of six (50%) of the chronic dissection cases for aortic dissection continued to dilate despite endograft exclusion of the aneurysm.²² In our series, all patients’ thoracic aortas continued to dilate and no abdominal false lumens thrombosed. The significance of aortic dilatation in the presence of false lumen thrombosis is difficult to explain and longitudinal follow up will be required to define whether false lumen thrombosis confers protection from aortic rupture in this setting.

This series demonstrates the uncertainty surrounding the use of endovascular techniques in patients with Marfan syndrome and chronic dissections of the distal aorta. The technique may confer protection from rupture through false lumen thrombosis, although this remains to be proven. Endovascular repair may offer a viable treatment option in patients who have contraindications to open surgery, but longer follow up of more patients is required to define the place of this therapy.

AUTHOR CONTRIBUTIONS

Conception and design: IN, RH, MT

Analysis and interpretation: IN, MT

Data collection: IN, MJ, RM

Writing the article: IN

Critical revision of the article: RH, PH, MJ, RM

Final approval of the article: IN, IL, MT

Statistical analysis: IN

Obtained funding: N/A

Overall responsibility: MT

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