Aortic Dissection in Patients With Connective Tissue Disorders

Techniques and considerations for the endovascular treatment of patients with genetically triggered aortic disease.

BY JAMES H. BLACK, III, MD, FACS

The connective tissue disorders (CTDs) describe human conditions in which the primary structural targets are the structural proteins fibrillin and elastin. These proteins are critical to aortic wall strength and homeostasis. Pathologically, thoracic aortic aneurysms (TAAs) and dissections (TADs) reveal marked destruction of normal architecture with extensive elastin fragmentation, usually without the atheromata seen in AAAs. Furthermore, presentations of TADs and TAAs may show classic Mendelian inheritance, suggesting the contribution of a single gene. These heritable disorders of connective tissue have emerged with a studied natural history, a defined basis for inheritance, and sufficiently understood pathophysiologic mechanisms to guide treatment. They have severe vascular manifestations: Marfan syndrome (MFS), Vascular Ehlers-Danlos syndrome (VEDS), Loeys-Dietz syndrome (LDS), and Familial Thoracic Aortic Aneurysm and Dissection syndrome (FTAAD).

Advances in aortic research have now broadened, extending beyond the historically disproportionate focus on elastic fiber fragmentation to reveal a very complex mechanism that drives development of TAAs and TADs in CTD patients and now affords opportunity for therapeutic medical intervention.

Identification of CTD patients is key to devise treatment strategies that invoke early medical therapies, address acute presentations with appropriate surgical and endovascular technology, and provide long-term success against late aortic events and secondary procedures. As the presence of CTDs was an exclusion criterion for the pivotal trials that led to all FDA-approved stent grafts, controversy remains concerning the merits and risks of stent graft placement in the CTD patient's biologically abnormal thoracic aorta after TAD (Figure 1). This article seeks to define the role of endovascular thera-

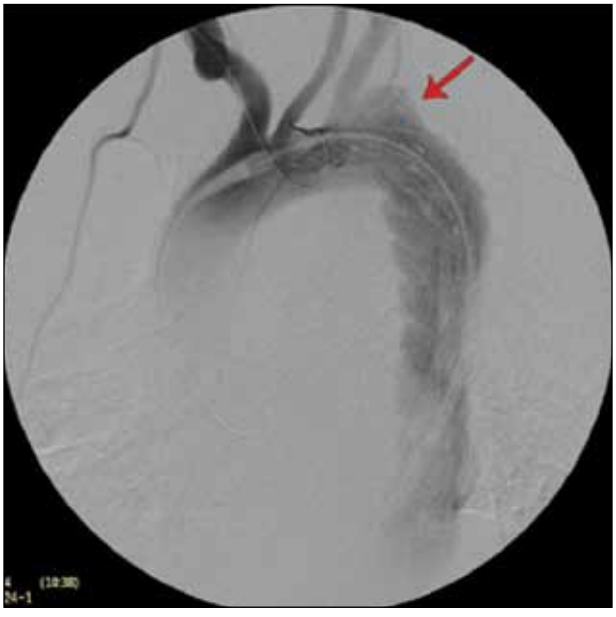
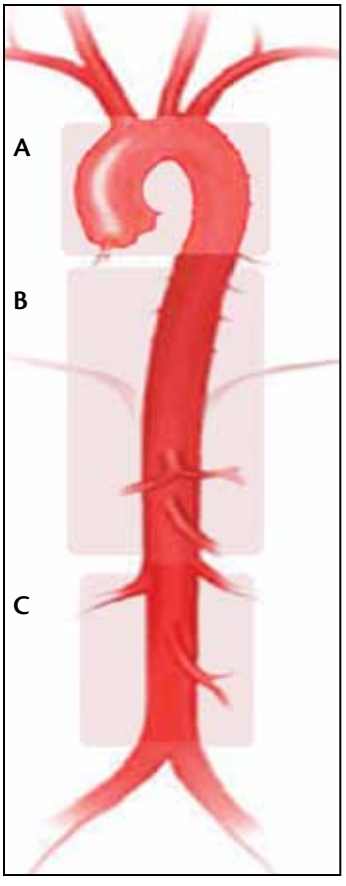


Figure 1. Stent graft perforation of the proximal descending thoracic aorta in an MFS patient. Reprinted from van Keulen JW, Moll FL, Jahrome AK, van Herwaarden JA. Proximal aortic perforation after endovascular repair of a type B dissection in a patient with Marfan syndrome. J Vasc Surg. 2009;50:190–192, with permission from Elsevier.

pies in patients with CTD upon presentation with aortic dissection.

NATURAL HISTORY OF TAD IN CTD

A biologic basis has been postulated for the development of aortic dissection, particularly type B aortic dissection (TBAD), in CTD.[1] Indeed, studies of cellular ontogeny have revealed areas in the proximal descending aorta with similar derivation as the aortic root. As an expected correlate, this shared heritage may be operant to yield TADs and TAAs originating in the proximal descending thoracic aorta (Figure 2). In patients with nonsyndromic TBADs, 30% to 40% of patients may degenerate to aneurysms, with great variability in the timing of these secondary events. Comparatively, in CTD patients, the development of aneurysmal change after TAD is not uncommon 2 to 3 years after the index dissection. Furthermore, this compares dramatically to descending thoracic aortic events after elective aortic root aneurysm repair (when nondissected), which postdate the index root surgery by 14 years.[2] CTD patients are at critical risk of late aortic events; similarly, MFS has been associated across multiple TEVAR studies as a risk factor for aortic progression and complications.



There are no studies that precisely detail the nature and extent of TAD in CTD patients. In the Johns Hopkins experience as a worldwide referral center for patients with MFS, the association of malperfusion syndrome after TAD is much more commonly appreciated than in nonsyndromic dissection patients. Comparatively, in a study of mostly nonsyndromic TAD (from the International Registry of Acute Aortic Dissection), the risk of complications after TBAD was paradoxically reduced in younger patients, with only 20% of the total events seen in patients under 50 years of age.[3] Many CTD patients will require aortic branch stenting in addition to aortic repair or TEVAR to alleviate malperfusion upon presentation with TAD. Medical therapy can be effective in many syndromic patients, and close follow-up for assessment of the trajectory of aortic root growth is required. In the author's experience, CTD aortic growth rates of 5 to 7 mm every 6 months through the first year after TAD are not unexpected. Consequently, high growth rates should further prompt consideration of a CTD if a previous diagnosis is not known.

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PROCEDURAL ISSUES IN ENDOVASCULAR REPAIR OF TBAD

Techniques to address TBADs in CTD patients include aortic fenestration, branch stenting, and endoluminal repair. Application of each treatment paradigm should be considered for specific patient anatomy. The primacy of TEVAR to address malperfusion syndrome in nonsyndromic patients has taken a central role over fenestration. Given the concerns regarding chronic, outward radial force of stent grafts in CTD patients, it remains a vital option to consider aortic fenestration by balloon septostomy to alleviate malperfusion, but when confronted with rupture, complex dissection anatomy, and multiple malperfusing territories, TEVAR may be the only life-saving option for the CTD patient. Careful technique is mandatory in any TAD patient, but the concomitant fragility of the host aortic tissue in CTD patients deserves special mention in the pantheon of aortic catastrophe. IVUS may be very informative for device delivery, and careful guidewire placement is key to avoid wire-induced complications, particularly on the ascending aorta. The basic tenets of TEVAR for

Figure 2. The aortic root and juxtaductal aorta emerge from the cardiac neural crest (A). The suprarenal aorta is derived from the somatic mesoderm (B). The infrarenal aorta is developed from the splanchnic mesoderm (C).

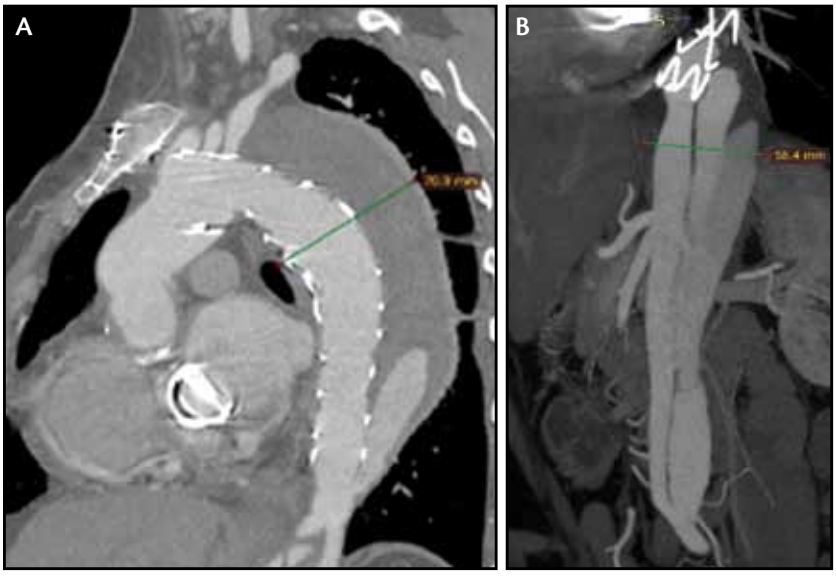

Figure 3. Progression of an aortic aneurysm in a 24-year-old MFS patient (A), with a new entry tear at the stent edge. The 2-cm growth in 3 months to 7 cm was asymptomatic. A 35-year-old MFS patient with acute back pain and new acute dissection flap appreciated inside chronic dissection (B).

TADs should include (1) stent graft coverage of the primary entry tear and any major secondary tear to the level of the celiac vessel; (2) in cases of rupture, additional false lumen embolization may be needed to reduce the risk of hemothorax; and (3) assessment of aortic branch perfusion by IVUS and/or angiography or pressure gradient interrogation.

In CTD patients, mechanical device issues may play a central role in the development of aortic complications during TEVAR for TAD. It has been proposed that certain endovascular devices are less flexible or conformable and thus expedite further aortic tears. In a series reported by Dong et al,[4] the most common complication in MFS patients was retrograde aortic dissection (rTAD). Other series have furthered the notion that rTAD is much more common in MFS patients than nonsyndromic patients (ie, MFS patients account for a much larger percentage of rTAD victims than their percentage of the total study population). However, studies of rTAD have failed to determine a role for the device, with nonsignificant statistical comparisons among vendors. Given the small numbers of rTAD patients, this may represent a type II statistical error. Accordingly, it is prudent to consider TEVAR in CTD only with devices without proximal bare springs, if logistically feasible. Because nearly 50% of rTAD dissections are detected beyond 30 days postimplantation, it is critical that CTD patients are closely followed. In the author's experience with CTD patients, very subtle anterior chest pain, neck pain, or shortness of breath can be indicative of a new rTAD event after aortic surgery.

While the proximal aorta is of great concern in CTD patients, the interplay of aortic stent grafts against the distal thoracic aortic dissection septum is also a source of aortic complications. The occurrence of new entry tears at the distal edge of the endoluminal device can occur. Again, this complication has not been proven to be device specific. In most instances, these are addressed by stent graft extension to the celiac vessel. Studies on stent graft-induced tears are generally derived from small study populations, so the length of stent grafting at the index operation and device position in the aorta (straight or curved segment) at the distal landing zone are difficult to ascertain. Certainly, in many acute TAD cases, the CTD aorta will be relatively straight, so a more distal landing zone in the mid-to-distal third may reduce conformability issues. Of course, extension of stent graft placement to a straight segment of the aorta may invoke coverage into the T8–T12 region. In these cases, cerebrospinal fluid drainage should be considered to reduce the risk of spinal cord injury.

LONG-TERM RESULTS

Series of MFS patients treated with endovascular therapy with reasonable follow-up periods to determine clinical effectiveness are now emerging. A report by Botta and colleagues[5] examined 12 patients treated for dissection of the descending thoracic aorta after previous open aortic root/arch surgery. Five procedures were performed urgently, and seven were done in elective scenarios. In the immediate postoperative period, no paraplegia was encountered. However, in follow-up (mean, 31 months), 25% of the patients developed new dissection (retrograde into the arch or distally into the abdominal aorta). Waterman and colleagues[6] have recently published the largest series of MFS patients with stent graft therapy, and the results are sobering: 44% of patients experienced primary failure of the stent graft, and many were converted to conventional surgical repairs. Among the primary treatment failures (7 of 16 patients), the mortality rate was 42%.

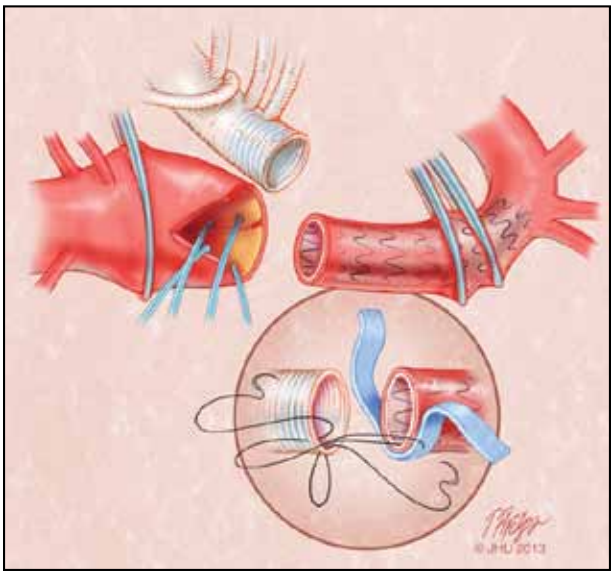

Figure 4. Technique for distal aortic conversion. The renovisceral circulation is supported on partial left heart bypass. The dissection septum and the metal edge are cut away to allow a secure circumferential anastomosis to the TEVAR graft. The intercostal vessels can be controlled (as in the figure) with occluding catheters or implanted, depending on the surgeon's judgment or monitor-evoked potentials guidance.

The issue of stent graft–induced new entry (SINE) tears seems to be a persistent theme in patients with MFS.[7] A report of 650 patients treated for TBADs with stent graft therapy revealed 22 events of SINE. The mortality of the new tears was substantial, with nearly 30% of patients dying from the event. The incidence of SINE in the patients with MFS was 33%, whereas only 3% of patients with TBADs and no underlying MFS developed SINE. The investigators concluded the stress-induced injury of the stent graft against the fragile aortic wall should be accounted for during design and placement of the endograft. While excessive oversizing should also be avoided, it is important to note the degree of oversizing was within IFU for the available devices to date. The same center has also elaborated their experience with stent graft therapy in MFS to state, "Poststent grafting RTAD (retrograde type A dissection) represented the most common complication among Marfan patients."

SURGICAL TECHNIQUES FOR DISTAL AORTIC SALVAGE

The distal aorta in CTD patients, beyond the TEVAR graft, remains at risk for further aortic dilation. In fact, many CTD patients eventually require repair of the abdominal segment. Among a group of MFS patients

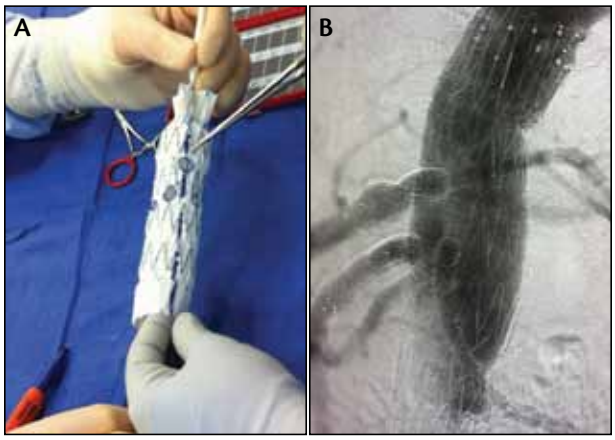

Figure 5. A 50-year-old MFS patient presented with a 7-cm aneurysm of the previous celiac-SMA-renal inclusion patch. Three-dimensional CT reconstruction was used to determine the fenestration locations (A) for subsequent stenting (B). The patient was discharged on postoperative day 2.

studied by Nordon et al, the distal aorta was appreciated to grow 7.2 mm per year after prior TEVAR.[8] This growth was appreciated despite false lumen thrombosis along the TEVAR region. In CTD patients, close surveillance is mandatory to address the abdominal aorta as required. Furthermore, the abdominal aorta is at ongoing risk of not only aneurysm but also acute dissection in addition to the previous chronic dissection (Figure 3).

In some instances, the progression of the abdominal aorta to aneurysm after TEVAR in CTD patients may be an isolated event. To wit, in the scenario of stable thoracic diameter or even total thoracic remodeling, the stent graft does not require extrication to address the distal aortic segment. All the FDA-approved stent grafts can be incorporated into a surgical anastomosis. Because this usually requires additional time to fashion the grafts, we have found that most of these repairs are best performed with distal circulatory support by left heart partial bypass (Figure 4).

FENESTRATED DEVICES FOR DISTAL AORTIC SALVAGE

The application of fenestrated or branched stent graft technology for addressing the CTD population is sparse after dissection. Because many CTD patients have had a proximal surgical procedure, the stability of a surgical graft as a proximal fixation zone for a downstream endovascular repair is very enticing. As most endovascular surgeons have become accustomed to fixation of TEVAR in an "elephant trunk" graft after previous arch repair, the extension of a device distally from

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a secure thoracic replacement is a natural next step. Recently, among a series of 15 patients managed with branched technology, six patients were identified with MFS or LDS.[8] Among these patients, all patients had the device secured proximally and distally within the surgical graft, and stability of the treated thoracoabdominal segment was implied, but patch aneurysms did not have a favorable morphologic response.

At Johns Hopkins, we have used fenestrated technology to address such patch aneurysms, and there are significant device-related issues to overcome; specifically, the fenestrations are usually very close to one another, and this may theoretically undermine long-term stability (Figure 5). On the other hand, since the segment of the patch is usually very narrow, the fenestrated device should have minimal excursion with systole and diastole to torque the multiple branches. Undoubtedly, revision and reoperative procedures in CTD patients can incur significant morbidity, and we look favorably to further complex technologies to handle this vexing subset of patients. Open surgical techniques are now generally assumed in CTD patients to include direct anastomosis to the renovisceral origins (Figure 4) to avoid any residual aortic tissue after thoracoabdominal aortic aneurysm repair, hopefully further reducing this current clinical need.

MATURATION OF CONSENSUS DOCUMENTS AND CTD PATIENTS

The appropriateness of endovascular therapies in CTD is under evolution. A previous summary publication[9] recommended endovascular repair only in instances of late localized pseudoaneurysm and stenting across native tissue aneurysm from "graft to graft," and a Society of Thoracic Surgeons (STS) Consensus Statement recommended strongly against endovascular repair unless operative risk was deemed truly prohibitive by a center experienced in management of complex aortic disease.[10] This placed smaller hospitals in the precarious position of transferring CTD patients with acute aortic pathology, particularly malperfusion and rupture after TADs. However, the stance was recently modified by the STS to support stent graft therapy in cases of aortic rupture in CTD patients.[10] To date, there exists no consensus opinion regarding the appropriateness of managing the scenario of chronic dissection with thoracoabdominal aortic aneurysm for the CTD patient, even if the endoluminal device can be secured in surgical grafts proximally and/or distally.

SUMMARY

CTD patients have benefited from a century of progress in the study of CTD pathogenesis and more recent refinements in surgical techniques to handle the cardinal manifestations within the cardiovascular system, such as aneurysm and dissection. Proper genetic counseling, surveillance, and prudent application of modern surgical techniques have greatly modified the natural history of the disorder and extended life expectancy to over 70 years of age. Endovascular therapy of aortic disease has yet to have a defined long-term role but acutely is of benefit in select instances of aortic rupture and dissection or as a bridge to definitive therapy. Among secondary aneurysms related to the initial conventional surgical repairs, CTD patients may draw significant benefit and inspiration from branched and fenestrated technologies. ■

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