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# New Paradigms in the Treatment of Acute Complicated and Uncomplicated Type B Aortic Dissection

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**Abstract** The treatment of acute type B aortic dissection is a rapidly evolving field, due in large part to the advent of thoracic endovascular aortic repair (TEVAR). This review will summarize the current literature on the management of both complicated and uncomplicated type B dissections, with special attention paid to emerging evidence supporting earlier aggressive treatment.

**Keywords** aortic dissection, aorta, thoracic endovascular aortic repair

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Since its first description in 1991,<sup>1</sup> the use of endovascular stenting has dramatically changed the way we view our ability to treat complex aortic pathology. Perhaps nowhere is this shift in approach more apparent than in the treatment of acute aortic dissections. In this review, we summarize the current literature available on the use of thoracic endovascular aortic repair (TEVAR) for treating descending thoracic dissections. This is an exciting and rapidly evolving field that has the potential to revolutionize the way we care for patients with this serious condition. To help illustrate the concepts later covered in this review, we describe the following example of a woman presenting with an acute type B aortic dissection.

## Illustrative Case

A 70-year-old woman presented to our emergency department after several hours of acute, severe, tearing back and chest pain. Past medical history was significant for uncontrolled hypertension as well as a known coarctation of the aorta located just distal to the left subclavian artery. According to the patient, she had undergone several attempts at dilatation of this coarctation in the past with no success, and her life had been plagued by the sequelae of a lack of distal perfusion. Specifically, she had chronic leg pain and

lower extremity weakness. On physical exam she was frail and in general distress, with weakened pulses in the lower extremities bilaterally.

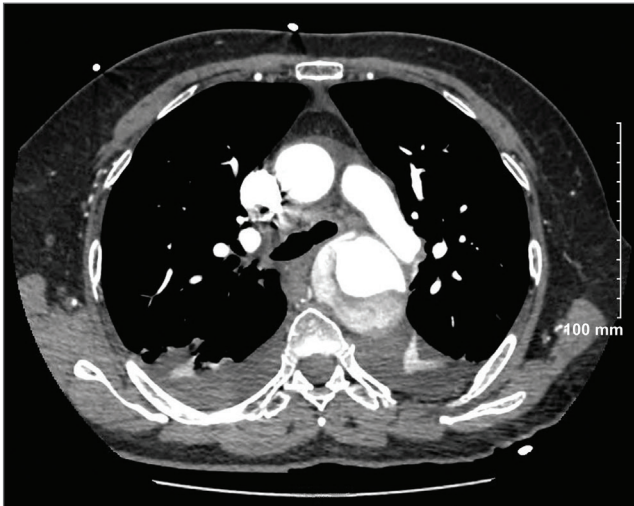
Assuming a differential diagnosis of myocardial infarction, pulmonary embolism and acute aortic syndrome, she underwent computed tomography (CT) of the chest with intravenous contrast (Figures 1 and 2), which revealed an acute Stanford type B aortic dissection, originating just distal to the coarctation, and a large descending thoracic aneurysm. As this was a complicated case, she was seen in the aortic center and discussed by a multidisciplinary team. Because of the large descending aortic diameter, ongoing pain and diminished pulses in the lower extremities bilaterally, the decision was made to pursue a therapeutic intervention. TEVAR was chosen, and two stent grafts were successfully deployed after dilatation of the coarctation. She had resolution of her symptoms and restoration of peripheral pulses; at 1-month follow-up, the patient had no endoleak, nor thrombosis of her false lumen.

## Defining Aortic Dissection

This case highlights the emerging use of TEVAR in management of type B aortic dissection. Acute aortic dissection occurs when a disruption in intimal integrity leads to a passage of blood into the medial layer of the aortic wall. This leads to a separation of layers and, subsequently, the formation of a true and false lumen within the aortic wall.<sup>2</sup> With lower resistance, blood preferentially flows down the false lumen, leading to a multitude of pathologic sequelae as true lumen flow is

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**Figure 1.** Computed tomography scan of chest showing large type B aortic dissection involving the descending thoracic aorta.

compromised. There are several classification schemes for describing acute aortic dissection; however, the most widely used and likely most clinically relevant is the Stanford classification, which divides aortic dissection into two principal types:<sup>3</sup> Type A, which is acute dissection involving the ascending thoracic aorta with or without involvement of the descending aorta, and type B, which is a dissection isolated to the descending thoracic aorta.

With the exception of special circumstances that necessitate the use of hybrid arch replacement, the treatment of type A dissections is largely reserved for open surgical approaches and is beyond the scope of this review. In contrast, the treatment of type B dissections has begun to rely more and more on endovascular approaches and will be the central focus herein.

### **Epidemiology**

Estimates of aortic dissection incidence are variable, ranging from 3.5/100,000 person-years to ~14/100,000 person-years.<sup>4-6</sup> Our best understanding of the current makeup of acute aortic dissection comes from the International Registry of Acute Aortic Dissection (IRAD) database, which was established in 1996, includes 30 centers located in 11 countries and has elucidated several key points about aortic dissection.<sup>7</sup> Known risk factors for dissection include genetic aortopathies, such as Marfan syndrome, Ehlers-



**Figure 2.** Three-dimensional reconstruction showing descending aortic dissection after coarctation.

Danlos syndrome and Loeys-Dietz syndrome among others, family history of aortic disease, uncontrolled hypertension, history of smoking, history of cocaine

use and history of trauma to the aorta. This is generally a disease of older individuals, with at least 65% being male, although genetic aortopathy patients present at younger ages.

### **Presentation**

The most frequent presentation of acute aortic dissection is either chest, back or abdominal pain that is often described as a tearing sensation and acute in onset. Unlike type A dissection in which chest pain is the most frequent complaint, type B dissections will typically present with back or abdominal pain. The timing of aortic dissection has been broken up into acute (within 14 days of onset), subacute (from 14 days to 6 weeks) and chronic (more than 6 weeks after onset) phases.<sup>8</sup> Recently, finer classification systems have been developed, primarily using the IRAD registry, to better characterize the clinical course of type B dissection. Specifically, the hyperacute phase lasts from onset of the dissection to 24 hours, the acute phase lasts for 2–7 days, the subacute phase 8–30 days, and the chronic phase past 30 days.<sup>9</sup> This new classification scheme may have important implications as we transition to an age of aggressive endovascular treatment of type B dissections.

### **Complicated Type B Aortic Dissection**

From a clinical standpoint the most important distinction in type B dissection is whether the dissection is complicated or uncomplicated. While the majority of dissections are uncomplicated, approximately 20% are complicated, defined as one with the presence of end organ or tissue ischemia, refractory hypertension (defined as blood pressure poorly controlled despite the use of three agents) or pain despite best medical treatment, hemodynamic instability, or rupture. Branch vessel ischemia can involve any region of aortic supply, including the spinal cord, the gastrointestinal track including the superior mesenteric or celiac arteries, the lower extremities via the iliac arteries, or the kidneys.<sup>10</sup> Occasionally, complicated type B dissections can present more subtly, with slight elevations of lactic acid (signifying bowel ischemia) or slight elevations in hepatic enzymes. Refractory pain appears to be a significant risk for mortality (35% risk), and patients with this symptom should be considered complicated as well.<sup>11</sup> Complicated type B aortic dissection is a medical emergency and the general goal of immediate

treatment is to lower blood pressure and heart rate to limit shear stress on the aorta and prevent dissection propagation, obstruction to the branch vessels and risk of rupture.<sup>2</sup>

Although a historically important approach for the treatment of acute type B aortic dissection, open surgical repair is being chosen less often by surgeons for this disease. In a recent study by Jones and colleagues utilizing Medicare data, the frequency of open surgical repair decreased by 26% between 2000 and 2010, although as of 2010 it still made up 73% of treatment choices.<sup>12</sup> The reason for this decrease has been the advent of TEVAR. Since the first published use for complicated type B dissection by Dake in 1999, TEVAR has dramatically altered the way we approach this disease process.<sup>13</sup> Although there are few randomized controlled trials comparing the two, TEVAR for acute complicated type B dissection has been studied in great detail, with superior results over open surgical repair consistently reported.<sup>14–16</sup> In a recent meta-analysis of the management of complicated type B aortic dissection, TEVAR showed a superior 30-day mortality rate to open repair (7.3% vs. 19%) with improvements in mid-term freedom from aortic events.<sup>17</sup> The analysis included more than 2,000 TEVAR patients and more than 1,200 who received open surgical repair. An expert consensus panel reviewed the literature on TEVAR for complicated type B dissection and found consistent results, with 10.2% early mortality for TEVAR relative to 17% for open repair.<sup>8</sup> Similarly, a study in 2010 examining 10,466 patients with type B dissection using the Nationwide Inpatient Sample showed a significantly lower mortality for TEVAR relative to open surgery (10.6% vs. 19%). In this study there was no significant difference in elective dissection cases and the survival advantage only applied to emergent type B dissections.<sup>18</sup> Finally, decision analysis based on best available evidence further revealed TEVAR led to an increase in quality adjusted life-years compared to open surgical repair.<sup>19</sup> Long-term data also is showing promise. A recent review of 50 patients at a single institution with 33.8 months of median follow-up showed overall survival at 5 and 7 years to be 84%. The reintervention rate was substantial at 26%, but no deaths were attributable to aortic pathology in this series.<sup>20</sup> These studies, along with additional registry evidence, led the U.S. Food

and Drug Administration to approve two endovascular devices for the management of type B dissection in 2014, and many physicians now consider TEVAR to be the optimal choice for the management of acute type B aortic dissection.<sup>21</sup> It should be noted, however, that despite this early excitement, long-term data is limited and TEVAR is not without complications such as paralysis, retrograde type A dissection, rupture and technical limitations. Further studies are needed to determine the true superiority for complicated dissections.

### **Uncomplicated Type B Aortic Dissection: New Indications for Aggressive Treatment**

Historically, uncomplicated type B aortic dissection has been managed medically with admission to an intensive care unit, pain control and decrease in systolic blood pressure and heart rates.<sup>22</sup> This strategy has worked well. Since the 1960s, the 30-day mortality rate associated with acute type B aortic dissection has dramatically decreased from 40% to approximately 10%.<sup>23</sup> Furthermore, in a recent review by Moulakakis et al. of 1,548 patients treated medically, the early mortality rate was only 6.4%, which was lower than the 10.2% and 17.5% mortality rate for TEVAR and surgical treatment, respectively.<sup>17</sup> It should be noted that this is not a surprising finding, as the authors' retrospective review could not account for the vast differences in patient characteristics treated medically versus surgically. However, it does set a benchmark for medical management by which we can compare other treatment options.

Advocates of TEVAR for acute uncomplicated type B dissections cite a 25–50% risk of progression of aortic disease,<sup>8,10,17,24</sup> a still unacceptably high rate of short- and long-term mortality<sup>25</sup> and favorable aortic remodeling that can occur with TEVAR.<sup>26-28</sup> For this reason, several studies have been conducted examining this specific issue.

Two trials examining this issue have failed to show a difference in early mortality but have showed a difference in aortic remodeling. The Acute Dissection: Stent graft OR Best medical therapy treatment (ADSORB) trial randomized 61 patients to either best medical therapy (BMT) or BMT with TEVAR.<sup>26,29</sup> Patients were randomized and underwent TEVAR

within 14 days, such that this was a trial of early endovascular intervention. The design mandated that there was at least a 2-cm proximal and distal landing zone and aortic diameter was less than 55 mm. Patients with connective tissue disorders such as Marfan's syndrome were excluded. The trial was designed to test the composite endpoint of lack of false lumen thrombosis, aortic dilatation and rupture, although mortality also was commented on. Although there was no significant difference in mortality at 30 days or 1 year, significant differences in aortic remodeling occurred, with incomplete false lumen thrombosis only occurring in 43% of the TEVAR group compared with 97% of the BMT-only group.

The two most complete studies examining this issue are the Investigation of Stent Grafts in Aortic Dissection (INSTEAD) trial, and INSTEAD-XL, which examined 5 years of follow-up from the original trial.<sup>30,31</sup> In INSTEAD, 140 patients at seven European centers were randomized in a 1:1 fashion to either optimal medical management (OMM) plus TEVAR or OMM alone. Similar to ADSORB, patients who met indications for surgery, such as aortic diameter > 5.5 cm or complications of dissection, were excluded. However, in contrast to ADSORB, TEVAR was performed after 14 days to allow dissection flap maturation. The primary endpoint was survival at 2 years, which did not differ significantly between medical management alone and the TEVAR group (95.6% vs. 88.7%, respectively, P=0.15). Further, there was no difference in aortic-related death or progression of disease.<sup>31</sup> As seen in ADSORB, there was a highly significant increase in the rate of false lumen thrombosis (signifying positive aortic remodeling) in the TEVAR group at 2 years (91.3% vs. 19.4%, P<0.001).<sup>31</sup> A modern series of 100 TEVAR patients similarly showed positive aortic remodeling, including in false lumen thrombosis and increased true lumen area for those receiving TEVAR in the acute or subacute setting.<sup>32</sup> This finding of consistent positive aortic remodeling could imply that with prolonged follow-up, the risk of aortic-related complications might be lower with TEVAR.

In response to this, an amendment to the INSTEAD trial protocol to extend follow-up to 5 years formed the basis of the INSTEAD-XL trial.<sup>30</sup> After 5-year follow-up, all-cause mortality was not lower in the TEVAR

plus OMM group compared to OMM alone (11.1% vs. 19.3%, respectively,  $P=0.13$ ); however, when examining just mortality at 2–5 years censored for early death, the TEVAR group had significantly lower mortality (0 vs. 16.9%,  $P<0.001$ ), with no patient in the TEVAR cohort dying from any cause from years 2 to 5. Furthermore, aortic-specific mortality was 12.4% lower in the TEVAR group (6.9 vs. 19.3%,  $P=0.04$ ). This suggests that the positive aortic remodeling with TEVAR leads to a survival benefit.

Thus, the crux of the debate over whether TEVAR is beneficial in uncomplicated type B dissection seems to center on whether one believes that aortic remodeling improves long-term survival. TEVAR is not complication-free, as rupture, paralysis and retrograde type A dissection are associated with the procedure. With mortality benefits not occurring until after year 2 in INSTEAD-XL, the aggressive employment of TEVAR for all type B dissections seems premature.

### **Blurring Lines Between Complicated and Uncomplicated**

Clearly, a key challenge in addressing this question is to identify those patients who may present with uncomplicated dissections but have features that predispose them to the development of late aortic complications. Several retrospective studies have sought to identify these risk factors. Specifically, aortic diameter of  $> 4$  cm at initial CT scan,<sup>33</sup> false lumen diameter of  $> 22$  mm,<sup>34</sup> influence of patent or partial false lumen thrombosis,<sup>35</sup> size of proximal entry tear,<sup>36</sup> location of primary tear along the convex portion of the aorta,<sup>37</sup> along with ongoing pain<sup>11</sup> are all risk factors for worse prognosis and likelihood of aortic complications. Uncontrolled hypertension appears to be an additional risk factor for worse prognosis. In a 2010 study using IRAD data, refractory hypertension was found to lead to a 23-fold increase in the rate of mortality compared to medical management.<sup>11</sup> Determining which patients benefit from early TEVAR is still a difficult and debatable clinical decision, and randomized controlled trials are necessary to develop algorithms for management of this complex disease.

### **Other Acute Aortic Syndromes**

Further complicating this issue is how to handle acute aortic syndromes that do not fall into the classification

of dissection. Acute aortic syndrome actually refers to a spectrum of diseases ranging from aortic rupture at one extreme to penetrating aortic ulcer with or without expansion at the other.<sup>38</sup> Intramural hematoma, for example, occurs when microscopic tears in the media allows blood to escape into the medial layer of the aorta without flowing back into the true lumen. Although a thorough discussion of acute aortic syndromes other than dissection are beyond the scope of this review, it is clear that with the advent of TEVAR, new treatment paradigms are being investigated in regard to these entities as well.

### **Conclusions**

This is an exciting time for the treatment of thoracic aortic disease. New technology is leading to substantial advances in the way we view acute aortic syndromes, and also has pushed the field to a place where it is difficult for any one person to be an all-encompassing expert. Perhaps the most exciting aspect of the preceding discussion is that these technological advancements have led to an important new clinical paradigm, aortic management by a multidisciplinary team. Different perspectives relating to advanced imaging, catheter-based interventions, preoperative planning and surgical decision-making all are necessary to treat a patient with an acute aortic dissection. It is unclear what the next 10 years hold for the treatment of aortic dissection, but what seems clear is that centers of excellence working as multidisciplinary teams will be necessary to provide optimal outcomes for these patients.

### **Patient-Friendly Recap**

- New technology has led to new approaches in treating aortic dissection, a serious condition in which a layer in the body's largest blood vessel tears.
- One such approach called thoracic endovascular aortic repair, or TEVAR, has proved beneficial for complicated descending thoracic dissection and may have merits for the uncomplicated type.
- Regardless of treatment strategy, a multidisciplinary team helps ensure optimal patient outcomes.

## Conflicts of Interest

Dr. Weiss serves as a consultant for Medtronic Inc., Minneapolis, MN.

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