Endovascular Repair in Acute Complicated Type B Aortic Dissection: 3-Year Results from the Valiant US Investigational Device Exemption Study

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Acute complicated type B aortic dissection (TBAD) is a potentially catastrophic, life-threatening condition. If left untreated, there is a high risk of aortic rupture, irreversible organ or limb damage, or death. Several risk factors have been associated with acute complicated TBAD, including age and refractory hypertension. In the acute phase, even uncomplicated patients are more prone to develop complications if hypertension and pain are left medically untreated. Innovations in stent graft technologies have incrementally improved outcomes since their first use for this condition in 1999, though improvement is needed in mitigating periprocedural complications, adverse events, and mortality. In the past decade, endovascular repair has become the preferred treatment because of its superior outcomes to open repair and medical therapy. The Valiant Captivia Thoracic Stent Graft System is a third-generation endovascular stent graft with advancements in minimally invasive delivery, conformability to the anatomy, and the minimization of adverse sequelae. Herein, this stent graft is briefly reviewed and its 3-year outcomes are presented. Freedom from all-cause and dissection-related mortality was 79.1% and 90.0%, respectively. The Valiant Captivia Stent Graft represents a safe, effective intervention for acute complicated TBAD. Continued surveillance is needed to verify its longer-term durability.

Key words: 1. Self expandable metallic stents 2. Aortic aneurysm, thoracic 3. Aortic dissection 4. Endovascular procedures 5. Valiant captivia

Introduction

1) The challenge of acute complicated type B aortic dissections

Acute aortic dissection is the most common type of potentially catastrophic aortic condition, and, if untreated, poses a high risk of early mortality. The widely adopted Stanford classification distinguishes type B aortic dissections (TBADs), which involve the descending aorta distal from the left subclavian artery (LSA), from type A dissections, which involve the aortic arch. TBADs may further be classified as complicated or uncomplicated based on their distinctive patterns of clinical presentation, and the prognosis may differ significantly. In-hospital mortality has been reported to be roughly 50% for complicated TBAD patients and 10% for uncomplicated TBAD patients [1-5]. Roughly one-quarter of all acute TBADs
may be considered complicated if there are signs of imminent rupture, any sign of organ or limb malperfusion, the presence of refractory hypertension, hypotension (<90 mm Hg systolic), or cardiogenic shock.

Acute complicated TBADs are challenging because of the formidable risk of organ or limb malperfusion, and/or the rapid expansion of the thoracic aorta, which may lead to rupture (a diameter of >4.5 cm or 5 cm). A timely intervention is critical for survival. Malperfusion is caused by the static or dynamic compression of the true lumen by the false lumen, which must be successfully managed to restore end-organ perfusion and avoid irreversible end-organ or limb damage [6]. Partial false lumen thrombosis independently predicts aortic growth and follow-up mortality in acute TBAD [7,8]. In 2007, Song et al. [9] reported that upper false lumen diameters ≥22 mm predicted late mortality (up to 9 years) versus diameters <22 mm (p<0.001).

Compared to patients with chronic expanding TBADs, patients with acute complicated TBADs are known to have poorer outcomes because of their presentation and aggressive course. In 2006, Bockler et al. [10] reported a 30-day mortality rate of 19% in patients with acute complicated TBADs versus 0% in patients with chronic TBADs. Systemic hypertension has been reported as one of the most important risk factors for acute TBAD, present in about 80% of patients [1], as well as increasing age, atherosclerosis, and taller stature [11-14].

2) Interventions for acute complicated type B aortic dissection

The mainstay life-saving treatments for acute complicated TBAD are open surgical repair (OSR), which was first performed in the 1950s, and thoracic endovascular aortic repair (TEVAR), first undertaken in 1999 by both Dake et al. [15] (a series of 19 acute complicated TBADs with early death occurring in 16% of the patients) and Nienaber et al. [16] (a case-control study of 24 subacute or chronic TBAD patients, 12 of whom underwent OSR, with a 33% mortality rate, and 12 of whom underwent TEVAR, with no early deaths). Medical therapy is typically a less aggressive modality reserved for uncomplicated acute, subacute, and chronic TBAD cases. However, medical therapy was employed for many patients before the debut of endovascular interventions. Currently, only a minority of patients with acute complicated TBAD are treated by medical therapy alone, if the use of either TEVAR and OSR is ruled out because of contraindicating patient comorbidities, anatomical considerations, or a lack of appropriate facilities, equipment, or expertise [17]. OSR and TEVAR each have their own rates of morbidity, treatment related complications, and mortality [15,18]. Although OSR is preferred for type A aortic dissections, endovascular repair has become the preferred first-line treatment for acute complicated TBADs and is increasingly employed for the distal arch, with OSR recommended to be reserved for patients unsuitable for endovascular repair [19].

Endovascular repair is now a standard therapy for acute complicated TBAD [20]. Fattori et al. [21,22] reported that TEVAR mortality rates when used to treat acute complicated TBADs are now similar to the mortality rates when TEVAR is used to treat uncomplicated TBADs, particularly with advancements in endovascular technologies. TEVAR offers a nearly a 4-fold increase in early survival for patients with acute complicated TBADs, which may be attributable to its myriad advantages [23]. TEVAR is less invasive than OSR. It is also a straightforward intervention to train for and perform, particularly with the availability of newer generation thoracic devices. The periprocedural advantages of TEVAR include a shorter procedure time, reduced blood loss, and faster patient recovery [24]. The technical success rates of TEVAR are high for both acute TBAD (ranging from 93.3% to 100.0%) [25-27] as well as for chronic TBAD (ranging from 77.6% to 100.0%) [28-30]. In addition, TEVAR for acute TBAD is surmised to promote aortic remodeling and have a prophylactic effect against late complications [31-33]. Although TEVAR is susceptible to periprocedural complications such as endoleak, new entry tears, and migration, technical success is commonly achieved.

3) Thoracic endovascular aortic repair versus open surgical repair versus medical therapy

Several studies have shown TEVAR survival outcomes to be superior to OSR in the short- to midterm time horizon [34-36]. Notable studies include a 2010 comparative analysis by Zeeshan et al. [37] at the University of Pennsylvania. In-hospital mortality was significantly different between groups, with mor-
tality rates of 4% for TEVAR, 40% for OSR, and 33% for medical therapy (p=0.006). For TEVAR patients, survival was reported at years 1, 3, and 5 to be 82%, 79%, and 79%, whereas the survival in patients receiving OSR or medical therapy (grouped together) was 58%, 52%, and 44% (p=0.008) at the same times [37]. These findings were confirmed in a 2014 comparative decision model study by Hogendoorn et al. [19], which concluded that TEVAR showed greater total effectiveness than OSR for all age groups.

In 2013, Fattori et al. [22] reported a propensity-matched analysis of the International Registry of Acute Aortic Dissection database (N=1,129 patients). Notably, this study revealed historical differences between TEVAR and medical therapy from 1995 to 2015; that is, from before the advent of TEVAR for acute TBADs, during the rising trend of TEVAR adoption in the 2000s, all the way to contemporary practice. TEVAR plus medical therapy (n=276, 25.2%) was compared to medical therapy alone (n=853, 74.8%) for both acute complicated and acute uncomplicated TBADs. Several baseline characteristics were significantly different between groups. It is interesting to note that TEVAR-treated TBADs were significantly more likely than medically managed dissections to be considered complicated (61.7% versus 37.2%, respectively; p<0.001), which is understandable given the scope of the time period and the seesaw-like shift in the usage of these respective interventions. Further differences between TEVAR and medical therapy can be seen in specific complication categories, including malperfusion (21.7% versus 8.4%, p<0.001), significantly worse reported pain (27.5% versus 15.7%, p<0.001), acute renal failure prior to treatment (21.4% versus 12.4%, p<0.001) and any pulse deficit on presentation (28.3% versus 13.4%, p<0.001), all of which were more prevalent in the interventional group. In-hospital mortality was statistically similar (10.9% versus 8.7%, p=0.273) despite the TEVAR group presenting with more complications. However, the cumulative probability of mortality at 5 years was significantly lower in the TEVAR group than in the group of patients who underwent medical therapy alone (29.0% versus 15.5%, p=0.018) [22].

Longer-term outcomes for TEVAR and OSR for acute complicated TBADs, however, are sparse and remain of great interest. Current long-term survival data suggest that no significant differences are present between TEVAR and OSR, which was recently confirmed in a 2016 meta analysis of 8 studies, in addition to a study conducted in a Chinese population of 118 inpatients (n=45 in the OSR group and n=73 in the TEVAR group) enrolled from January 2004 to January 2015. They concluded that there was no significant difference in the 10-year survival between OSR and TEVAR (56.7% and 26.1%, respectively; log-rank p=0.953) [38].

Only in recent years has oversizing been scrutinized and debated in terms of its relationship with severe complications over time, including stent-graft-induced new entry (SINE) tears, retrograde type A dissection, and proximal neck dilatation [17,39]. Excessive distal oversizing has been reported to be an independent predictor of SINE events, which usually require reintervention. It is believed that SINE events occur because of the fragility of the dissected intimal membrane in acute dissection as opposed to chronic dissection [39,40], although SINE events have been reported to be more common in chronic dissection [41]. However, a 2016 study of type B dissection cases reported that a distal-first rather than proximal-first deployment approach resulted in significantly fewer SINE events [42]. A better understanding of the long-term durability of TEVAR is needed to appropriately advance the technology and practice to achieve better durability and outcomes.

**The US DISSECTION trial 3-year results of Valiant Captivia for acute complicated type B aortic dissection**

The DISSECTION trial is an ongoing prospective, nonrandomized, multicenter evaluation of 50 patients (80% male) with acute complicated TBAD treated with the Valiant Captivia Thoracic Stent Graft System (Medtronic, Santa Rosa, CA, USA). Bavaria et al. [43] have described the design and methods of the trial and reported the 30-day and 1-year results. The study has continued with plans for a 5-year follow-up. Valiant Captivia received US Food and Drug Administration (FDA) investigational device exemption (IDE) in January 2014 and DISSECTION trial enrollment began in 16 centers in the United States.
1) The Valiant Captivia Thoracic Stent Graft System

Valiant Captivia is a third-generation stent graft system with approved indications for use in Europe and US for thoracic aortic aneurysms, transections, and dissections. As the successor to the Talent Thoracic Stent Graft System (Medtronic), Valiant has been evaluated in a number of critical research studies specifically aimed at elucidating its feasibility, safety, and effectiveness in the thoracic aorta, all with satisfactory results: VALOR II (US IDE for descending thoracic aneurysms, n=160) [44,45], VIRTUE (European registry for all types of TBADs, n=100) [46-48], the VALIANT CAPTIVIA registry (mid- to high-risk all-comer cohort, n=100) [28], the RESCUE trial (blunt thoracic aortic injury, n=50) [49,50], and the Valiant Mona LSA first-in-human feasibility trial using a modified Valiant Captivia System with branching to allow LSA patency (US FDA IDE via the new Innovation Pathway, n=9) [51]. The VIRTUE registry was a prospective cohort study comparing 3 groups of TBADs: complicated acute (n=50), subacute (n=24), and chronic (n=26). All-cause mortality at 3 years was 18%, 4%, and 24%, respectively, and dissection-related mortality was 12%, 4%, and 9%, respectively [46].

The DISSECTION trial included patients diagnosed with an acute complicated TBAD who were treated with a stent graft within 14 days from presentation. The included patients had malperfusion (visceral, renal, spinal cord, and/or lower limb ischemia) or rupture; patients were excluded if they had a history of a connective tissue disorder. The Valiant Captivia Thoracic Stent Graft System consists of a modular, self-expanding endograft preloaded into the Captivia Delivery System. The endograft size matrix was expanded in 2014, significantly broadening the size and configuration choices to address a wider range of anatomical variants. The proximal end of the endograft is composed of its bare-spring 8-Peak FreeFlo configuration, which was designed and bench-tested to successfully distribute force radially across its multiple apices. The distal end consists of either a closed web configuration devoid of bare springs or an 8-peak bare-spring configuration at the distal end.

2) Baseline characteristics and index procedure

A total of 50 patients (80% males) were enrolled; 62% were Caucasian, 12% Asian, 22% black, and 4% other. Their mean age was 57.2±12.9 years. The vast majority of patients had a medical history of hypertension (90%), while relatively few had a history of myocardial infarction (6.0%) or congestive heart failure (8.0%). There were a variety of patient presentations, with 1 in 5 patients presenting with an impending rupture (20%), and fewer with paraparesis (12%). Abdominal pain at presentation was present in 36% of patients. The mean time from the onset of symptoms to the index procedure was 4.7 days. The majority of patients complained of back or chest pain (88%). Malperfusion was diagnosed in 86% of patients, of whom visceral ischemia was present in 40%, renal ischemia in 42%, lower limb ischemia in 40%, and spinal cord ischemia in 6%. Medical therapy was administered to 84% of patients (antihypertensives), and 16% required inotropic support. At the baseline index procedure, the primary entry tear was covered in all dissections, and all cases achieved 100% delivery and deployment success with no misaligned deployments. Device oversizing was 12.0±10.3% and the length of coverage was 196.9±67.1 mm. Through year 3 post-index, a total of 28 of the 32 eligible patients (87.5%) have reportedly completed their follow-up appointment. Since the previous report by Bavaria et al. [43], there have been no post-index ruptures or conversions to OSR.

3) Mortality through 3 years

All-cause mortality was 8% in the first 30 days and 14.6% (7 of 48) in the first year. Throughout
Table 1. Aortic remodeling through 3 years

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<tr>
<td>False lumen maximum diameter (decreased or stable)</td>
<td>75.8 (25/33)</td>
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<tr>
<td>True lumen maximum diameter (increased or stable)</td>
<td>93.9 (31/33)</td>
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<td>False lumen thrombosis (partial or complete)</td>
<td>75.8 (25/33)</td>
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Values are presented as % (number).

Adverse events, reinterventions, and aortic remodeling through 3 years

Within the first 30 days, there were 3 cerebrovascular accidents (6%), 1 report of chronic venous insufficiency (2% [1 of 50]), and 1 retrograde type A dissection (2.2% [1 of 46]). After 30 days and within the first year, 1 additional retrograde dissection was reported, as well as 1 case of acute renal failure. In years 2 and 3, however, there were no further serious adverse events. Notably, there were no postoperative ruptures throughout the entire study period. Four reinterventions were performed after the first year, one of which was an LSA plug and not deemed dissection-related; the other 3 reinterventions were extension endografts. There were no conversions to OSR. Favorable remodeling was observed over stented segments at 12 months and through 3 years (Table 1).

For patients with acute complicated TBAD, the Valiant Captivia Thoracic Stent Graft System demonstrated acceptable rates of adverse events and positive outcomes through 3 years. There were no ruptures or conversions to OSR. Freedom from all-cause mortality was 79.4%, and freedom from dissection-related mortality was 90.0%. Only 1 dissection-related death occurred more than 30 days after the index procedure. There was a very low incidence of endovascular reinterventions, and favorable aortic remodeling was observed over the stented segment.

Conclusion

Acute complicated TBADs are the most common emergency aortic syndrome and pose a formidable treatment challenge. The 3-year midterm results of the Medtronic DISSECTION trial continue to demonstrate the safety and effectiveness of the Valiant Captivia Thoracic Stent Graft System for patients with acute complicated TBAD. The follow-up through 3 years demonstrates acceptable mortality given the serious risks that accompany acute complicated TBADs and the treatment thereof. Annual follow-up is planned for up to 5 years. Longer-term results are anticipated to be forthcoming to determine if this trend of durability can be sustained.

Conflict of interest

No potential conflicts of interest relevant to this article are reported.
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References