⟩⟩ *Review Article* ⟨⟨

Uncomplicated Acute Type B Aortic Dissection: Selection Guidelines for TEVAR

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Traditionally, the surgical management of acute type B aortic dissections was reserved for patients with signs of malperfusion, rapid expansion, retrograde dissection or rupture. The adjunct of endovascular techniques has brought a paradigm shift, leaning towards preventing long term dissection complications. Multiple risk factors have been proposed to identify patients at risk for long term aortic complications. The patients, who are offered a prophylactic endovascular therapy for uncomplicated aortic dissection, should be selected carefully, and offered intervention by an experienced team in a high-volume center. (This is a review article based on the invited lecture of the 57th Annual Meeting of Japanese College of Angiology.)

Keywords: uncomplicated aortic dissection, type B aortic dissection, thoracic endovascular aortic repair, aortic remodeling

Introduction

Traditionally, the surgical management of acute type B aortic dissections was reserved for patients with signs of malperfusion, rapid expansion, retrograde dissection or rupture. Open surgical repair of type B dissections carries a significant 30-day mortality of 14–67%, and has not changed significantly since being first described.[1,2] The thoracic endovascular aortic repair (TEVAR) of type B aortic dissection has brought a paradigm shift from only treating complications of type B dissection to both preventing and treating those complications. The advent of endovascular repair has reduced the perioperative morbidity and mortality significantly.[3–5]

The term "Uncomplicated Type B aortic dissection"

(UTBAD) was first proposed by Trimarchi et al., and described Stanford type B dissection presenting without hemodynamic instability or malperfusion syndrome.[3] This type of aortic dissection has traditionally been treated with optimal medical management with acceptable early mortality ranging around 10%.[3,4]

Despite the initial success of optimal medical management of UTBAD, aortic degeneration and aneurysmal formation of dissected aorta remain a clinical challenge.[6] As reported by DeBakey et al. in 1982[7] and Juvonen et al. in 1999[8] over 40% of patient with UTBAD will progress to aneurysm formation within 5 years from the index event. Further studies suggested that 20–50% of patients will require aortic repair, and rupture rate will reach up to 30% once the aneurysmal degeneration of the aorta reaches the diameter of 6 cm.[9–11] Thus selecting patients with UTBAD who could benefit from TEVAR becomes pertinent.

Optimal Medical Therapy vs. TEVAR for UTBAD

The Investigation of Stent Grafts in Aortic Dissection Trial (INSTEAD) published in 2009 was the first prospective, randomized controlled trial that compared optimal medical management with TEVAR for patients with type B aortic dissection. These patients were in stable clinical condition and their index dissection occurred at least 2 weeks prior.[12] Only patients with uncomplicated chronic dissection were considered for analysis, and study group included 72 patients randomized into the operative group and 68 patients randomized into the optimal medical therapy group. The primary end point of the study was all-cause mortality at 2 years. Aortic related mortality, aortic remodeling and disease progression (need for conversion, or additional procedures) were secondary end points. This study failed to show survival benefit among patients who underwent TEVAR. Furthermore, the aortic related mortality rate was not different amongst the groups. However, the TEVAR group showed significantly higher rates of aortic remodeling with true lumen expansion and false lumen thrombosis and regression. The limitations of the INSTEAD trial included its lack of power—the initial

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power analysis was based on a mortality calculation of at least 20%, which was not reached, and its relatively short follow up of two years. Despite its small sample size, it did show a positive aortic remodeling benefit after operative intervention on UTBAD.

The long term results of this study population were published in 2013 in the Investigation of Stent Grafts in Aortic Dissection Trial with extended length of follow up (INSTEAD-XL) Trial.[13] The analysis of long term results in the intervention group showed reduced all-cause mortality (11.1% in TEVAR vs. 19.3% in optimal medical management [OMT] group), aortic specific mortality (6.9% in TEVAR vs. 19.3% in OMT group), and increased freedom from disease progression and aorta-specific events (95.9% in TEVAR and 71.9% in OMT group). Both improved survival and freedom from progression after 5 years were associated with false lumen thrombosis induced by stent graft in over 90% of cases. Morphological evidence of aortic remodeling was present in almost 80% of patients in TEVAR group at 5 years, compared to only 10% of patients in best medical management group.

Mid-term outcomes of the VIRTUE registry, published in 2014, described all-cause mortality, dissection related mortality and aortic morphology after TEVAR in 100 patients treated for aortic dissection with Valiant endograft.[14] Patients were divided into three groups basing on the onset of symptoms: acute (<15 days), subacute (15–92 days) and chronic (>92 days) and their clinical outcomes were described at 3 year follow up. The authors noted that patients in the acute and subacute group had relatively low all-cause mortality following their index operation. Patients in the chronic dissection group, however, showed an increased (although not statistically significant) all-cause mortality from non-aortic pathology, as well as higher reintervention rate. The authors linked this outcome with reduced aortic remodeling, observed in patient with chronic dissection, comparing to acute and subacute group. The indications to intervene in the acute dissection group were: aortic rupture, malperfusion syndrome, impending rupture (persistent pain) and refractory hypertension. For the subacute group, the indications included: complicated/symptomatic dissection, aortic expansion > 5.5 cm, as well as aortic diameter > 4 cm with true lumen and false lumen both patent. Indications for the chronic group were: complicated/symptomatic dissection, aortic diameter > 5.5 cm or expanding > 0.5 cm/year. The authors also noted that the aortic remodeling was similar between acute and subacute groups.

Most recently, Acute Dissection Stent Grafting or Best Medical Treatment (ADSORB) results identified the number of vessels originating from the false lumen as an independent predictor of false lumen growth in UTBAD.[15] The study described clear benefit of stent placement on

aortic remodeling and increased rates of false lumen thrombosis in the intervention group compared to optimal medical management.

Clinical Predictors of Progression of UTBAD

The selection of patients, who may benefit from intervention with UTBAD remains the key in reducing complications and maximizing the benefits in aortic repair. Trimarchi et al. in 2014 summarized demographic, clinical, pharmacological and radiological risk factors predicting aortic enlargement and potentially influencing the decision to intervene in a selected group of patients.[16] Demographic risk factors for disease progression include age <60 years and white race. Patients who presented with UTBAD at age younger than 60 years exhibit an increased aortic growth rate on follow up, compared to older age groups,[9] a possible explanation for this is the relative inelasticity of aortic wall with aging and thus less prone to dilatation. Moreover, the younger age group harbors the risk of connective tissue disorder, which may contribute to faster degeneration of the aortic wall. Individuals with those genetic abnormalities exhibit accelerated aortic growth rate and increased aortic related mortality.[17]

Certain pharmacological treatment options and specific laboratory tests have been identified as risk factors for aortic enlargement. Patients treated with calcium channel blockers have less aortic growth.[18] One study by Kitada et al. identified fibrinogen–fibrin degradation product level > 20 mg/ml on admission as associated with aortic enlargement in the long-term follow up, whereas factors such as thrombin–antithrombin III complex, D-dimer, platelet count and co-reactive protein seemed to have protective effects and were associated with decreased aortic enlargement at follow up.[19]

Radiologic Risk Factors

Trimarchi lists several radiologic findings, as being unfavorable. These findings have been validated by several other authors[10,20–24]: 1) aortic diameter ≥40 mm during acute phase, 2) an elliptical configuration of the true lumen/round configuration of the false lumen, 3) patent false lumen, 4) partially thrombosed false lumen, 5) proximal descending thoracic aorta false lumen diameter ≥22 mm on initial imaging, 6) sac formation in partially thrombosed false lumen, 7) single entry tear, 8) false lumen/intimal tear located in the inner aortic curvature, 9) large entry tear (≥10 mm) located in the proximal part of the dissection.

While a maximal aortic diameter of ≥40 mm was considered a predictor of aortic growth, it was also noted by several authors that patients presenting at a higher

initial maximal diameter, reach a maximum diameter of >60 mm faster, and therefore qualified for aortic intervention sooner, than the rest of the patients.[10,20] Song et al. determined that the diameter of the false lumen on the initial computer tomography (CT) scan correlated with the rate of aortic growth on follow up.[21] Recently Ray et al. showed that a false lumen diameter >22 mm and maximal aortic diameter >44 mm on admission correlated with a decreased intervention free survival in 294 patients with UTBAD followed for 3.7 years on average.[22] Additionally, same authors determined that large false lumen diameter reflected high pressure in the false lumen and played an essential role in further aortic growth. Other factor that could indirectly reflect intraluminal pressure was the configuration of the false lumen.[23] Elliptical configuration of the true lumen, when combined with circular configuration of the false lumen, was described as indirect determinant of intraluminal pressurization of the false lumen. That in turn subjected the false lumen to higher radial forces and potentially led to higher aortic growth rate.

Presence of blood flow in the false lumen has been mentioned as a risk factor by several authors. Patent false lumen has been described as causing direct hemodynamic stress on the aortic wall and contributing to aortic enlargement.[9,10,20,24] In the same studies, a completely thrombosed false lumen has been associated with less aortic enlargement and positive aortic wall remodeling on follow-up imaging. Unfortunately, patients with a completely thrombosed false lumen were also excluded from the INSTEAD and INSTEAD-XL trials.[12,13] Inconclusive data exists on a partially thrombosed false lumen, however certain authors have found an association between partial thrombosis and an eccentric/saccular degeneration of the thoracic aorta.[9,23] Lastly, the number and size of entry/re-entry tears have been associated with aortic growth.[13,25] Tolenaar et al.[25] discovered that one entry tear at presentation is associated with higher aortic growth rate, likely due to turbulent blood flow pattern and increased pressurization of the false lumen, in the absence of re-entry. An entry tear of ≥10 mm was also associated with increased flow in the false lumen, and was associated with aortic enlargement even with presence of distal re-entry.[13]

There are limitations to utilizing strict diameter measurements of the true and false lumen to characterize aortic remodeling and predict aortic enlargement. Our group[26] proposed a volumetric analysis of the initial index CT as a method of predicting patients at a high risk of aortic growth who would benefit from an early aortic intervention. Using 3D reconstruction software, initial CT of 117 patients were analyzed. Measurements of true lumen volume (TLV) and total aortic volume (TAV) were obtained using the summation of area technique, and false lumen volume (FLV) was calculated by subtracting TLV from TAV. The authors found that a TLV/FLV ratio of <0.8 was highly predictive (odds ratio 12.2; confidence interval 5–26; P<0.001) for the need of an eventual aortic intervention (**Fig. 1**). Conversely, TLV/FLV ratio of >1.6 was highly predictive for freedom from intervention. Further analysis showed that there was no significant differences between study subgroups in 1- and 2-year freedom from aortic related mortality, reflecting the successful surveillance program and proceeding with TEVAR before rupture or death (**Fig. 2**). To date, the method of volumetric assessment had been utilized only to assess aortic remodeling after TEVAR, but never prior to intervention.[27]

Currently in our practice, the majority of patients with uncomplicated acute type B aortic dissection are not treated with TEVAR. We select patients carefully based on anatomic suitability for TEVAR and presence of radiologic or clinical factors, which are predictive of aortic dilation and need for late aortic intervention. The decision to offer a prophylactic TEVAR for an asymptomatic patient with uncomplicated acute TBAD must be made judiciously and the procedure must be done with minimal morbidity and no mortality, by a very experienced team in high-volume institution. For this reason, anatomy must be favorable for TEVAR, and we perform the procedure in delayed fashion, between 30 to 60 days after initial diagnosis. Therefore, in our institution we treat UTBAD with TEVAR in young patients, with low TLV/FLV ratio and with significant
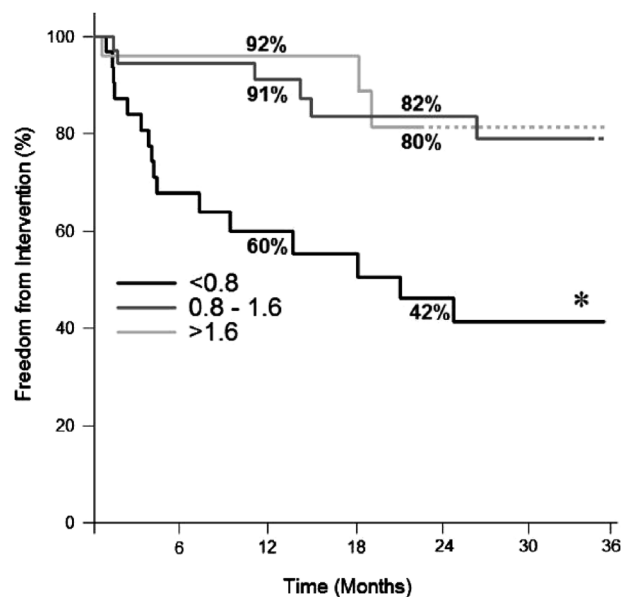

Fig. 1 Kaplan–Meier analysis for freedom from intervention (%) stratified between study participants with TLV/FLV ratios listed. The dashed line indicated the point at which standard error exceeded 10%. *Statistically different from other groups (P<0.001). [reported with permission from J Vasc Surg 2015; **62**: 893–9].
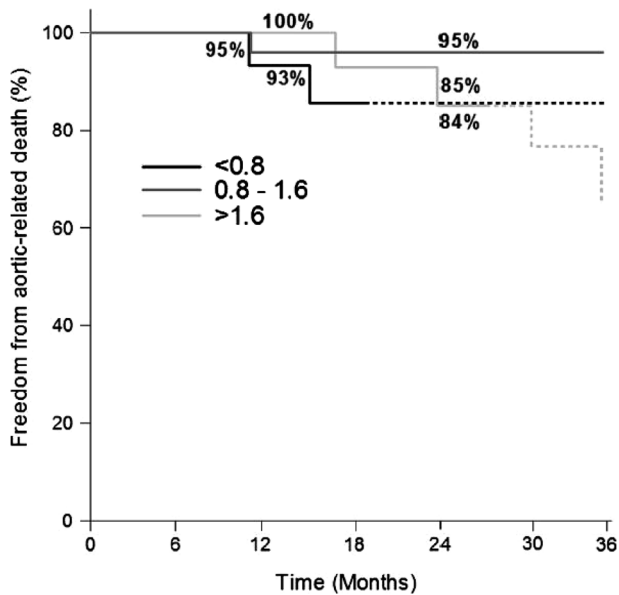
Fig. 2 Kaplan–Meier analysis for freedom from aortic-related mortality (%) stratified between study participants with TLV/FLV listed. The dashed line indicates the time point at which standard error exceeds 10%. [reported with permission from J Vasc Surg 2015; **62**: 893–9].

Fig. 3 Uncomplicated acute type B aortic dissection.

Fig. 4 Excellent remodelling of the aorta after TEVAR.

case basis, by the vascular surgery team. Incorporation of the new branched and fenestrated grafts techniques may allow patients with anatomy formerly considered prohibitive, to potentially benefit from endovascular therapy in the future.

Disclosure Statement

Author Contributions

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aortic enlargement (40–45 mm) on initial CT scan. **Figure 3** shows a dissection in the thoracoabdominal aorta, with ulcer-like projections, large entry tear in patient showing aortic enlargement of ≥ 5 mm between the index CT scan and the discharge CT scan. **Figure 4** demonstrates excellent aortic remodeling after intervention. In addition to those general guidelines, the decision is made on case-to

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