# The Use of TEVAR in Acute Uncomplicated Type B Aortic Dissection

Data and perspectives on the utility of endovascular repair in this challenging pathology.

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Thoracic endovascular aneurysm repair (TEVAR) is a lifesaving therapy and currently the preferred treatment modality for patients with Type B aortic dissection presenting with complications such as aortic rupture or malperfusion syndrome.[1-4] Its role to treat uncomplicated acute Type B aortic dissection (ABAD), however, is not yet fully clarified. Consensus has been established to manage ABAD with surveillance and optimal medical treatment (OMT) with control of hypertension and heart rate.[5,6] Despite adequate antihypertensive treatment, however, delayed aortic dilatation will develop in 20% to 50% of patients with uncomplicated ABAD, which can lead to aortic rupture or late-term complications.[2,7] Attempts have been made to evaluate the use of early aortic repair compared to conventional medical therapy in uncomplicated ABAD with the ADSORB trial.[8,9]

## ADSORB TRIAL

The ADSORB trial is the first randomized controlled trial on acute aortic dissection and compares OMT with OMT plus TEVAR, performed with the aim to cover the primary entry tear in patients with uncomplicated ABAD.[8,9] Important exclusion criteria of this study were retrograde extension of dissection proximal to the left subclavian artery and presence of a connective tissue disorder. The primary endpoint was a combination of the following variables: (1) incomplete/no false lumen (FL) thrombosis; (2) aortic dilatation (≥ 5 mm/year or descending aorta ≥ 55 mm); or (3) aortic rupture at one year.[9] One-year results demonstrated that thrombosis of the FL and reduction of its diameter are induced by the stent-graft in uncomplicated ABAD patients, but long-term results are needed.[8] Given the small sample size and duration of follow-up, the trial is not powered to detect differences in aortic-related and all-cause mortality. Therefore, a larger prospective, randomized, controlled trial with longer follow-up should be conducted to assess the preferred treatment modality for uncomplicated ABAD.

## INSTEAD TRIAL

The INSTEAD trial was the original study that compared medical management alone with additional TEVAR for long-term outcomes in uncomplicated subacute and early chronic Type B aortic dissection.[10] The rationale behind this randomized trial is that coverage of the primary entry tear with a stent-graft will induce FL thrombosis and aortic remodeling. Despite this potential benefit, TEVAR may nevertheless be associated with complications, including aortic rupture, retrograde dissection, endoleaks, and stent-graft migration; therefore, a conservative approach in many patients is still advocated.

In the INSTEAD trial, patients with uncomplicated Type B aortic dissection were randomly assigned to TEVAR in addition to OMT between two and 52 weeks from symptom onset. Patients were unsuitable for randomization in the presence of an aortic diameter > 55 mm or with other emerging recurrent complications.[10] TEVAR in addition to OMT was associated with adverse early survival at two years and adverse event rates, despite favorable aortic remodeling.[10] This excess early mortality was mainly attributable to periprocedural deaths. In contrast, improved five-year aorta-specific survival and delayed disease progression was found.[11] Congruently, data from the International Registry of Acute Aortic Dissection (IRAD) showed improved late mortality if TEVAR was performed in addition to OMT, while similar results were seen between groups regarding early mortality.[12] The INSTEAD trial suggests that OMT and surveillance were associated with failure to prevent late complications, including aneurysmal growth, rupture,

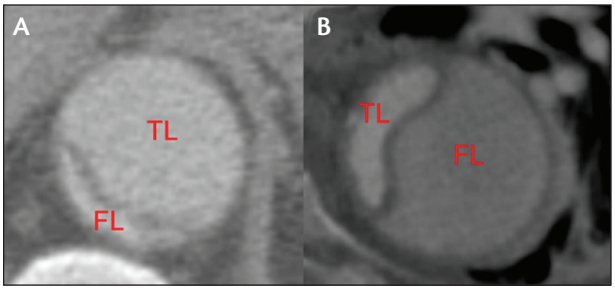


**Figure 1. Computed tomography images show the configuration of the TL and FL. A circular-shaped TL is shown (A). An elliptic shape results when the FL compresses the TL (B). Adapted from J Vasc Surg, Volume 58, Tolenaar et al, Morphologic predictors of aortic dilatation in type B aortic dissection, pages 1220-1225, Copyright 2013, with permission from Elsevier.[17]**

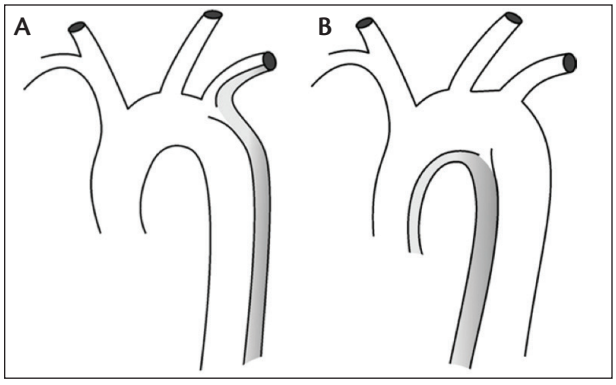


**Figure 2. Scheme of different sites of the primary entry tear of acute Type B aortic dissections (A). Primary entry tear at the outer circumference of the distal aortic arch defined as "convex." The retrograde component of the dissection is stopped by the left subclavian artery (B). Primary entry tear at the inner circumference of the distal aortic arch defined as "concave," allowing progression of the retrograde component of the dissection into the aortic arch and the ascending aorta. Adapted from Ann Thorac Surg, Volume 93, Loewe et al, A new mechanism by which an acute type B aortic dissection is primarily complicated, becomes complicated, or remains uncomplicated, pages 1215-1222, Copyright 2012, with permission from Elsevier.[20]**

and late conversion to emergent TEVAR, conveying a higher aorta-specific mortality. Thus, initial clinical stability ("uncomplicated") does not preclude emergent silent expansion and even rupture, and both events might be preventable by TEVAR in the early phase. Therefore, preemptive TEVAR should be considered in stable Type B dissection with suitable anatomy to avoid late complications. OMT alone may delay progressive aortic expansion, at best; conversely, TEVAR induces aortic remodeling. It should be noted that the INSTEAD trial included patients undergoing TEVAR in the subacute and early chronic phase, and therefore, their results cannot be completely generalized for the acute phase of Type B aortic dissection. Larger randomized, controlled trials should be established to address this open issue.

## CLINICAL AND RADIOLOGICAL PREDICTORS OF AORTIC GROWTH

To identify a cohort of uncomplicated ABAD patients at high risk for aortic growth and subsequent aortic rupture, several studies have been conducted.[13-17] Certain clinical and radiological predictors of aortic growth in ABAD patients have been identified (Table 1).[18] Recently, Tolenaar and colleagues found that the number of entry tears at initial imaging was associated with aortic growth during follow-up.[19] Patients with one entry tear at presentation showed a higher growth rate compared to patients with multiple entry tears.[19] The presence of only one patent entry tear might pressurize the FL and change the normal laminar flow into turbulent flow, leading to higher stress of the aortic wall and, due to a weakened dissected aortic wall, also to aortic enlargement. Additionally, Evangelista and colleagues demonstrated that patients with a primary entry tear ≥ 10 mm in the proximal part of the dissection presented more frequently with dissection-related events and experienced a higher growth rate than those with an entry tear < 10 mm.[13] A larger tear size suggests that more blood enters the FL, causing increased FL pressurization and subsequent aortic enlargement. Interestingly, in the majority of patients, at least three-year follow-up was required before complications occurred, which indicates that structural and hemodynamic changes in the aortic wall and aorta require time to appear.[13]

Different radiologic predictors, including patent FL, FL diameter > 22 mm, elliptic true lumen (TL) combined with round FL (Figure 1), one entry tear, and entry tear size > 10 mm all seem interrelated due to pressurization of the FL, with subsequent aortic growth of the dissected segment.[17,18] Recent studies have shown that those patients with an entry tear at the concavity/undersurface of the distal aortic arch have more frequent development of complications (Figure 2).[20,21] This cohort of patients at high risk for aortic growth might benefit from closer follow-up and early intervention, even if those patients initially presented without complications. This approach deserves even more consideration because a significant number of patients will develop aneurysmal degeneration along the dissected segments during follow-up, and may lose the opportunity for endovascular treatment if not identified at an early stage.[18]

**TABLE 1. PREDICTORS OF AORTIC GROWTH IN UNCOMPLICATED TYPE B AORTIC DISSECTION**

| | Predictor | Negative Predictor |
|---|---|---|
| **Patient characteristics** | Age < 60 y | Increasing age (≥ 60 y) |
| | White race | |
| | Heart rate ≥ 60 bpm | Heart rate < 60 bpm |
| **Medical history** | Marfan syndrome | |
| **Clinical information** | | Use of calcium-channel blockers |
| **Blood test** | FDP level ≥ 20 µg/mL on admission | |
| **Radiologic signs** | Aortic diameter ≥ 40 mm during acute phase | Diameter < 40 mm (debated) |
| | Patent FL | Closed/thrombosed FL |
| | Partially thrombosed FL (debated) | |
| | Proximal descending thoracic aorta FL diameter (≥ 22 mm) on initial imaging | |
| | | IMH |
| | Sac formation in partially thrombosed FL | |
| | One entry tear | Increased number of entry tears |
| | FL/intimal tear located at the inner aortic curvature | FL/intimal tear located at the outer curvature |
| | An elliptic configuration of the TL/round configuration FL | A circular configuration of the TL/elliptic configuration FL |
| | Areas with localized dissection/ULP | |
| | Degree of fusiform dilatation of the proximal descending aorta (FI ≥ 0.64) | FI < 0.64 |
| | Large entry tear (≥ 10 mm) located in the proximal part of the dissection | |

*Abbreviations: BPM, beats per minute; FDP, fibrinogen-fibrin degradation product; FI, fusiform index; FL, false lumen; IMH, intramural hematoma; TL, true lumen; ULP, ulcer-like projections.*
*Adapted from J Vasc Surg, Volume 59, van Bogerijen GH et al, Predictors of aortic growth in ucomplicated type B aortic dissection, pages 1134-1143, Copyright 2014, with permission from Elsevier.*[18]

## RETROGRADE TYPE A DISSECTION

Retrograde Type A dissection is a feared complication after TEVAR and is one of the factors limiting the routine use of this treatment modality for uncomplicated ABAD.[22] Despite its rare occurrence (estimated 1%–2%), it has a high risk of mortality (around 40%).[22] Considering other stent-graft-related complications such as endoleaks and stent-graft migration, further modification of current device design and endovascular approach is warranted.

## FUTURE PERSPECTIVES

To assess the management controversies of uncomplicated ABAD, larger randomized, controlled trials should be conducted. The timing of the procedure is especially of interest in studies about uncomplicated Type B dissection and can be classified into acute (0–2 weeks); subacute (2–8 weeks), and chronic Type B dissection (> 8 weeks).[23] Other temporal classifications have also been used. Recently, the IRAD registry described a new temporal classification system of acute dissection

based on survival curves demonstrating that survival decreases significantly up to 30 days after presentation, with chronic dissection defined > 30 days after symptom onset.[24] A recent European multidisciplinary expert group defined acute Type B dissection as < two weeks, subacute two to six weeks, and chronic > six weeks from symptom onset.[25] Taking into consideration these and other temporal classification systems, an updated consensus definition of dissection acuity based on survival and aortic event rates, as well as the temporal relationship between the aortic remodelling after endovascular therapy and dissection chronicity is needed. Studies should be focused also on early and late outcomes related to the timing of TEVAR, either in the acute, subacute, or chronic phase.

Over the last year, the United States Food and Drug Administration approved both the Conformable Gore® TAG® Thoracic Endoprosthesis (Gore & Associates) and Valiant Thoracic Stent Graft (Medtronic) devices for the treatment of acute and chronic, complicated and uncomplicated, Type B aortic dissections. However, the clinical trials leading to approval of the devices included only acute, complicated Type B dissection cases. Robust data to support the indication of TEVAR for uncomplicated ABAD are not currently present, and future studies will help determine appropriate therapeutic pathways. ■

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