

## EDITORIAL

## Are Risks Reduced by Delaying Thoracic Endovascular Aneurysm Repair in Patients with Acute Type B Dissection: Who Can Wait?

The treatment of type B aortic dissection (TBAD) has changed since the advent of thoracic endovascular aneurysm repair (TEVAR). Medical treatment alone is under scrutiny, as some 28% of patients with initially uncomplicated TBAD develop aortic related delayed complications, and another 12.5% will die from aortic rupture before undergoing TEVAR.<sup>1</sup> Therefore currently, selected patients with initially uncomplicated TBAD, but specific clinical features or anatomy resulting in a higher risk of developing dissection related complications, are treated more often with TEVAR.<sup>2–4</sup> Clinical features include persistent pain, increasing pleural effusion, or uncontrollable hypertension; anatomical features include an aortic diameter of >4.0 cm with true and false lumens both patent, a primary entry tear with a diameter  $\geq 10$  mm, a false lumen diameter  $\geq 22$  mm, and partial false lumen thrombosis.

Timing for TEVAR in this cohort of patients remains controversial but may be important in view of the impact on aortic remodelling.<sup>5,6</sup> In the acute phase an increased risk of retrograde aortic dissection has been reported.<sup>7</sup> Those who recommend waiting at least two weeks for the dissection process to cool down justify their choice based on lower peri-operative complications with still acceptable aortic remodelling rates.<sup>8</sup> Those who recommend treating patients in the acute phase believe the risks are acceptable and aortic remodelling will be maximised the sooner the TEVAR is done.<sup>9</sup> An additional argument is that technical success is decreased when patients are treated in a more chronic dissection phase.<sup>5</sup>

So far, there is no strong evidence to guide a decision on who to treat and what the optimal timing of TEVAR is in patients with initially uncomplicated TBAD. Most of the available data focusing on timing of TEVAR originate from two multicentre studies, one registry, and a few smaller case series.

The Virtue registry analysed the outcomes of TEVAR performed in patients with uncomplicated TBAD based on its chronicity.<sup>10</sup> Mid term analysis of this registry was based on a comparison of patients treated during the acute (<2 weeks,  $n = 50$ ), subacute (2–6 weeks,  $n = 24$ ) or chronic (>6 weeks,  $n = 26$ ) dissection phase. No difference in false lumen area or expansion of the true lumen was found between patients treated in the acute and subacute phase. Retrograde aortic dissection did occur in two patients

treated in the acute phase, but it did not occur in patients treated in the subacute or chronic phases. Both acute and subacute groups had a greater reduction in false lumen area than the chronic clinical cohort. Thus, performing TEVAR in the subacute phase (>2 weeks) appears to be safer, while keeping the same potential of aortic remodelling, as TEVAR done during the acute phase.

The INvestigation of StEnt grafts in Aortic Dissection (INSTEAD) trial was the first multicentre, randomised trial to study TEVAR in patients with uncomplicated TBAD.<sup>8</sup> In this trial the same strategy of performing TEVAR during a subacute or early chronic phase (range 2–52 weeks; mostly 10–12 weeks) was used.<sup>8</sup> At the five year follow up, the risks of all cause mortality (11.1% vs. 19.3%;  $p = .13$ ), aorta specific mortality (6.9% vs. 19.3%;  $p = .04$ ), and progression (27.0% vs. 46.1%;  $p = .04$ ) were lower in the TEVAR group than in those receiving best medical treatment (BMT) alone. In the TEVAR group, complete false lumen thrombosis occurred in 90.6% of patients, with morphological evidence of aortic remodelling in 79.2% at five years.<sup>8</sup> The message conveyed by the INSTEAD trial was that TEVAR is safe, if done in a more subacute/chronic phase and, at the same time, very effective with regard to aortic remodelling.

The Acute Dissection: Stent graft OR Best medical therapy (ADSORB) trial was a randomised trial that compared BMT alone vs. BMT plus TEVAR. Different from the INSTEAD trial, this study enrolled patients who were treated within two weeks of the onset of symptoms (acute phase).<sup>11</sup> No strokes, no paraplegia, and no deaths occurred in either group regardless of which phase TEVAR was done. The trial demonstrated that aortic remodelling was noticeably more frequent in patients undergoing acute phase TEVAR at the one year follow up.<sup>11</sup> Following the same line of thought as the ADSORB trial, a recent study analysed data from 338 patients treated by TEVAR during the acute dissection phase (TEVAR [ $n = 184$ ] vs. BMT [ $n = 154$ ]).<sup>9</sup> In the TEVAR group, organ failure occurred in one (0.5%) patient and stroke in another (0.5%), but no aortic rupture was reported and the 30 day mortality rate was 0.5%. Overall, fewer aortic related adverse events (TEVAR 23.9% vs. BMT 38.3%;  $p = .005$ ) and lower all cause mortality rates were demonstrated in patients undergoing TEVAR (<14 days from initial presentation) than in those receiving BMT alone (4.3% vs. 12.3%;  $p = .03$ ).<sup>9</sup> **Supplementary Table 1** summarises the outcomes of the two multicentre trials,<sup>8,11</sup> and the Virtue registry.<sup>10</sup>

A series by Zhu *et al.* reported 47 patients with uncomplicated TBAD treated by TEVAR during the acute phase. Again, no deaths, stroke, retrograde type A aortic

dissection, or distal stent induced new entries were seen, which showed that TEVAR was safe and effective during acute phase dissection.<sup>12</sup> Another small case control study comparing a group of 22 patients with TBAD who were treated in the acute phase (<2 weeks) with a second group of 16 patients treated by TEVAR in the subacute phase (2 weeks–3 months) has been reported.<sup>13</sup> Complication rates were similar, but aortic remodelling following TEVAR was more pronounced in the acute phase than in the subacute phase cohort. Thus, these results, coupled with those of the ADSORB trial,<sup>9</sup> along with other centres,<sup>9,12,13</sup> favour TEVAR during the acute dissection phase as a safe and efficacious treatment strategy.

So, where do we stand in terms of timing for TEVAR in patients with uncomplicated TBAD at this time? We cannot yet answer this question because of the heterogeneity of the available data discussed and lack of head to head comparison between patients treated during acute and subacute phases. Intuitively, the answer would be to wait, because the majority of the patients can. However, missing the best time window to elicit maximum aortic remodelling may not be desirable. For now, the priority will continue to be to find a way to determine accurately which patients with initially uncomplicated TBAD should be treated by TEVAR, without losing focus on research efforts aimed toward answering whether those patients requiring TEVAR should be treated in the acute or subacute phase.

#### CONFLICTS OF INTEREST

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#### APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejvs.2019.07.020>.

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