ASK THE EXPERTS

Does Early TEVAR Prevent Aneurysmal Degeneration?

Selection criteria, results of studies comparing medical therapy with TEVAR, and what future studies should seek to evaluate.

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The traditional recommended management of type B aortic dissection (TBAD) is initial medical management, reserving intervention for acute complicated dissections mainly to resolve malperfusion and prevent or treat rupture. Patients with uncomplicated TBAD are continued on medical therapy, and intervention is performed in cases of aneurysmal dilation, malperfusion, intractable pain, or patient preference. The initial results of the INSTEAD trial, which randomized subacute patients (beyond the first 2 weeks) to optimal medical therapy (OMT) or OMT plus endovascular repair (anatomically suitable and clinically stable patients), showed no difference in overall survival at 2 years. However, a subsequent analysis at 5 years showed improved survival in patients who had endovascular repair in addition to OMT. Several important observations resulted from this trial. No difference in survival was seen between the two groups within the first 6 to 8 weeks after the dissection. This was mostly due to the morbidity and mortality associated with endovascular intervention within this early interval. Aneurysmal degeneration occurred in around 40% of patients whose false lumen (FL) was > 22 mm, whereas it was only seen in about 5% of patients with a FL < 22 mm. In addition, proximal tears > 10 mm were associated with a higher risk of rupture, and all patients who crossed over from the OMT to the endovascular group had tears > 10 mm. Other investigators have suggested that the presence of multiple tears, particularly with a partially thrombosed FL, also identifies patients at a higher risk of aneurysmal degeneration. In our experience, patients undergoing infrarenal aortic replacement (which decompresses the FL) with retrograde debranching as a hybrid strategy to treat TBAD will rarely have aneurysmal degeneration of the intervening segment in the descending thoracic aorta. This observation suggests that decompression of the FL significantly decreases the risk of aneurysmal dilation.

Prophylactic thoracic endovascular aortic repair (TEVAR) after TBAD to prevent aneurysmal degeneration is not supported by available data. A systematic review of

aneurysmal degeneration of TBADs after TEVAR concluded that the risk of aneurysmal degeneration over time in the thoracic aorta after endovascular repair approaches or is equal to the risk of treating with medical therapy alone. In fact, this was true for both thoracic and abdominal segments of the aorta following a TBAD. However, the fact remains that there appears to be a survival benefit for patients treated with an endovascular intervention after the first 6 to 8 weeks from the initial event. Therefore, it is plausible to have a selective approach in which anatomically suitable patients with > 2-year life expectancy can be offered endovascular repair in combination with best medical therapy. This is particularly the case in patients who are identified as having a higher risk of aneurysmal degeneration based on their initial presentation, considering the size of the FL and/or the size of the proximal tear. Management of patients with TBAD beyond the acute presentation is rapidly evolving. I anticipate that as more clinical information on long-term outcomes becomes available, there will be further refinements in the selection criteria for patients who will benefit from a combined medical and endovascular approach.

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In the last 2 decades, we have learned a lot about uncomplicated TBAD. We know that medical therapy alone will result in aortic-related delayed complications in about 30% of patients and mortality before treatment in > 10% of patients.[1] Selected patients with initially uncomplicated TBAD but specific clinical features or anatomy resulting in higher risk of developing dissection-related complications are currently treated more often with TEVAR.[2]

So far, there is no strong evidence to guide the decision on who to treat and the optimal timing of TEVAR in patients with initially uncomplicated TBAD. Timing of treatment seems to be a trade-off between delayed treatment with potentially lower risk of retrograde dissection and earliest possible treatment to increase chances of remodeling.[3] Both the INSTEAD and ADSORB trials documented favorable remodeling after TEVAR compared with medical treatment, as well as lower aortic-related events during follow-up, but there are no data on prevention of long-term aneurysmal degeneration.[4,5]

Does early TEVAR prevent aneurysmal degeneration? The answer is probably "no" for most cases, if we take into account that several series have reported postdissection thoracoabdominal aortic aneurysm (PDTAAA) after TEVAR and that a number of patients will not develop PDTAAA after medical treatment only. Therefore, at least at this moment, it is absolutely impossible to prove that early TEVAR increases the proportion of patients that will not develop a PDTAAA. Conversely, closing the entry tear with TEVAR in the absence of distal reentry tears may result in healing of the aorta. An extra argument to support my "no" answer is the ongoing search for adjunctive endovascular techniques to counteract distal aortic dilatation. The PETTICOAT technique with additional stenting over the visceral arteries using the Zenith dissection stent (Cook Medical) demonstrated benefits with regard to true lumen diameter, but failed to demonstrate a clear advantage in preventing aneurysmal dilatation.[6] The "new kid on the block" is the stent-assisted balloon-induced intimal disruption and relamination in aortic dissection repair (STABILISE) technique.[7] The concept of STABILISE includes the use of a stent graft to cover the proximal entry tear (TEVAR), followed by a noncovered stent over the visceral arteries (eg, PETTICOAT), and then additional ballooning with a larger balloon to disrupt the dissection flap with the aim of obliterating the FL and restoring single lumen flow. In theory, the technique seems to be a serious attempt to "cure" dissection patients and prevent late aneurysmal degeneration, but more studies are required to prove both safety and efficacy. A European registry on STABILISE created by Melissano and colleagues aims to collect data from multiple European centers and monitor the technique in the long term, hoping to provide some answers to the aforementioned questions.

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Much has been learned regarding treatment of TBADs over the last decade. Clearly, TEVAR has become the treatment of choice for complicated dissections. However, the debate exists as to whether to treat uncomplicated TBADs. Without question, aneurysmal degeneration can lead to significant morbidity and mortality, and left alone, some proportion of uncomplicated TBADs will progress to chronic TAAAs.

Looking at the data, it seems we can predict which anatomies are more prone to aneurysmal progression with some reliability. Treatment modalities have improved resulting in higher success (ie, FL thrombosis) and reduced periprocedural risk. When taken together, it would seem reasonable to treat patients who have moderate- to high-risk anatomy and reasonable life expectancy. Early treatment would entail true lumen expansion with TEVAR. Adjunctive procedures are also often beneficial including sealing of additional fenestrations. We have endorsed treating patients within the first 7 to 14 days when the flap is most mobile, thus increasing the probability of true lumen expansion and pressurization. All in all, we believe that the benefits of early treatment clearly outweigh the small risks of treatment and have moved toward this paradigm.

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The questions of aortic remodeling and prevention of aneurysmal degeneration after TEVAR are vital in the uncomplicated chronic TBAD population. Uncomplicated TBADs are defined by a tear in the thoracic aorta distal to the left subclavian artery that does not result in end-organ malperfusion or impending rupture of the aorta. The dissection flap has to be present for > 2 weeks after the onset of symptoms for it to be deemed chronic. The INSTEAD trial randomized 140 patients with early chronic uncomplicated TBAD into OMT or TEVAR with OMT. The initial 2-year results failed to demonstrate a survival benefit between the OMT and TEVAR groups. Furthermore, there was no difference between the maximal aortic diameters at this 2-year break point. Due to an overestimation of the projected event rate of primary and secondary endpoints at 2 years, the trial was underpowered to discriminate these differences. However, the trial was able to detect a benefit to aortic remodeling within the TEVAR group. The investigators observed increased true luminal diameter, decreased FL diameter, and increased rate of FL thrombosis.

In light of the limitations surrounding the 2-year results, the 5-year follow-up results from the INSTEAD-XL trial provided more insight and clarity regarding the primary and secondary endpoints. The 5-year data from the INSTEAD-XL trial were suggestive of a late survival benefit in both all-cause and aortic-specific mortality in the TEVAR arm. Furthermore, the 5-year results demonstrated that the TEVAR group again showed improved aortic remodeling. However, in contrast to the 2-year results, there was a notable increase in the maximum aortic diameter in the OMT arm at 5 years compared with the TEVAR arm. The decreased growth of the maximum aortic diameter in the TEVAR group supports the role that TEVAR plays in preventing aneurysmal degeneration over long-term follow-up.

The next challenge, which is beyond the scope of this article, is in the realm of acute aortic dissection. A recent analysis of statewide administrative data from California, found a survival benefit at 5 years in acute TBAD patients treated with TEVAR compared with OMT. Thus, it is our opinion that TEVAR does reduce aneurysmal degeneration in chronic TBADs, but more information and research are needed to determine whether there should be a paradigm shift within the initial management of uncomplicated acute TBADs. If a change in acute TBAD practice occurs, the trials evaluating the chronic condition will need to be revisited.

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Since its inception, TEVAR has gained popularity in treating various aortic pathologies, from aneurysmal disease to aortic dissection. Currently, TEVAR is widely adopted for complicated aortic dissection, whereas aggressive medical management continues to be the standard for uncomplicated acute TBAD. Given the relatively high incidence of late aneurysm degeneration and 30% to 40% long-term mortality,[1] there is a considerable interest in treating uncomplicated acute TBAD with TEVAR with the assumption that early TEVAR would prevent long-term aneurysmal degeneration.

Multiple studies have evaluated aortic remodeling, but most have encountered the challenges of short follow-up and inadequate sample size. The most noticeable trials are the ADSORB and INSTEAD trials. The ADSORB trial evaluated 50 patients with TBAD and showed a favorable FL thrombosis but did not show significant reduction in overall aortic diameter in the TEVAR group compared with the medically treated group.[2] The INSTEAD trial enrolled 140 patients with TBAD and showed no survival benefit for early TEVAR compared with OMT during the initial 2 years. However, the follow-up study, INSTEAD-XL, showed an improvement of aortic specific mortality (6.9%) and progression (27%) in the TEVAR group compared with those in the OMT group (19.3% and 46.1%, respectively) at 5 years.[3] However, a systematic review of 17 studies on TEVAR for TBAD concluded that TEVAR did not prevent aneurysmal degeneration.[4] With increased experiences of using TEVAR for acute TBAD, retrograde type A dissection and stent graft–induced new entry have become increasingly visible complications that bear a devastating outcome. Currently, the data are still limited. Although TEVAR has shown promise in preventing late aortic aneurysmal degeneration, TEVAR for uncomplicated acute TBAD should not be a routine practice. Timing of the intervention and patient-specific strategy need to be considered.[5] With increased clinical proficiency, improved technology, and dissection-specific stent, early TEVAR may become a standard care in the future.

It is worth mentioning that China has the largest experience of aortic dissection. A more aggressive endovascular approach has been adopted in treating TBAD. More than 11,000 TEVAR cases in China were reported in the literature in 2018.[6] These reported cases are largely concentrated in several key regions. Chinese patients receiving TEVAR are younger and have less atherosclerotic disease than those of Western countries, and impressively low major complication, in-hospital mortality, and follow-up mortality rates have been reported from China.[6] However, due to the lack of standard practice guidelines and long-term follow-up, only a few of the cases are effectively used to produce high-level clinical evidence.

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Medical therapy continues to be the standard of care for patients with uncomplicated acute TBAD. However, follow-up studies reveal a more worrisome outlook with medically treated patients, demonstrating significant aneurysmal degeneration and often surgical intervention in up to 40% of patients.[1] Recent studies have challenged the medical therapy paradigm, suggesting that the natural history of asymptomatic aortic dissection may be favorably altered by TEVAR. The objectives of TEVAR include coverage of the proximal intimal tear to allow for decreased FL flow, subsequent expansion of the true lumen, and hopefully eventual FL thrombosis. Obliteration of the FL appears to be the most important factor and desired objective with TEVAR.

Aneurysmal degeneration appears to be directly correlated with persistent FL perfusion. Can we therefore change this natural history with TEVAR? Whereas the INSTEAD trial demonstrated no survival benefit at 1 year, it did reveal a 5-year survival benefit and specifically in aorta-specific survival. Additionally, it demonstrated a marked decrease in the FL diameter from 29.3 to 10.4 mm, and complete FL thrombosis was achieved in 91% of patients at 5 years.[2] Five-year follow-up of patients who had TEVAR for repair of acute complicated TBAD demonstrated that all patients who required late intervention had a patent FL.[3] In a recent study looking at "real-world" results from a large series of patients in California, patients treated with TEVAR exhibited a survival advantage over patients treated medically.[4]

Numerous studies have demonstrated the safety and efficacy of early TEVAR in acute complicated TBAD. When considering treating asymptomatic patients with uncomplicated TBAD, one must consider the risk of inducing complications such as retrograde type A aortic dissection, spinal cord ischemia, stroke, and malperfusion. We have learned our lessons over the last decade. We now know that we should generally only oversize 5% to 10% proximally and, ideally, distally as well. The risk of stroke and spinal cord ischemia do not seem as prohibitive as once thought, and because of true lumen expansion and the presence of distal reentry tears, malperfusion is rarely worsened after TEVAR.

In my practice, I continue to be aggressive in attempting to change the natural history of uncomplicated TBAD in patients with worrisome anatomic features such as aortic diameter > 40 mm in the thoracic aorta, large patent FL > 22 mm, and proximal entry tear > 10 mm. I also tend to be more aggressive in younger and healthier patients. I believe these patients in particular have a high risk of long-term aneurysmal dilatation in the future and can benefit from early TEVAR.

Long-term data are especially needed in this patient population to decipher whether TEVAR changes the natural history with respect to remodeling and decreased aneurysmal degeneration. In addition, we look forward to future studies as well as long-term follow-up of ongoing studies, which will shed light on the optimal timing of intervention, whether there is benefit to staging interventions with respect to increased thoracic aortic coverage with a covered stent, and the effect that a distal self-expanding bare stent may have on FL obliteration with or without dissection septum ballooning within the covered and bare stent (STABILISE technique). ■

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