Need for and update on clinical trials for uncomplicated type B aortic dissection

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ABSTRACT

The mainstay of management for uncomplicated type B aortic dissection is currently optimal medical therapy, targeting blood pressure and heart rate, along with serial imaging. There is a paucity of data that informs whether early intervention with thoracic endografting in this group of patients will promote aortic remodeling and better long-term outcomes. Investigations to date, including the Investigation of Stent Grafts in Aortic Dissection (INSTEAD), INSTEAD-XL, and Acute Dissection: Stent Graft or Best Medical Therapy (ADSORB) studies, have compared thoracic endovascular aortic repair (TEVAR) with optimal medical therapy in patients with uncomplicated type B aortic dissection but have not shown a benefit for TEVAR conclusively. We discuss three major new randomized trials, which will recruit concurrently in Scandinavia (the Scandinavian trial of uncomplicated aortic dissection therapy [SUNDAY] trial), in the United States (the IMPRoving outcomes in vascular DisEase - aortic dissection [IMPROVE-AD] trial) and the United Kingdom (the Early aortic repair in patients needing endovascular surgery for type B aortic dissection [EARNEST] trial), which promise to provide conclusive, level 1 evidence to decipher whether early TEVAR in this cohort of patients in beneficial. (JVS-Vascular Insights 2024;2:100130.)

Keywords: Uncomplicated type B aortic dissection; TEVAR; Aortic surgery; Optimal medical therapy

Type B aortic dissections (TBADs), that occur when an entry tear in the intimal layer of the aorta distal to the left subclavian artery propagates blood from the true lumen to the consequent false lumen, can acutely lead to aortic rupture or malperfusion and ischemia of end-organs.[1,2] Such complicated TBADs are associated with increased morbidity and mortality.[3] In uncomplicated TBADs, where the tear and consequent changes in aortic hemodynamics do not lead to the aforementioned sequalae, management tends to be optimal medical therapy (OMT), using pharmacological manipulation of heart rate and blood pressure and serial surveillance imaging.[4] This approach, however, has been under scrutiny for a number of years. Issues surrounding compliance with drugs, loss to follow-up and disease progression are real concerns, with some survival analyses suggesting a mortality rate of 25% and 50% at 3 and 5 years, respectively, for uncomplicated TBAD patients discharged solely on OMT.[5-7] Data on the natural history of uncomplicated TBADs that were initially managed medically indicates that, at 5 years, a significant proportion of patients will have failed medical management and required aortic intervention (24%) and that overall survival is better with intervention compared with no intervention (76% and 58%, respectively).[8] With reports suggesting such high incidence of late interventions and mortality during follow-up of medically managed patients, it is little wonder that there is an appetite for evidence that informs the role of pre-emptive thoracic endovascular aortic repair (TEVAR) in this group of patients. Key trials including Investigation of Stent Grafts in Aortic Dissection (INSTEAD), INSTEAD-XL, and Acute Dissection: Stent Graft or Best Medical Therapy (ADSORB) have evaluated the role of TEVAR in uncomplicated TBAD, but these data are not of sufficient quality to inform best practice and there remains equipoise as to whether uncomplicated dissection is treated best with OMT or surgical intervention.

RANDOMISED TRIALS INFORMING THE BENEFIT OF TEVAR FOR UNCOMPLICATED TBAD

The INSTEAD and INSTEAD-XL trials. The first randomized comparison between TEVAR and OMT in uncomplicated TBAD, the INSTEAD trial,[9] demonstrated that at 2 years there was no difference in all-cause mortality, aortic-related death, or progression of dissection between TEVAR with OMT and OMT alone. There was, however, favorable remodeling in the TEVAR group, with false lumen thrombosis seen in 91% (vs 19% in the OMT alone group). INSTEAD enrolled 140 patients from 7

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centers in France, Germany, and Italy, and reported its findings in 2009. The trial recruited patients with uncomplicated TBAD with symptom onset between 2 and 52 weeks and without classic indications for TEVAR. However, there were limitations in the trial, including a lack of statistical power and a short follow-up of only 2 years. Recruiting patients with symptom onsets that encompass both subacute and chronic dissections may have created a heterogenous group of noncomparable patients, as well as excluding all of those who may have benefitted from TEVAR in the acute stage.

Extending the INSTEAD study using the same patient cohort, INSTEAD-XL[10] was a follow-up retrospective analysis of longer term outcomes at 2 to 5 years. Although no difference in all-cause mortality was found at 5 years, there was a significantly lower aortic-related mortality (7% vs 19%; $P = .04$) and disease progression (27% vs 46%; $P = .04$) in the TEVAR with OMT group compared with the OMT alone group, with landmark statistical analysis showing a significant long-term survival benefit between years 2 and 5.

The ADSORB trial. ADSORB[11] was a randomized controlled trial of patients with acute uncomplicated TBAD (n = 61), instigated in 2014, comparing TEVAR (Gore TAG device; W. L. Gore & Associates, Flagstaff, AZ) plus OMT (n = 31) against OMT alone (n = 30). Only patients with a symptom history of <14 days were included and treatments were performed within 48 hours of randomization. This study used a composite primary end point encompassing false lumen thrombosis, aortic dilatation, and aortic rupture. At 1 year, there was greater false lumen thrombosis ($P < .001$) and decrease in false lumen size ($P < .001$) in the TEVAR group, with no aortic ruptures or aortic-related mortality in either group. A further analysis in 2017[12] demonstrated that the number of vessels originating from the false lumen was an independent predictor of false lumen growth, and advancing age was a negative predictor of aortic growth. The main conclusion from the ADSORB trial was that TEVAR promotes false lumen thrombosis and decreases the risk of aortic dilatation, although it did not demonstrate a survival advantage and was not powered to do so.

SELECTED RETROSPECTIVE STUDIES ATTEMPTING TO INFORM THE BENEFIT OF TEVAR FOR UNCOMPLICATED TBAD

All-cause and aortic-related mortality. Retrospective studies have compared all-cause mortality in acute uncomplicated TBADs between different treatment strategies. Qin et al[13] evaluated acute uncomplicated TBADs (n = 338) in three centers treated with TEVAR (n = 184) and OMT alone (n = 154) and found all-cause mortality to be significantly higher ($P = .01$) in OMT alone patients compared with the TEVAR group over 11 years. Iannuzzi et al[14] also evaluated acute uncomplicated TBADs (n = 9165) treated with OMT alone (95%), TEVAR (2.9%), or open surgical repair (2%) from the California Office of Statewide Hospital Planning Database, demonstrating that all-cause mortality was significantly lower ($P < .01$) with TEVAR (19%; median follow-up, 1.5 years) compared with OMT (37%; median follow-up, 2.3 years), and open surgical repair (34%; median follow-up, 2.3 years). Xiang et al[15] similarly showed that among acute uncomplicated TBADs (n = 357), the freedom from all-cause mortality was significantly higher with TEVAR (n = 191) compared with OMT alone (n = 166) at 1, 3, and 5 years ($P = .028$).

In 338 acute uncomplicated TBADs treated with TEVAR (n = 184) or OMT (n = 154), the cumulative freedom from aortic-related adverse events at 5 years was 71.8% and 62.2% ($P = .025$), respectively, indicating that patients treated with OMT alone had more aortic-related adverse events than those treated with TEVAR.[13] This retrospective analysis also showed that aortic-related mortality with TEVAR was 4.3% as opposed to a significantly higher rate of 12.3% with OMT alone. Similarly, among 357 acute uncomplicated TBADs treated with TEVAR (n = 191) or OMT (n = 166), the freedom from aortic-related mortality after 5 years was significantly higher ($P = .044$) with TEVAR (94.1%) than with OMT (86.1%).[15]

Torrent et al[16] analyzed Vascular Quality Initiative data pertaining to 688 patients with uncomplicated TBAD who were treated with TEVAR either acutely (1-14 days) or subacutely (15-90 days). Although acute repair was associated with a higher reintervention rate, no difference in the 1-year mortality rate was observed between the groups (13.3% vs 8.2%; $P = .129$). Xie et al[17] also showed no significant difference between uncomplicated TBADs (n = 267) treated with TEVAR acutely (n = 130) and subacutely (n = 137) in all-cause mortality (4.2% and 8.3%, respectively) over a median follow-up period of 48.2 ± 25.9 months (range, 1-106 months). Similarly, Xiang et al[18] demonstrated that in uncomplicated TBADs (n = 238) treated with TEVAR acutely (n = 142) and subacutely (n = 96), there was no significant difference ($P = .39$) in all-cause mortality (7.3% and 12.4%, respectively) after 5 years. These retrospective reports of nonrandomized data indicate a signal that the all-cause mortality rates in uncomplicated TBAD patients 1 to 5 years after TEVAR are relatively low, irrespective of whether the repair was carried out acutely or subacutely.

Potential predictive factors (high-risk features) influencing operative selection. The Society for Vascular Surgery (SVS) has outlined a number of high-risk features potentially predicting the need for surgical intervention in their TBAD reporting standards. Clinical high-risk features include refractory pain and hypertension. Radiographic high-risk features include an aortic diameter of >40 mm, a proximal entry tear of >10 mm, a primary entry tear at the concavity of the distal aortic arch, and

radiographic evidence of bloody pleural effusion. The evidence for these high-risk features is broadly based on observational studies.[19-23] In addition to their retrospective nature, these studies are limited by their relatively small sample sizes and the heterogeneity of the populations involved in terms of dissection chronicity and TEVAR indications. Furthermore, follow-up periods are often short in these studies, limiting a genuine appreciation of long-term outcomes, although the causes of death are also often unknown.[24]

Given these limitations of these studies, the SVS reporting standards advise caution when relying on these high-risk features to decide on treatment owing to a lack of consensus and a paucity of strong evidence on the impact of each feature. Despite this caveat, retrospective studies have correlated the presence of high-risk features with poor long-term outcomes (including 10-year mortality and aneurysmal degeneration) in patients with uncomplicated TBAD.[25] Notably, data from the International Registry of Acute Aortic Dissection suggested that recurrent pain and refractory hypertension were predictive of rupture.[26]

As well as these high-risk features, further studies have also suggested consideration of a false lumen diameter of >22 mm,[27] partial false lumen thrombosis,[28] and involvement of the abdominal aorta[29] as potentially indicative of a need for surgical intervention. Imaging techniques such as computed tomography with positron emission tomography scans have been used to decipher aortic wall inflammation and presumed instability and risk of rupture, but these data are experimental.[30] In short, these data also represent low quality evidence and these indications cannot be considered definitive for intervention.

Meta-analyses of published studies. Systematic reviews and meta-analyses have yielded contrasting conclusions on the benefit of TEVAR in acute uncomplicated TBAD. Enezate et al[31] found, after evaluating six studies, that for uncomplicated TBAD there was no significant difference in all-cause mortality between those treated with TEVAR compared with OMT at 1 year (5.1% vs 5.4%; $P = .96$) and 5 years (15.3% vs 26.3%; $P = .75$). There was, however, an increased risk of rupture at 1 year in patients treated with OMT alone compared with TEVAR (odds ratio [OR], 2.49; 95% confidence interval [CI], 1.23-5.06; $P = .01$). Conversely, Hossack et al,[32] after evaluating six studies (largely different from those reviewed by Enezate et al), reported that all-cause mortality rates were significantly higher in acute uncomplicated TBAD treated with OMT alone compared with TEVAR (hazard ratio [HR], 1.54; 95% CI, 1.27-1.86; $P < .001$). Aortic-related mortality was also significantly higher in the OMT alone group compared with TEVAR (HR, 2.71; 95% CI, 1.49-4.94; $P = .01$). It should be noted that stroke rates were significantly lower in the OMT group as opposed to the TEVAR group. It does also highlight the paucity in suitable, high-quality studies, which limits its conclusions, a recurring theme in the literature for this subject.

In sum, focusing on the all-cause mortality in the mid-long term, the consensus seems to be that patients with acute or subacute uncomplicated TBAD may benefit from treatment with TEVAR. The current evidence informing this opinion is summarized in the Table. This conclusion must be tempered by the fact that the evidence outlined is of low quality and definitive evidence would be provided by randomized, controlled trials.

SELECTED CONSIDERATIONS FOR PERFORMING TEVAR

Performing TEVAR for an uncomplicated TBAD necessitates a consideration of the balance of risk and benefit in an asymptomatic patient. After all, the intervention exposes the patient to an immediate risk to circumvent a perceived risk of longer term adverse aortic events. For this reason, it is important, particularly whilst we await higher quality evidence related to these benefits, that the decision to intervene is considered by multidisciplinary teams.

Stroke. Zha et al[33] showed that, among 445 patients treated with TEVAR for TBAD, the incidence of stroke was 11.5%, although most cases were those of transient neurological dysfunction (10.6%) as opposed to permanent neurological dysfunction (0.9%). Left subclavian artery coverage was an independent predictor of stroke in this series. In the Study to Assess Outcomes After Endovascular Repair for Multiple Thoracic Aortic Diseases (SUMMIT), among 126 patient with acute TBAD, the stroke rate was 8.7%.[34] Takazawa et al[35] reported post-TEVAR stroke rates of 0.6% in TABDs from a single-center experience over a mean of 5.7 years. It should be noted, however, that these studies did not pertain to uncomplicated TBAD specifically. Indeed, a meta-analysis by Howard et al[3] of >16,000 patients with TBAD treated with TEVAR demonstrated that stroke rates were significantly higher in patients with complicated TBADs compared with uncomplicated TBADs (5.85% vs 3.92%; $P = .008$).

Paraplegia. Spinal cord ischemia (SCI) leading to permanent paraplegia is one of the most devastating complications of aortic surgery. For endovascular interventions, SCI is related predominantly to coverage of segmental arteries supplying the spinal cord, with previous studies suggesting a direct correlation between length of aortic stent graft coverage and risk of SCI.[36,37] Coverage of the left subclavian artery, and therefore limiting spinal cord perfusion through the left vertebral artery, is also thought to increase the risk of SCI, with some studies reporting this observation.[38] The ADSORB trial did not report on SCI, and the INSTEAD trial reported two cases (2.8%) of SCI after TEVAR (one paraplegia and

Table. Summary of selected studies pertinent to uncomplicated type B aortic dissection (TBAD) management

Year	Author	Study type	Sample size	Summary
2009	Nienaber et al (INSTEAD trial)[9]	Randomized controlled trial	Total: 140 TEVAR: 72 OMT only: 68	At 2 years, no difference in all-cause mortality, aortic-related death, or progression of dissection between TEVAR with OMT and OMT only groups.
2013	Nienaber et al (INSTEAD-XL trial)[10]	Randomized controlled trial	Total: 140 TEVAR: 72 OMT only: 68	At 5 years, no difference in all-cause mortality, but significantly lower aortic-related mortality and disease progression in TEVAR with OMT compared with OMT alone.
2014	Brunkwall et al (ADSORB trial)[11]	Randomized controlled trial	Total: 61 TEVAR: 31 OMT only: 30	At 1 year, greater false lumen thrombosis and false lumen size reduction in TEVAR with OMT compared with OMT alone, although no survival difference.
2016	Qin et al.[13]	Observational	Total: 338 TEVAR: 184 OMT: 154	At and beyond 30 days, significantly lower mortality rate and aortic-related events in TEVAR compared with OMT. Nonsignificantly ($P = .064$) increased aortic-related events before 30 days in TEVAR compared with OMT.
2018	Iannuzzi et al.[14]	Observational	Total: 9165 TEVAR: 2.9% OMT: 95% Open repair: 2%	All-cause mortality significantly lower with TEVAR compared with OMT and open repair.
2021	Xiang et al.[15]	Observational	Total: 357 TEVAR: 191 OMT: 166	At 1, 3, and 5 years, freedom from all-cause mortality significantly higher with TEVAR compared with OMT.
2021	Torrent et al.[16]	Observational	Total: 688 TEVAR (acute): 446 TEVAR (subacute): 242	At 1 year, no difference in mortality rate between acute and subacute TEVAR, although association of higher reintervention rate with acute TEVAR.
2021	Xie et al.[17]	Observational	Total: 267 TEVAR (acute): 130 TEVAR (subacute): 137	No difference in all-cause mortality between acute and subacute TEVAR over median of 48.2 ± 25.9 months.
2021	Xiang et al.[15]	Observational	Total: 238 TEVAR (acute): 142 TEVAR (subacute): 96	After 5 years, no difference in all-cause mortality between acute and subacute TEVAR.
2018	Enezate et al.[31]	Meta-analysis (6 studies)	Total: 1960 TEVAR: 740 OMT: 1220	At 1 and 5 years, no difference in mortality between TEVAR and OMT. At 1 year, significantly lower risk of rupture with TEVAR compared with OMT.
2020	Hossack et al.[32]	Meta-analysis (6 studies)	Total: 14,706 TEVAR: 1066 OMT: 13,640	Significantly lower all-cause mortality and aortic-related mortality in TEVAR compared with OMT.

OMT, Optimal medical therapy; *TEVAR*, thoracic endovascular aortic repair.

one transient paraparesis). Other studies have reported SCI rates of ≤10% after TEVAR.[39] Although conclusive evidence specifically relating to SCI in uncomplicated TBAD is lacking, strategies that have been demonstrated to potentially decrease the risk of SCI include minimizing the length of aortic coverage, left subclavian artery revascularization and prophylactic cerebrospinal fluid drainage when extensive aortic coverage is planned.[39-41]

False lumen thrombosis. Both the INSTEAD and ADSORB trials demonstrated that TEVAR in patients with uncomplicated TBAD promotes false lumen thrombosis and aortic remodeling, defined as a reduction of >5 mm in aortic diameter during follow-up. Although these landmark trials did not find a mortality advantage, subgroup analyses from other studies have reported increased survival in patients with successful false lumen thrombosis and aortic remodeling after TEVAR.[42] False lumen thrombosis has also been reported to be more likely when TEVAR is performed in the acute and subacute phase of TBAD compared with chronic dissections.[43] These findings highlight the importance of false lumen thrombosis and raise questions about the need for reintervention in patients with persistent false lumen perfusion. They also further add to the discourse on the optimal timing of TEVAR in patients with TBAD. In selected cases, operators have described techniques for false lumen embolization and balloon fracture fenestration in the endeavor to promote false lumen thrombosis and aortic remodelling.[44] Further delineating the clinical and anatomical features that predict false lumen thrombosis and refining operative strategies to promote aortic remodeling may improve long-term survival in this cohort of patients after TEVAR.

Persistent false lumen perfusion. Qin et al[13] reported late type I entry flow (previously endoleak) in 11 of 184 TEVARs (6%) for uncomplicated TBAD (mean follow-up, 28.5 ± 40.2 months). Among 145 uncomplicated TBADs treated with TEVAR studied by Xiang et al,[15] the cumulative incidence of type I entry flow was 6.1% at 3 years and 13.2% at 5 years. Song et al[22] found 9 of 135 TEVARs (6.7%) for uncomplicated TBAD developed a type I entry flow (mean follow-up, 49.2 ± 39.3 months). Gao et al,[45] however, showed among 751 uncomplicated TBADs treated with TEVAR that only 9 developed type I entry flow and 1 developed type II entry flow (together 1.3%) over a mean follow-up of 70 months. There does not seem to be a difference in likelihood of persistent flow depending on whether TEVAR is performed acutely or subacutely.[17] It must be considered that the risks associated with TEVAR are likely to vary for each patient depending on anatomical variables, including the nature of the proximal landing zone.

Rupture after TEVAR. Rupture after TEVAR for uncomplicated TBAD is an aortic-related adverse event associated with high mortality.[45] Although some studies have reported a decrease aortic-related mortality with TEVAR, there continues to be a risk of aneurysmal degeneration and rupture even after TEVAR, often associated with persistent entry flow into the false lumen.[13] The incidence of rupture in observational studies varies between 2.5% and 5.0%,[13,15,46] with one study reporting the cumulative incidence of aortic rupture after TEVAR as 2.1% after 1 year and 5.1% after 5 years.[15] It has been suggested that the variation in incidence could be due to differing follow-up periods and time of interventions between studies.[24]

Retrograde type A aortic dissection. Post-TEVAR retrograde type A aortic dissection (RTAD) can occur acutely or after several months.[47-49] The high mortality of RTAD after TEVAR (42%)[47] merits close attention regardless of its low incidence (1.33%-3.17%).[24,47,48] It can also present more discretely, being found incidentally during follow-up on imaging.[49,50]

Stent graft design features may influence RTAD risk after TEVAR. Chen et al[51] in their metanalysis of 50 publications on TEVAR patients showed that those treated with proximal bare stents were more likely to develop RTAD (n = 1728 [2.31%]) than those treated with proximal covered stents (n = 1126 [1.24%]) (relative risk, 2.06; 95% CI, 1.22-3.50). Of note, the underlying aortic pathology here was heterogeneous, and not solely uncomplicated TBADs. In contrast, Ma et al[48] found no significant difference ($P = .64$) in post-TEVAR RTAD incidence between proximal bare stent (n = 531 [3.4%]) and proximal covered stent use (n = 321 [2.8%]). This experience did highlight the high mortality associated with RTAD, with 7 of the 27 (25%) dying from aortic rupture or cardiac tamponade.

Yammine et al[49] suggested that a greater proportion of post-TEVAR RTAD patients had a ≥4 cm ascending aortic diameter (n = 15 [47%]) than those who did not develop RTAD after TEVAR (n = 171 [21%]) ($P = .05$). The precise location of pathology is also thought to influence outcomes, with Weiss et al[52] showing that a primary entry tear at the concavity of the distal aortic arch predisposes to complications including RTAD, multiorgan failure, and mortality after TEVAR, although one should note that this study looked at complicated TBADs.

The proximal landing zone has been shown to influence RTAD rates. The Ishimaru classification describes proximal landing zones for stents in the thoracic aorta.[53] In a series of 186 patients[49] who underwent TEVAR for TBAD, patients who went on to develop RTAD were significantly more likely to have proximal stent landing in zone 0, 1, or 2 (n = 15 [93.3%]), compared with patients who did not develop RTAD (n = 171 [63.7%]) ($P = .02$).

RANDOMIZED CONTROLLED TRIALS ON THE HORIZON THAT WILL INFORM TREATMENT OF UNCOMPLICATED TBAD

As the only randomized clinical trial in acute uncomplicated TBAD, ADSORB provides some positive evidence of the aortic remodeling benefits of early TEVAR in terms of false lumen thrombosis and size reduction. However, given the short follow-up period of 1 year and the lack of statistical power for mortality differences, it falls short

of providing conclusive proof of a clinical benefit from early TEVAR in patients with acute TBAD. The INSTEAD trial, focusing on uncomplicated TBAD of 2 to 52 weeks' duration, has similarly shown a favorable remodeling advantage with false lumen thrombosis in the TEVAR group compared with OMT only. However, it also had a short follow-up (2 years) and was underpowered to detect a mortality difference. Retrospective analysis of this cohort at the 5-year mark (INSTEAD-XL) did show lower aortic-related mortality and disease progression associated with stent graft-induced false lumen thrombosis in the TEVAR group. Although these studies and others have supported the use of TEVAR in uncomplicated TBAD over OMT alone, the evidence remains inconclusive. Guidelines from the European Society of Vascular Surgery advise that TEVAR may be considered selectively for these patients, leaving the decision to individual clinician preference.[41] An international survey of vascular operators revealed that more than one-half do not use TEVAR routinely in the context of uncomplicated TBAD and 89% felt there was equipoise in this decision.[54] To address this controversy, three major randomized controlled trials have been constructed.

Scandinavian trial of uncomplicated aortic dissection therapy. The Scandinavian trial of uncomplicated aortic dissection therapy (SUNDAY) trial has begun recruiting with an estimated completion date of April 2026.[55] This randomized controlled trial involves 23 aortic centers in Denmark, Sweden, Norway, Iceland, and Finland. The trial aims to recruit 550 patients with uncomplicated TBAD of <4 weeks' duration, randomized to either OMT or OMT plus TEVAR to be done within 12 weeks of the onset of symptoms. The choice of specific graft type will be left to the operator's discretion. The primary outcome is all-cause mortality at 5 years; included secondary outcomes are aortic-related mortality, aortic intervention, any reintervention related to dissection, neurological injury, and quality of life. An economic evaluation of cost effectiveness will also be made.

Improving outcomes in vascular disease - aortic dissection. Improving outcomes in vascular disease - aortic dissection (IMPROVE-AD) is another randomized controlled trial that has commenced recruitment.[56] This study aims to recruit 1100 patients from 60 North American vascular units. Patients with uncomplicated TBAD will be randomized within 48 hours to 6 weeks of index symptoms to be treated with either OMT and TEVAR or OMT alone. The primary end point for the study is a composite of all-cause mortality or major aortic complications, including rupture, malperfusion, SCI, stroke, and need for aortic intervention. Secondary end points include the component parts of the primary end point as well as cardiovascular death, cardiovascular hospitalizations, and quality of life. The median follow-up is expected to be 4 years with the study concluding in June 2030. As well as determining the optimal treatment for uncomplicated TBAD to achieve the best clinical outcome, this trial aims to assess the impact of high-risk dissection features, as described by the SVS reporting standards on aortic dissection.[57] These high-risk features include both clinical and radiographic indicators, as discussed previously. Despite the SVS reporting standards advising caution when using these high-risk features to guide operative management, they have been used in some centers as an indication for early TEVAR, which may be associated with a higher stroke rate when performed within 48 hours.[58] As such, more definitive evidence on the impact of these high-risk features is required and their incorporation into IMPROVE-AD trial is promising. The inclusion of quality-of-life assessments in this trial is compelling and an important aspect of management, although this assessment would be strengthened by disease-specific questionnaires that do not exist currently.[59]

Early aortic repair in patients needing endovascular surgery for type B aortic dissection trial. Early aortic repair in patients needing endovascular surgery for type B aortic dissection (EARNEST) is a randomized controlled trial that will be based in the United Kingdom, that also aims to assess the benefits of TEVAR for patients with uncomplicated TBAD compared with OMT.[60] The trial is currently in the final stages of instigation with a plan to follow-up participants over a 5-year period. The primary end point will be a composite of death from aortic disease, major stroke, paralysis, or serious heart and lung illness. As well as investigating for clinical benefits, this trial also aims to perform an economic analysis assessing the cost effectiveness of early TEVAR for these patients in the context of the National Health Service. This factor is particularly important when considering the upfront cost of early TEVAR compared with the potential for an even more costly complex aortic repair owing to aneurysmal degeneration several years later.

These promising trials aim to address the main limitations of the INSTEAD and ADSORB trials by recruiting considerably greater patient numbers and evaluating longer follow-up periods. As such, they have the potential to provide conclusive evidence for the optimal management of patients with uncomplicated TBAD. The similarities in the overarching question may facilitate pooling of data from these independent trials and it is imperative that the lead investigators make an effort to facilitate combining their efforts so data at scale can inform practice.

CONCLUSIONS

The role of TEVAR in uncomplicated TBAD remains controversial. Existing randomized trials such as INSTEAD, INSTEAD-XL, and ADSORB as well as other observational studies have suggested beneficial aortic

remodeling effects of TEVAR, but have not established a mortality advantage clearly in patients with uncomplicated TBAD. The upcoming SUNDAY, IMPROVE-AD, and EARNEST trials are aiming to address some of the criticisms of previous trials and show promise to provide conclusive evidence guiding the management of patients with uncomplicated TBAD.

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Conception and design: MR, MA, BM
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Writing the article: MR, MA, BM
Critical revision of the article: MR, MA, BM
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