Biomechanical Changes After Thoracic Endovascular Aortic Repair in Type B Dissection: A Systematic Review

Foeke J. H. Nauta, MD, Michele Conti, PhD, Arnoud V. Kamman, MD, Guido H. W. van Bogerijen, MD, Jip L. Tolenaar, MD, Ferdinando Auricchio, PhD, C. Alberto Figueroa, PhD, Joost A. van Herwaarden, MD, Frans L. Moll, MD, and Santi Trimarchi, MD

Abstract
Thoracic endovascular aortic repair (TEVAR) has evolved into an established treatment option for type B aortic dissection (TBAD) since it was first introduced 2 decades ago. Morbidity and mortality have decreased due to the minimally invasive character of TEVAR, with adequate stabilization of the dissection, restoration of true lumen perfusion, and subsequent positive aortic remodeling. However, several studies have reported severe setbacks of this technique. Indeed, little is known about the biomechanical behavior of implanted thoracic stent-grafts and the impact on the vascular system. This study sought to systematically review the performance and behavior of implanted thoracic stent-grafts and related biomechanical aortic changes in TBAD patients in order to update current knowledge and future perspectives.

Keywords
complications, thoracic endovascular aortic repair, type B dissection, thoracic aorta, stent-graft performance, systematic review

Introduction
Aortic dissection is the result of a tear in the intimal layer that allows blood to flow within the medial layer, creating a flap that divides the aorta into a true lumen (TL) and a false lumen (FL). Stanford type B aortic dissection (TBAD) involves the descending aorta only and accounts for about one-third of all aortic dissections. The estimated incidence of TBAD is about 2 per 100,000 persons per year. Risk factors have been well described and include hypertension (present in 80% of TBAD patients), advanced age, male gender, and atherosclerosis. The most important risks of TBAD are aortic rupture and malperfusion, both associated with high morbidity and mortality.

Thoracic endovascular aortic repair (TEVAR) was introduced by Dake et al in 1994 and has emerged as the preferred management strategy for TBAD when complicated by malperfusion, ongoing growth, aortic rupture, or refractory hypertension/pain. The introduction of TEVAR decreased early mortality for complicated TBAD considerably, with reduction of 30-day mortality from 29% to 3% when endovascular treatment was performed instead of open surgery. Clinical benefits include hemodynamic restabilization, reversal of end-organ ischemia, restoration of TL perfusion, positive aortic remodeling, reduced morbidity and mortality, minimal access procedure, interventional treatment of surgically unfit patients,

1Thoracic Aortic Research Center, Policlinico San Donato IRCCS, University of Milan, Italy
2Department of Surgery and Biomedical Engineering, University of Michigan, Ann Arbor, MI, USA
3Department of Vascular Surgery, University Medical Center Utrecht, the Netherlands
4Department of Civil Engineering and Architecture, University of Pavia, Italy
5Department of General Surgery, University Medical Center Groningen, the Netherlands
6Department of General Surgery, St. Antonius Hospital, Nieuwegein, the Netherlands

Corresponding Author:
Santi Trimarchi, Thoracic Aortic Research Center, Policlinico San Donato IRCCS, University of Milan, Piazza Malan 2, 20097 San Donato Milanese, Milan, Italy.
Email: santi.trimarchi@unimi.it
short procedure time with minimal blood loss, decreased recovery time, and potential financial savings.

Based on these advantages and good outcomes, TEVAR is now considered the management of choice for complicated TBAD, with 80% to 90% in-hospital survival.24–27 Management of uncomplicated TBAD is primarily medical therapy.13 Nevertheless, data from the ADSORB28 and INSTEAD-XL29 trials and the IRAD (International Registry of Aortic Dissection) registry30 demonstrated that TEVAR, in addition to medical therapy, is associated with improved 1-year and 5-year aorta-specific survival, delayed disease progression, and improved positive aortic remodeling. These promising results have led to a global debate on whether all TBAD patients should be considered for TEVAR.31,32 However, the INSTEAD-XL trial also revealed that early mortality and reintervention rates were higher in the cohort managed with TEVAR in addition to medical therapy.29 Therefore, a patient-specific approach is currently advised for TEVAR in TBAD, treating only patients with complications or those suspected of complications during follow-up.31 TEVAR has been reported as feasible following acute catastrophes, such as ruptured TBAD,33,34 as well as in Marfan patients.35 However, Marfan aortas tend to dilate after TEVAR,36 and reintervention rates are higher in this cohort.37 Therefore, the gold standard for patients with connective tissue disorder–related TBAD remains open surgical repair.8,13

Despite the improved in-hospital outcomes, TBAD patients may present follow-up complications due to both disease progression, such as aortic dilatation and rupture, and stent-graft–related complications including migration, stent-graft collapse/fracture, retrograde aortic dissection (AD), extended dissection, and stent-graft–induced new entry tears.38–53 Endoleaks may be associated with both clinical and biomechanical stent-graft conditions. The final success of TEVAR, as well as the development of aortic complications, is determined by the biomechanical behavior and interaction of the “rigid” implanted stent-grafts with the “elastic and fragile” thoracic aortic wall. The increasing practice of TEVAR for TBAD34 and the complexity of the aortic anatomy and related hemodynamic forces call for a deeper understanding of the changes in aortic pulsatility due to an implanted stent-graft. In this article, we present a comprehensive review of the biomechanical behavior and performance of implanted thoracic stent-grafts in patients with TBAD, highlighting the unsolved issues and the added value of combining clinical and experimental studies.

**Literature Search**

The PubMed and Embase electronic databases were systematically searched up to April 2015 for reports on biomechanical, endovascular, vascular, and science studies pertaining to the research topic. Non-English articles were excluded. Keywords used were the following: “thoracic aortic dissection,” “thoracic aortic graft,” “thoracic endovascular aortic repair,” “stent-graft,” “endoleak,” “graft migration,” “aortic rupture,” “biomechanical,” “in vitro,” “ex vivo,” “in vivo,” and corresponding synonyms. The following search terms were used on Medline: ((aortic dissection OR type B aortic dissection) AND (TEVAR OR thoracic endovascular aortic repair) AND (outcome OR biomechanical OR complication OR stent-graft OR endoleak OR graft failure OR aortic rupture OR stent graft induced new entry tear OR retrograde type A dissection)). A similar search was used for the Embase database. After removal of duplicates, 2 reviewers (F.N. and M.C.) independently screened titles and abstracts of the remaining articles for the following keywords in title or abstract: aortic dissection, device failures, reintervention procedures, dissection/stent-graft morphology, stent-graft type, complications of TEVAR, migration, endoleak, retrograde dissection, extension dissection, stent-graft–induced new entry tear, or aortic remodeling. All abstracts were read and relevant articles were downloaded in full. Articles about type A aortic dissection, aortic aneurysm, hybrid treatment, or open surgery were excluded. The reference lists of the included articles were screened and relevant publications not identified in the primary electronic search were included through cross-references. All full-text articles were studied by 2 independent physicians, and in case of disagreement, a decision was reached by consensus. Engineering and basic science articles were classified as experimental or computational modeling.

A total of 1739 articles were identified through the electronic search, of which 692 were removed as duplicates. After screening of titles and abstracts, 188 full-text articles were selected, of which 91 matched the inclusion criteria. Cross-referencing of all included articles yielded an additional 20 articles, resulting in 111 included articles (Figure 1).

**In Vivo Biomechanical Changes After TEVAR for TBAD**

In vivo biomechanical changes of the stented aorta following TBAD are still to be determined. For thoracic aortic aneurysms (TAA), van Prehn et al55 demonstrated that significant distension (area change ranging from 2%–20%) of the aortic arch and descending aorta during the cardiac cycle was preserved after TEVAR, suggesting that forces on stent-grafts may be much higher than initially expected.

Morphologically, the aorta remodels significantly after TEVAR for TBAD, which is considered beneficial if the TL expands and the FL completely thromboses and eventually resorbs.56,57 Such positive aortic remodeling is associated with improved long-term outcomes.58 Complete FL thrombosis results in decreased diameter of the entire aorta, whereas patent and partial thrombosed FLs are associated...
with aortic dilatation, rupture, and increased mortality.\textsuperscript{59–62} Several factors seem to influence thrombosis of the FL. Tolenaar et al.\textsuperscript{63} reported that branch vessel involvement or a patent entry tear after TEVAR is associated with decreased complete FL thrombosis, suggesting consideration of a more extensive procedure and more intensive follow-up for this cohort. Furthermore, TEVAR for acute TBAD promotes early aortic remodeling.\textsuperscript{64–66} However, this process is continuous, being completed in 6 to 12 months in most cases.\textsuperscript{53,67,68} For chronic TBAD, more extended coverage of the descending aorta is associated with a higher incidence of FL thrombosis\textsuperscript{69} and beneficial reduction in aortic volume,\textsuperscript{67} although it is also a risk factor for spinal cord ischemia.\textsuperscript{40,48,70} Another positive predictor of FL thrombosis seems to be the rate of TL expansion after TEVAR.\textsuperscript{71}

For uncomplicated TBAD, the INSTEAD\textsuperscript{72} and the ADSORB\textsuperscript{28} trials reported higher rates of FL thrombosis in patients treated with TEVAR in addition to medical therapy. This was most evident in those treated within the acute and subacute phase.\textsuperscript{53,68,73,74} Such an observation may suggest that decreased aortic compliance of chronic dissected aortas, with thickened intimal dissection flaps and multiple fenestrations, may inhibit positive remodeling.\textsuperscript{75} Retention of this aortic compliance in the subacute group lengthens the therapeutic window for the treatment of uncomplicated TBAD.\textsuperscript{68} Beneficial factors for achieving complete obliteration of the FL include absence of a primary entry tear at the outer distal arch curvature, young age, small aortic diameter, and absence of the abdominal aortic branches arising from the FL.\textsuperscript{76}
Typically, the thoracic aorta remodels significantly after TEVAR for TBAD, whereas the abdominal aorta tends to expand over time. Several studies have reported abdominal aortic expansion after TEVAR for TBAD. IRAD showed that in 63% of acute TBAD patients managed with TEVAR, aortic growth or new aneurysm formation occurred at 5-year follow-up, highlighting the risk of disease progression in the thoracoabdominal aorta. To stabilize distal collapsed dissection flaps while allowing blood flow to target abdominal and spinal vessels, distal bare metal stents extending into the thoracoabdominal aorta have been introduced, such as the PETTICOAT (provisional extension to induce complete attachment) technique. The long-term goal of such a technique is to prevent aortic expansion and rupture and to decrease reintervention rates. A number of studies have reported positive remodeling of distal bare metal stenting for TBAD, with complete thoracic FL thrombosis ranging from 31% to 75%. However, the FL of the abdominal segment distal to the stent-graft showed the tendency to expand, leading to continuous dilatation of the abdominal aortic volume. These volume changes seem to be influenced by the length of stent-graft coverage and the presence of re-entry tears.

Complications of TEVAR

Although TEVAR has emerged as the main management tool for complicated TBAD, several drawbacks are described. TEVAR-related complications range from endoleak, dissection extension, newly induced dissection, malapposition, and aortic rupture to stent-graft defects. Some of these complications may be managed conservatively by careful monitoring, while others call for reintervention. In this section, the most common complications and reinterventions related with TEVAR for TBAD are discussed.

Endoleak

The most important types of endoleaks in TBAD are types Ia or b and II. Type Ia endoleak is caused by antegrade perfusion of the FL and is a significant predictor of death in TBAD. The most common causes of type Ia endoleak are malapposition of the proximal segment of the stent-graft, mainly due to short proximal landing zone and severe angulation. To prevent malapposition, oversizing in TBAD should not be greater than 20% to reduce the risk of proximal neck dilatation. Another recent study showed that immediate type Ia endoleak was related to larger preoperative distal FL area (498±274 vs 284±123 mm², p=0.02) and distal aortic area (759±275 vs 624±185 mm², p=0.03). One-year follow-up showed that patients with immediate type Ia endoleak had smaller TL indices and larger FL areas and indices. Retrograde flow from distal entry tears in TBAD patients (type Ib endoleaks) is still under debate. Refilling of the FL from the distal aorta has been associated with increasing aortic diameter over time; on the other hand, other authors place a low importance on type Ib endoleak but consider closer monitoring justified. Type II endoleak is caused by perfusion via arterial side branches, with the left subclavian artery (LSA) and spinal arteries as main sources. In cases of intentional LSA coverage, preoperative debranching with embolization of the LSA is recommended. In the presence of type II endoleak, the patent branch can be coil embolized, sutured, or treated with glue embolization. Type IIIa endoleak is defined as leakage due to junctional separation of the modular components and is a major cause of reintervention, in particular after multistenting with an overlap <5 cm. Type IV endoleak is caused by graft wall porosity and is a first-generation stent material problem that seems to have been resolved with the new-generation stent-grafts.

Bird-Beak Sign

This complication arises from poor apposition of the proximal stent-graft along the inner arch curvature, producing to a wedge-shaped gap (Figure 2A). This condition may lead to complications, such as endoleak, migration, collapse, and infolding, and is associated with both under- and oversizing. The exact cause of a bird-beak formation remains speculative, although landing in zone 2 or 3 of the aortic arch seems to increase the risk. Also, a preoperative distal arch angle <151° has been described as a predictor of bird-beak configuration (sensitivity 86%, specificity 83%). Hsu et al hypothesized that the proximal end of the stent-graft pivots on the inner arch curvature, induced by the “wind-sock effect,” hemodynamic forces that pull the graft distally before deployment is complete. Stiffness of the stent-graft might straighten the distal aortic arch and enlarge the angle of the bird-beak, which seems to progress over time.

Others reported delivery systems as potential causes of bird-beaking. For instance, the Zenith Z-Trak delivery system was associated with an increased risk of bird-beak configuration when compared to the new-generation Zenith TX2 Pro-Form. The latter was designed specifically to achieve good proximal apposition due to a diameter reducing tie on the inner curve that forces the stent-graft to partially intussuscept, allowing a more angulated fixation. Interestingly, although complete stent-graft apposition was significantly higher in the group that was treated with the Pro-Form delivery system (65% of Pro-Form patients vs 18% Z-Trak vs 6% Gore TAG, p<0.0001), there was no difference in terms of type Ia endoleak occurrence. On the contrary, Ueda et al demonstrated that mean bird-beak length was significantly longer in patients with type Ia or II endoleak (14.3 and 13.9 mm, respectively) than in patients without endoleaks (8.4 mm). The bird-beak sign might be a precursor of an increased risk of rupture and therefore demands close follow-up. In the event...
of excessive bird-beaking, stent-graft realignment with a similar stent or a Palmaz stent should be considered.47 This would apply especially to younger patients, as the aorta might expand over the years,96 potentially resulting in higher displacement forces on the stent-graft and subsequent complications.97,98

**TEVAR-Related Retrograde Aortic Dissection**

The incidence of this lethal complication is 2% to 16%, with mortality ranging from 20% to 57%.56,99–104 It may present intraoperatively or during follow-up, and patients with TBAD are predisposed, probably due to the fragile
dissected aortic wall.\textsuperscript{102,100,101,103–105} Retrograde AD after TEVAR can be associated with inappropriate aortic wall selection (ie, connective tissue disorder), catheter injury (ie, iatrogenic dissection), female gender, severely angulated arch, ascending aortic diameter $\geq$ 4 cm, proximal landing in zone 0, wire or stent-graft manipulation, poor perioperative antihypertensive control, proximal balloon dilation, and excessive stent-graft oversizing.\textsuperscript{42,99–104} Proximal bare spring stenting might also be a cause of retrograde AD\textsuperscript{42,101}; however, this is still an issue of debate.\textsuperscript{106,107} Large-sample studies without the use of bare springs (Gore TAG device) reported similar retrograde AD rates compared with studies that did use bare springs (Medtronic Talent device), with an incidence of 2% and 3%, respectively.\textsuperscript{100,101} Importantly, in the multicentered EuRec study, only 46% of the retrograde AD patients presented within 30 days after TEVAR.\textsuperscript{42} On this, the MOTHER registry (consisting of 5 prospective studies and a single institution series) showed that retrograde AD after TEVAR for acute TBAD was the cause of death in 16% in the acute setting and up to 12% after 30 days, emphasizing the risk for late retrograde AD formation.\textsuperscript{104} The standard of care for retrograde AD is open surgery, although good results have been described with TEVAR in highly selected patients with an entry tear in the descending aorta.\textsuperscript{108}

**Stent-Graft–Induced New Entry Tear**

Stent-graft–induced new entry tear (SINE), an iatrogenic new entry tear caused by the stent-graft,\textsuperscript{45} is associated with Marfan disease, high taper ratio of the TL, high stent-graft–aorta angle, bare spring stenting, and excessive oversizing at the distal landing zone.\textsuperscript{45,50,51,104–111} Distal SINE typically occurs as a late complication and is associated with aortic expansion.\textsuperscript{51} Its incidence varies from 6.3% to 27%.\textsuperscript{50,51} The latter was reported after implantation of stent-grafts with distal bare stents and barbs. Dong et al\textsuperscript{35} reported a 3% incidence of proximal and distal SINE with a mortality rate of 26%, without a difference in proximal and distal SINE-related mortality. Four types of “spring back” stents were used [Medtronic Talent and Valiant, the Hercules (Microport, Shanghai, China), and the Cook Zenith TX2]. The Talent, Valiant, and Hercules stent-grafts have a proximal bare spring and the Talent and Hercules stents have a longitudinal connecting bar that prevents twisting and kinking but impairs flexibility. Interestingly, all 16 cases of proximal SINE occurred at the greater curve, suggesting the spring back effect as a possible trigger. Restrictive bare stenting as an adjunctive technique to TEVAR has been shown to reduce distal SINE in dissected aortas.\textsuperscript{111} Notably, there is ongoing debate on this topic, as it is challenging to accurately identify the stent-graft as a cause of new entry tears.\textsuperscript{112}

**Aortic Rupture**

Risk factors for this thankfully rare but devastating perioperative complication of TEVAR for TBAD include TBAD with arch involvement, ascending aortic diameter $>4$ cm, multistent placement, proximal bare spring stenting, and balloon dilation.\textsuperscript{49} In a cohort of 563 TBAD patients treated with TEVAR, 1% died perioperatively from aortic rupture, of which 50% were associated with retrograde AD.\textsuperscript{49} Close examination of the aortic wall and dissection anatomy and careful intraprocedural device manipulation and balloon molding may help to prevent this potentially life-threatening complication.\textsuperscript{113}

**Stent-Graft Defects**

Component separation has been reported for all aortic stent-graft systems.\textsuperscript{114} Junctions that lie in or near a curvature are prone to separate, most likely due to the pulsatility of the blood flow and the pressure gradient resulting in countering radial forces on the stent-graft. Adequate overlap between devices and prophylactic correction of impending separation may prevent such a complication.\textsuperscript{114}

Wire fractures were reported with the use of first-generation stent-grafts, mainly caused by repetitive torsional and bending motions on longitudinal column bars, causing metal fatigue. Fabric tears leading to type III endoleaks were broadly reported in early devices and probably were caused by repetitive friction against calcified lesions or fractured stents. This problem has been solved by stronger fabric designs and elimination of stiff longitudinal column bars. For bare metal stenting, the rate of device failure was 9% in a group of 108 aortic dissection patients in pooled data of a recent systematic review.\textsuperscript{115} Component separation or device migration necessitating secondary interventions was reported in 5 patients. One case consisted of a focally ruptured stent-graft and 4 cases of a stent body misalignment.

Thoracic stent-graft collapse is an infrequent but hazardous complication after TBAD. It is most commonly reported with the Gore TAG device, with a low incidence of 0.4% but high early mortality ranging from 7% to 8% in cohorts including TBAD.\textsuperscript{46,47} It should be noted that off-label use might have pushed the boundaries of this device.

**Stent-Graft Collapse**

This event, which can present directly postoperatively or after years,\textsuperscript{43} occurs primarily as a result of excessive oversizing and severe proximal aortic angulation.\textsuperscript{39,46,47} Muhs et al\textsuperscript{39} demonstrated that a small distal aortic sealing zone diameter and intragraft aortic diameter predicted collapse.\textsuperscript{39} Sze et al\textsuperscript{43} concluded that the main cause might be use in
young patients who generally have small aortic diameter, tight curvatures, high peak velocities, and greater aortic wall elasticity than older patients with degenerative, atherosclerotic aneurysmal disease. Newly designed stent-grafts, such as the Gore Conformable TAG, offer greater radial force, better conformance to the inner curvature of angulated aortic arches, greater tolerance for device oversizing, and smaller device diameter, with promising results. For collapse management, a secondary TEVAR procedure with high radial force should be considered as first choice of therapy.  

**Spinal Cord Ischemia**

This complication of TEVAR leads to severe morbidity and may be reduced by preoperative revascularization, although there is limited data to support this. The risk of neurological malperfusion may be increased after coverage of the LSA by a stent-graft and can be managed by LSA revascularization. To minimize this risk, preoperative screening of intact contralateral posterior circulation is key. Perioperative hypotension (mean arterial pressure <70 mm Hg) and length of aortic coverage (with 205 mm as a threshold for increased risk) have been reported as independent predictors of spinal cord ischemia. Moreover, preoperative evaluation of the Adamkiewicz artery might allow extended stent-graft coverage with decreased risk of spinal cord ischemia and improved aortic remodeling. Distal bare stenting has also been associated with a decreased rate of spinal cord ischemia.

**Rare Complications**

Aortoesophageal fistula is a rare but lethal complication of TEVAR and might be caused by ischemic necrosis of the stented midesophageal arteries. Six (2%) out of a group of 268 patients who underwent TEVAR for various thoracic aortic diseases developed aortoesophageal fistula, of which 4 had received TEVAR for TBAD. Although treated with surgery, all patients died due to bleeding or mediastinitis. Aortobronchial fistula following TEVAR for TBAD is even rarer, with a reported incidence ranging from 0.2% to 0.8%. Both complications may also develop after TEVAR from resorption of hematoma, as this resorption may cause wall fatigue and fistulation.

Stent-graft explantation may be necessary in particular cases of stent-graft failure. In a cohort of 500 patients with thoracic aortic diseases, 4 patients required stent-graft explantation due to device failure (the deployment system could not be disengaged), aortoesophageal fistula, retrograde AD, and severe type I endoleak (aneurysmal patient). Other reported indications for stent-graft explantation include deployment-related problems, stent-graft infection, migration, collapse, kinking, aortic rupture, and fracture. In the presence of highly unstable hemodynamic conditions, TEVAR has also been proposed as a bridge to open surgery.

Reintervention rates for TEVAR following TBAD remain high and seem mainly associated with excessive oversizing, bare spring stent-grafting in the proximal landing zone, large aortic dilatation, and anticoagulant therapy. Marfan disease, smoking, and type I endoleak are the main predictors. High conversion rates to open surgical repair are reported (8%–14%), mainly due to retrograde AD. Suboptimal stent-graft placement may require TEVAR extension, which is associated with overstenting of arteries, increased risk of stroke, paraplegia/paraparesis, subclavian steal syndrome, and need for subsequent revascularization. The VIRTUE registry showed that the need for additional thoracic stent-grafts was greater in patients with chronic TBAD than in those with (sub)acute TBAD, with >30% of these patients requiring additional procedures. In most cases, additional stent-grafts were required for distal aneurysmal degeneration of the chronic dissection below the primary stent-graft. Greater aortic coverage in the primary procedure might reduce the rate of reintervention in the chronic cohort.

**Experimental Analyses of Aortic Wall and Stent-Graft Failures**

Experimental studies offer analysis of hemodynamics and aortic and stent-graft behavior in a controlled environment (Table 1). In the development stage of TEVAR, Marty-Ané et al reported an in vivo canine study that complete dissection obliteration could be accomplished only when the entire length of the dissected aorta was treated, as otherwise a false channel continued to exist. Faure et al studied the efficiency of bare metal stenting in 15 human aortic ex vivo models and the impact on visceral and renal arterial patency. Reexpansion of the TL with FL collapse was achieved in all cases. Overall, a significant pressure gradient drop was reported in 25% of all the aortic branch vessels after bare metal stenting (n=15). In addition, a significant pressure drop in at least one renal artery was observed in 9 (60%) aortas. After TEVAR, visceral and renal arteries perfused by the FL showed a significant pressure drop in 55% (12 of 22).

Autopsy and animal studies help to understand stent-graft performance and biomechanical aortic changes considerably. Rubin et al reported a fatal case of retrograde AD after TEVAR plus balloon dilation for TBAD. Autopsy revealed several intimal lesions with a new 2-mm entry tear caused by the proximal bare spring. Sincos et al studied the influence of thoracic stent-grafts on the structure of the aortic wall in an in vivo porcine study (n=25). They demonstrated that oversizing was associated with a significant decrease in smooth muscle, elastic fibers, and α-actin expression. Histological studies have shown that aortic
dissection is associated with a stiffer and weaker aortic wall due to lower amounts of elastin and collagen, making it more prone to intimal lesions when challenged by high mechanical stress, such as hypertension.142,143 Modern 3-dimensional printers offer accurate replicas of pathological aortas (Figure 2B).144 Chung et al145 used a rigid transparent and a compliant opaque dissection model, constructed with synthetic tubes and polytetrafluoroethylene, to assess prevention or treatment options for TL collapse in TBAD. Stent-graft placement effectively relieved TL collapse, especially in cases without communication between the TL and FL or in cases with communication through only the distal reentry branch. Experimental studies have furthermore been conducted to investigate the magnitude of loads acting on thoracic stent-grafts, their resistance to dislodgment, as well as their stability and movement.98,146–151 Sincos et al150 studied the effect of oversizing on stent-graft (Medtronic Valiant) displacement force and aortic wall strength on in vivo porcine models. Displacement forces between 10% and 40% oversizing were similar (41–46 N), but maximum wall shear strength, stress, and tension showed negative and linear correlation with oversizing and were significantly lower than in the control group.150

Canaud et al148 assessed the proximal fixation of stent-grafts in human cadaveric thoracic aortas and showed significant increase of stent-graft malapposition due to oversizing for 3 of the 4 tested stent-grafts. Lack of proximal apposition was primarily caused by an aortic arch angulation, that is >80° for the Bolton Relay (bare spring) and >90° for the Gore TAG device (scalloped flares). Lack of body apposition was first observed in the Cook Zenith stent-graft (no open bare stent) above 70°. The Medtronic Valiant stent-graft (open bare stent) remained well apposed through both oversizing and angulation challenges.148 Veerapen et al146 carried out mechanical testing in an ex vivo model on 4 commercially available stent-grafts. The median displacement force ranged from 6.5 N for the Excluder to 26.5 N for the Zenith (8.0 N for the Talent, 11.8 N for the Ancure, and 8.1–10.7 N for the various homemade Palmaz stent-graft designs). The Zenith and Ancure devices required significantly higher displacement force (~25%). Addition of a bare Palmaz stent to the proximal fixation site improved displacement force significantly for all devices.

**Computational Modeling**

Computational modeling is an emerging technique that enables detailed analysis of hemodynamics and biomechanics of the aorta. Three-dimensional models of the aorta are reconstructed from cardiac-gated computed tomography angiography or magnetic resonance data. Once these computer models are created, computational fluid dynamics (CFD) can be performed to simulate blood flow, blood pressure, and vessel wall dynamics (Figure 2C).152 Kung et al153 demonstrated the accuracy of CFD by comparing computed pressure and wall motion with in vitro measurements. Good predictions of flow and pressure waveforms indicated that the numerical simulation captured both the vessel wall motions and wave reflections accurately.153

Several computational studies have analyzed forces on aortic stent-grafts, predominantly in the abdominal aorta affected by aortic aneurysms. The main findings of these computational studies are that pressure-related forces are much higher than flow-related forces (eg, wall shear stress) and that blood pressure, radial aortic compliance, inlet graft diameter, and angulation are determining factors of drag forces (DF) on abdominal stent-grafts.154–158 On this, Morris et al157 showed that DF on bifurcated abdominal stent-grafts decreased from 14 to 8 N when placed in vessels with small angles (<40°) and small proximal neck diameters (<28 mm). In addition, their group showed through CFD studies that the DF was unidirectional in idealized smooth stent-graft models, while this was found to act in 3 directions in realistic implanted stent-graft simulations.158 As a result, the DF was up to 26% higher in the realistic stent-grafts, on which the input velocity of the flow had no effect, which suggests that geometry has major influence on the DF in abdominal stent-grafts.158 The main factors of DF on

<table>
<thead>
<tr>
<th>Triggering Mechanisms</th>
<th>Biomechanical Response</th>
<th>Factors With Minor Impact</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oversizing ≥10%</td>
<td>Decreased vascular wall strength</td>
<td>141, 150</td>
<td></td>
</tr>
<tr>
<td>Oversizing, aortic arch angulation</td>
<td>Malapposition</td>
<td>148</td>
<td></td>
</tr>
<tr>
<td>Cardiac pulsation, blood pressure, increased stent-graft diameter and length, stent-graft curvature, proximal landing zone</td>
<td>Drag force</td>
<td>Shear stress, stent-graft length</td>
<td>149, 157–159</td>
</tr>
<tr>
<td>During follow-up</td>
<td>Stent-graft area expansion</td>
<td>157</td>
<td></td>
</tr>
<tr>
<td>Incomplete stent-graft expansion (not including collapse)</td>
<td>High flow velocities</td>
<td>161</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: TBAD, type B aortic dissection; TEVAR, thoracic endovascular aortic repair.
thoracic stent-grafts arise from cardiac pulsation, increasing from 11 N (diastole) to 18 N (systole) in a representative model.\textsuperscript{159} Whereas frictional forces of fluid on the blood vessel contributed <0.5\% of the total DF, suggesting that shear stress and friction contribute negligibly, as also described by other studies.\textsuperscript{149,157–159} In addition, the effect of contact surface of the stent-graft, and therefore the length, appeared to be minor in determining DF.\textsuperscript{159} On the contrary, Figueroa et al\textsuperscript{149} showed in 3-dimensional computational simulation that DF increased with increasing stent-graft diameter and length.\textsuperscript{149} Interestingly, in patients with TAA treated with thoracic stent-grafts, it seems that cranial directions of DF might be more important than caudal and/or sideways DF, potentially causing migration.\textsuperscript{149}

Displacement force vectors appear to be largely determined by the curvature of the stent-graft. In general, the more proximal the stent-graft was implanted, the greater the cranial component of displacement. Furthermore, increased simulated blood pressure was approximately linearly proportional to the increase in DF vector.\textsuperscript{149} In general, the longer the stent-graft and the larger the curvature, the higher the displacement forces acting on the stent-graft.\textsuperscript{149,159–161} In addition, the orientation of the DF typically follows the main curvature of the stent-graft.\textsuperscript{156,161} Pasta et al\textsuperscript{162} assessed stent-graft collapse with CFD and suggested that both increased stent-graft angle and extension into the aortic arch lead to increased transmural pressure across the stent-graft wall, potentially evoking collapse. Patient-specific computational modeling may allow for identification of patients at high risk for stent-graft collapse and guide preventive intervention.

Regarding TEVAR for TBAD, Cheng et al\textsuperscript{159} studied 12 patients with (sub)acute or chronic dissection and showed through CFD analysis that stent-graft diameter increases significantly after TEVAR, which is associated with an increase in hemodynamic DF, similar to studies on abdominal stent-graft DF.\textsuperscript{155,160} However, resultant DF was much higher than in abdominal stent-grafts, measuring 10.3 N when the graft diameter was 26 mm, increasing to 26.8 N with a graft diameter of 42 mm,\textsuperscript{159} while DF on abdominal stent-grafts are on the order of 3 to 9 N.\textsuperscript{154} They also showed that proximal deployment position is associated with increased DF, measuring 17.3 N at the top of the arch (angle of 90°) and 2.3 N in the descending aorta (angle of 180°).\textsuperscript{159} Follow-up imaging showed a general increase in both inlet and outlet graft areas postoperatively [increase of 11.0\% (p=0.05) and 58.0\% (p=0.01), respectively]. The general shape of the stent-grafts remained conical, although the inlet:outlet area ratio decreased from 1.93 (range 0.94–3.59) to 1.50 (range 0.76–3.26). Remarkably, graft expansion was significantly associated with increasing DF from 21.0±3.5 to 24.8±3.4 N (p=0.002), suggesting that aortic remodeling after TBAD increases DF on stent-grafts.\textsuperscript{159}

van Bogerijen et al\textsuperscript{163} demonstrated blood flow disturbance after TEVAR for TBAD through CFD analyses. Disturbance was seen at the partially covered origin of the LSA, which produced a backward-facing step geometry of the lumen profile. In addition, high velocities have been identified at the stent-graft–induced stenosis of the distal descending aorta.\textsuperscript{163} It is notable that the studies of Cheng,\textsuperscript{159} Figueroa,\textsuperscript{149} and Prasad\textsuperscript{161} used rigid artery wall and stent-graft models, while stent-grafts pulsate with diameter changes of up to 5 mm.\textsuperscript{165} However, engineering studies have supposed that it is reasonable to believe that the artery wall- and graft-compliance have little contribution to the overall DF.\textsuperscript{149}

Image-based computational modeling is evolving rapidly as a promising tool for the prediction of implanted stent-graft and aortic behavior. Computational solid mechanics and CFD are key developments in understanding the complex hemodynamics and biomechanics of the aorta.\textsuperscript{151} As aortic pulsation is a dynamic process influenced by surrounding structures, mathematical models should include the tethering of the external tissues and organs. Moireau et al\textsuperscript{165} developed a fluid-structure interaction model of blood flow compatible with large displacements of the vessel walls. They reported a methodological guide focusing on identification of external tissue support parameters using data assimilation techniques. By implementing their framework with estimated parameters in a realistic case, they demonstrated that direct modeling simulations were more accurate than previous manual expert calibration methods.\textsuperscript{166} Valdez-Jasso et al\textsuperscript{167} showed that linear and nonlinear viscoelastic models are able to predict pressure-area dynamics of the descending aorta. Such mathematical models offer an understanding of the interactions between aortic morphology, hemodynamics, and implanted material (eg, stent-graft stability and aortic wall stiffening) and might lead to the development of the so-called fluid-solid-growth models.\textsuperscript{151,168}

**Discussion**

With the increasing use of TEVAR for TBAD, it is vital to better understand the impact of implanted thoracic stent-grafts on aortic physiology. Although TEVAR has improved TBAD-related morbidity and mortality significantly, still one-third of patients presenting with TBAD expire within 5 years.\textsuperscript{3} Patient and device selection, stent-graft performance, and biomechanical changes of the aorta seem of major influence on these outcomes. Efforts are made by clinicians and engineers to study stent-graft performance and aortic changes after TEVAR for TBAD by exploring clinical and experimental data. The present study aims to clarify and update current knowledge on this topic by reviewing the literature.

We found that modern imaging techniques disclose the dynamics of the thoracic aorta and stress the importance of
such observations in order to decrease stent-graft–related complications and to improve future stent-graft design.55 Large-scale clinical studies and registries have given insights into early- and long-term outcomes, which are key to patient stratification. For instance, the INSTEAD and the ADSORB trials demonstrated the added value of TEVAR for uncomplicated TBAD.28,72 Furthermore, the VIRTUE registry showed that aortic remodeling is similar in the acute and subacute phases after TEVAR for TBAD.68 IRAD highlighted the risk of aortic expansion after TEVAR for acute TBAD by showing that dilatation occurred in 73% of these patients within 5 years.30

Several issues seem to influence post-dissection aortic expansion; however, currently no definitive consensus exists on what exactly causes this phenomenon. In the STABLE study, for example, which reported on TBAD patients treated with a thoracic stent-graft and an abdominal bare metal stent (the PETTICOAT technique), many patients demonstrated persistent abdominal FL flow without aortic expansion during follow-up.53 An association between patent FL or partial thrombosed FL and aortic expansion has also been reported.63 In general, TBAD impacts on patients lifelong and should be considered as a chronic disease and TEVAR as management rather than treatment because the risk of aortic expansion may persist even after TEVAR. New procedures, such as the PETTICOAT technique, aim to further improve outcomes after TEVAR; however, such an approach should be studied further regarding the risk of aortic expansion and malperfusion over time.53,79,80,140 Importantly, a better understanding of post-dissecting expansion is necessary to improve TEVAR-related outcomes.

Stent-graft–related complications can lead to hazardous outcomes and call for improvement of patient selection and TEVAR, including stent-graft design. Endoleak type Ia and Ib have been reported as significant predictors of morbidity and mortality in TBAD patients; therefore, early intervention should be considered in these patients.44,52,165 Stent-graft collapse and migration are rare complications for TEVAR following TBAD as the proximal neck does not usually dilate postoperatively. However, oversizing >20% should be avoided in TBAD patients because it is related to proximal neck dilatation and subsequent stent-graft migration.36,170

To date, no clear consensus exists for thoracic stent-graft sizing for TBAD, so further investigation is warranted. Generally, oversizing <10% is recommended to decrease the risk of retrograde AD and SINE.45,107 In the absence of long-term evidence, it can be speculated that TBAD patients are typically younger than TAA patients and their aortas are more compliant, potentially more prone to future dilatation, especially when using severely oversized devices.36,98 Bird-beaking remains a precursor of stent-graft–related complications and should therefore be minimized by adequate landing zone and device selection. Severe angulated arches with short landing zones and severe mis-sizing should be avoided.

Stent-graft design should improve to facilitate stenting in anatomically challenging aortic arches. Retrograde AD and SINE are harmful complications, partly caused by the intervention itself, considering the fragility of dissected aortic walls. Restricted bare metal stenting, straight distal prosthetic aortic alignment, and possible future dissection-specific devices with lower radial force, higher flexibility, and more tapering may reduce the incidence of such complications.45,110,111 Nevertheless, an important part of these complications could very well be caused by the natural course of disease progression and the spontaneous dissection extension. Increasing experience with TEVAR seems to have improved stent-graft design, leading to fewer reports of graft failure and stent-graft collapse. However, junctions placed in curvatures combined with high pressure and pulsatility may still lead to component separation. Future studies should focus on further improvement of stent-graft design for curved aortas and adequate postoperative blood pressure and heart rate control, which requires close follow-up and monitoring.

Aortic wall analyses contribute to a better understanding of thoracic aortic diseases and their new stented physiology, emphasizing the risk of severe forces on this fragile environment.109,141 Modern techniques such as 3-dimensional printing might play important roles in the future to further analyze biomechanical changes in the aorta (Figure 2B).144 However, the types of printable materials limit these printed models and therefore caution should be maintained with regard to the translation of such studies to clinical outcomes.

In vitro and ex vivo studies have demonstrated that oversizing does not lead to better proximal fixation and that it is even negatively linearly correlated with wall shear strength, stress, and tension and associated with malapposition and intimal damage (Figure 2D).141,148,150 Meanwhile, computational studies flourish in analyzing hemodynamic and biomechanical changes after TEVAR (Figure 2C). Pressure-related forces and cardiac pulsation seem to be major determining factors of stent-graft stability, which stresses the importance of blood pressure and heart rate control after stent-graft implantation.149,156,159 Moreover, large inlet diameter is related with increased DF as well as postoperative stent-graft expansion, which is also associated with increasing DF.149,157,159 These findings may underline the long-term risks of oversizing. The observations that the DF on thoracic stent-grafts is mainly cranial might suggest that DF are counteracted by fixation forces from the stents and hooks and barbs at the proximal end, of which the consequences are undetermined. A longer distal landing zone may improve stent-graft stability, and the addition of a series of bare metal stents in the distal aorta (ie, PETTICOAT technique) may
also help to maintain the position of the stent-graft.\textsuperscript{159} Patient-specific computational modeling and overall easier accessibility with faster processing and improved clinical interpretation of these computational techniques are continuously under exploration. Nevertheless, clinical correlation and in vivo and in vitro studies are needed to complement this computational approach. Currently, there is no published or ongoing randomized controlled trial that investigates the biomechanical impact of different thoracic stent-grafts, and only a few studies have compared their clinical performance.\textsuperscript{171–173} This lack of knowledge calls for a deeper investigation of the performance and behavior of different types of thoracic stent-grafts.

**Conclusion**

Thoracic endovascular aortic repair is an established endovascular technique that has improved outcomes for TBAD significantly. However, this technique is associated with severe biomechanical setbacks and unknown long-term outcomes. Therefore, both clinical and experimental studies are warranted to further investigate the biomechanical behavior of implanted thoracic stent-grafts and stented aortic dissections to improve stent-graft design and to identify which patients benefit most from TEVAR.

**Declaration of Conflicting Interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding**

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Ferdinando Auricchio and Michele Conti have received support from the Ministero dell’Istruzione, dell’Università e della Ricerca through Project No. 2010BFXRHS; ERC Starting Grant through the Project ISOBIO: Isogeometric Methods for Biomechanics (No. 259229); and the iCardioCloud project by Cariplo Foundation (No. 2013-1779) and Lombardy Region (No. 42938382; No. 46554874).

**References**


