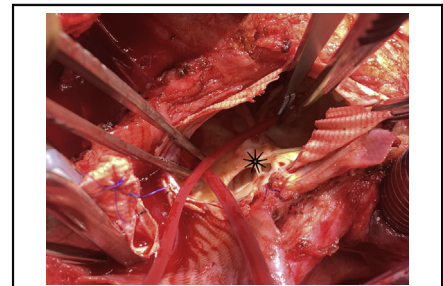


# Acute type A aortic dissection and the consequences of a patent false lumen



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Acute type A aortic dissection (ATAAD) is a life-threatening condition associated with high mortality and morbidity.<sup>1</sup> Without immediate surgical repair, mortality rates approach 50% within the first 48 hours.<sup>2-5</sup> Despite improvements in surgical technique and critical care, the short- and long-term mortality and morbidity associated with ATAAD, particularly the DeBakey I subgroup, remains high. Although standard repair for ATAAD involves resection of the primary intimal tear in the proximal aorta, persistence of flow through a large distal tear or a new entry tear at the distal aortic anastomosis may lead to persistent false lumen (FL) perfusion with unfavorable downstream consequences.<sup>6</sup> This manuscript aims to discuss the following concepts: (1) aortic true lumen (TL) and FL behavior after repair of ATAAD; (2) the concept of distal anastomotic new entry tear (DANE) following standard hemiarch repair; (3) how this impacts short- and long-term outcome of patients; and (4) strategies to prevent DANE. Better understanding of these hemodynamic conditions may serve to improve surgical technique, guide the creation of novel devices toward new therapeutic targets, reduce surgical risk, and ultimately improve patient outcomes.



Asterisk indicates an intraoperative example of a proximal anastomosis new entry tear.

## CENTRAL MESSAGE

This manuscript introduces the concept of DANE following standard hemiarch repair and how it contributes to the significant mortality and morbidity associated with ATAAD.

See Commentaries on pages 9, 11, 13, and 15.

## OUTCOMES FOLLOWING STANDARD HEMIARCH REPAIR

### Short-Term: Malperfusion and Stroke

Early mortality after surgical treatment of ATAAD has remained relatively unchanged since the early reports of hemiarch repair. Contemporary reports of several large registries have demonstrated in-hospital mortality ranging from 18% to 26% associated with repair of ATAAD.<sup>5,7-10</sup> The International Registry of Acute Aortic Dissection database recently reported on outcomes of >4000 patients from 1995 to 2013<sup>8</sup> and observed a decrease in the surgical mortality rate from 25% to 18% over the study period.

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Similar overall mortality has been reported by the German Registry for Acute Aortic Dissection Type A registry, with a 30-day mortality of 16.9%.<sup>9</sup> These findings were further corroborated by the Society of Thoracic Surgeons and Canadian Thoracic Aortic Collaborative databases, reporting an overall operative mortality of 17.4% and 17.8%, respectively.<sup>5,10</sup> The greatest early mortality is still attributed to malperfusion, leading to end-organ ischemia and an adverse systemic response.

Malperfusion can be static or dynamic and is defined as a critical decrease of blood supply to 1 or more organs. The compromised blood flow is caused by the compression of the aortic TL or aortic branch vessel obstruction secondary to the dissection.<sup>11</sup> Visceral or peripheral malperfusion complicates 30% to 40% of ATAADs and significantly increases mortality.<sup>1</sup> Mortality resulting from organ ischemia and failure has been reported as high as 45% when any malperfusion is present at the time of ATAAD presentation. Over time, when malperfusion of a vascular bed results in end-organ ischemia and cell necrosis, malperfusion syndrome (MPS) occurs.<sup>11</sup>

The potential of recovery from malperfusion associated with ATAAD is largely dependent on the degree of end-organ flow reduction, the time between onset of dissection to restoration of TL flow, and the effectiveness of restoring flow to the malperfused organ(s). The shorter the time between symptoms, diagnosis, and surgical therapy and the more effective the restoration of TL flow, the greater the chances of systemic improvement. Despite restoration of blood flow through the TL with proximal aortic repair, peripheral malperfusion may persist into the postoperative period related to unpredictable distal flow dynamics and multiple re-entry tears. Proximal aortic repair in the presence of vessel malperfusion preoperatively may only worsen postoperatively due to the period of hypothermic circulatory arrest and any resultant hypotension, a secondary insult to an already-compromised vascular system.<sup>12</sup> If there is any doubt about the effectiveness of TL flow restoration, the resolution of malperfusion should be assessed objectively after central aortic repair with imaging. It is because of this that certain groups are advocating managing the malperfusion before the proximal aortic repair.<sup>12,13</sup>

Cerebral malperfusion in particular carries a catastrophic prognosis, resulting in stroke and death in up to 47% and 50% of patients, respectively, after repair.<sup>5,14-16</sup> Supra-aortic vessel dissection has been shown to be associated with poor neurologic outcome, and cerebral malperfusion may be a potentially reversible cause of cerebral injury following repair of ATAAD.<sup>17</sup> The high mortality and postoperative stroke rates associated with the standard hemiarach procedure in patients with cerebral malperfusion suggest that there is room for improvement with regards to the current approach.

The Michigan group has a unique approach in which they advocate for early distal aortic fenestration and/or stenting by interventional radiology before proximal aortic repair in patients with MPS who are hemodynamically stable.<sup>13</sup> Fenestration is achieved by creating a tear in the dissection flap to equalize the blood pressures and allow blood flow between the TL and FL. Patients were allowed to recover from their MPS before proximal aortic repair, if hemodynamically stable. Compared with the standard approach from an earlier decade, in patients with MPS treated with an interventional radiology-first strategy, they observed a nonsignificant but 8% reduction in in-hospital mortality. An important observation was that the risk of dying from aortic rupture was ~7 times lower than the risk of death from organ failure. The Michigan group suggests that patients with MPS who are stable, without rupture or tamponade, benefit from a staged approach: endovascular reperfusion followed by proximal aortic repair, the exception being patients who present with cerebral malperfusion, in whom a staged approach was found to be deleterious. Grimm and colleagues,<sup>18</sup> using an "aortic-first" strategy for malperfusion management, showed resolution in only 57% of survivors.

An additional strategy for the management of mesenteric malperfusion is abdominal surgery first with visceral artery branch bypass with or without bowel resection in patients who are hemodynamically stable, followed by aortic repair.<sup>19</sup> There are 2 different types of organ malperfusion: (1) dissection that extends into the branch arteries where the TL is compressed by the FL and (2) organ malperfusion is caused by a collapsed TL in the aorta, not the branch vessel.<sup>20</sup> In the latter type, central aortic repair is more likely to alleviate the malperfusion and in the former, the malperfusion should be addressed directly via laparotomy. In this small series of patients, those who initially received visceral artery branch bypass had an uneventful postoperative recovery.<sup>20</sup> The patients who received a central aortic repair first had extensive bowel necrosis postoperative, and both of those patients died.<sup>20</sup> Ultimately, malperfusion remains a huge challenge for management of ATAAD, and what both approaches have in common is earlier detection and restoration of mesenteric blood flow.<sup>21</sup>

### Mid- and Long-Term: Aortic Growth, Reintervention, and Survival

The pressurized FL also influences long-term survival and the rate of aortic reinterventions. Over time, the pressurized FL increases the risk of aortic growth, necessitating secondary aortic operations in up to 25% to 50% of patients and involving the aortic arch in up to 74% of cases.<sup>22-28</sup> Long-term mortality after ATAAD repair is much lower than what is expected in the general population. Earlier reports have reported 10-year survival in all-comers ranging from 42% to 68%.<sup>29-32</sup> However, the recently reported Nordic Consortium for Acute Type A Aortic Dissection registry revealed medium-term survival at 5 and 8 years of 86% and 76%, respectively.<sup>33</sup> One of the contributing factors to long-term mortality after ATAAD repair remains a patent FL and lack of adequate surveillance and follow-up in patients who would otherwise require a surgical reintervention for aortic growth.<sup>22,27,28</sup> Secondary aortic reoperation occurs in 25% to 50% of patients, with increasing hazard over time.<sup>22-32</sup> The cumulative risk of reintervention has a significant impact on long-term mortality and morbidity, with additional intervention requiring a redo sternotomy or left thoracotomy. Interestingly, in patients undergoing an aortic reintervention, the FL was patent in 92% to 96% of cases, reinforcing the importance of sealing the FL at the initial life-saving operation.<sup>27,28</sup>

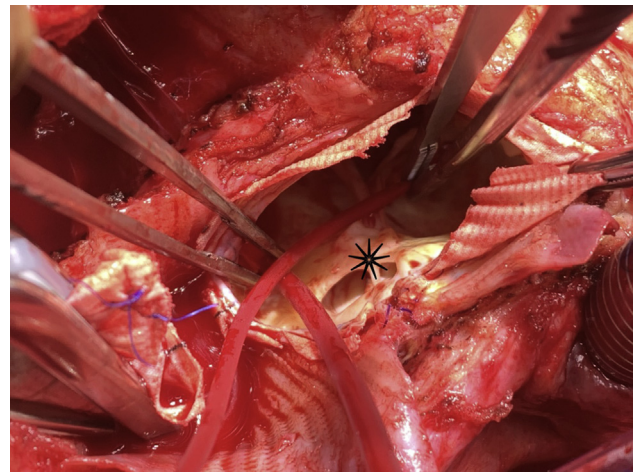
### ANASTOMOTIC INSUFFICIENCY AND FL PRESSURIZATION

The immediate goals of standard surgical repair of ATAAD are to prevent or treat fatal complications, including aortic rupture, coronary malperfusion, severe acute aortic regurgitation, and cardiac tamponade. To achieve these goals, the surgical strategy should successfully resect and

exclude the ascending primary intimal entry tear, seal the FL at the distal anastomosis, eliminating the antegrade pulsatile flow into and thereby depressurizing the FL, and rapidly expand and pressurize the TL to remedy malperfusion.

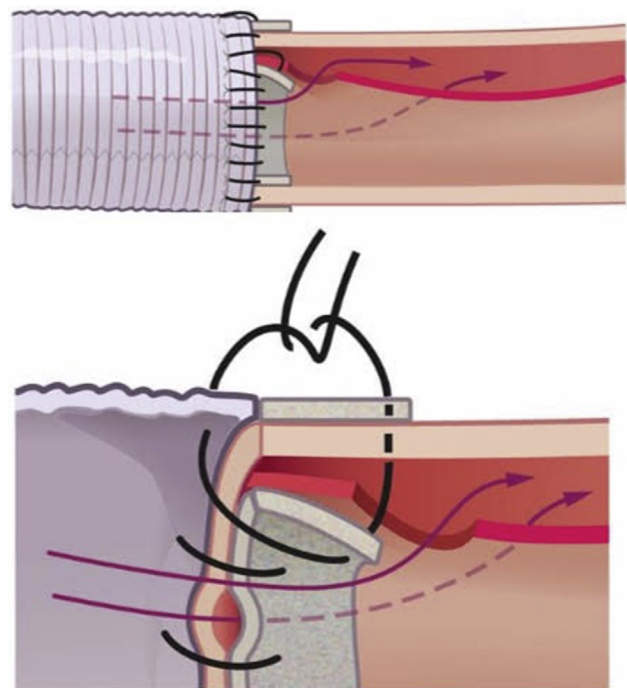
Despite meticulous suturing technique, creation of a proximal anastomosis new entry tear (PANE) or a DANE still occurs in a significant number of patients (Figures 1 and 2). The presence of a DANE allows for continued FL pressurization through a tear at the distal anastomosis that acts as a new primary intimal tear, leading to decreased long-term remodeling. One such suturing technique includes the creation of a neomedia through use of Teflon felt placed between the layers of the TL and FL and on the outside of the aorta to help bring the layers of dissected aorta together. Teflon felt is thought to add further support to the aortic suture line by minimizing bleeding intraoperatively and preventing late pseudoaneurysm formation/suture line disruption.<sup>34</sup> Another described technique using felt is a double-sandwich technique that includes a pericardial cap that is wrapped over the dissected layers as well as a Teflon felt strip on the outside.<sup>35</sup> This method has been shown to reduce suture line bleeding, which in turn led to a reduction in blood loss and fewer blood product transfusions. An infrequently used surgical technique is the adventitial inversion technique.<sup>36</sup> In this described technique, the intima is trimmed more distal than the adventitia and then the redundant adventitial layer is folded inwards and tacked to the intimal layer. It has previously been shown that although overall outcomes do not differ between the double-sandwich technique and adventitial inversion technique, the latter is thought to facilitate FL thrombosis.<sup>37</sup> Another surgical adjunct is the use of sealants such as BioGlue (CryoLife Inc, Kennesaw, Ga), first described in the early 2000s, although its use is controversial. Proponents of BioGlue suggest it helps with hemostasis and remodeling, especially of the aortic root.<sup>38,39</sup> While some surgeons prefer to use BioGlue to reinforce the dissected layers in the aortic root, many surgeons worry about embolization into the head and neck vessels if used at the distal anastomosis.<sup>40-43</sup> Regardless of surgical technique, the creation of a DANE still occurs, likely as a result of a tear forming during suturing of the distal anastomosis both from the needle itself and as a result of weakened medial layers or inadequate reapproximation of all 3 layers.<sup>18,44</sup>

The DANE behaves similar to a primary entry tear, allowing antegrade pulsatile flow and pressurization (patency) of the FL (Figure 3). The presence of a DANE has been identified in more than 70% of standard hemiarach repairs and results in significant rates of negative remodeling and accelerated growth.<sup>45</sup> Several factors have been identified that contribute to ongoing FL pressurization after surgical repair, including the presence of a DANE,<sup>46-48</sup> re-entry tear size,<sup>3,46,49</sup> and primary and re-entry tear location.<sup>44,48,50</sup> In addition to the DANE, distal re-entry tears

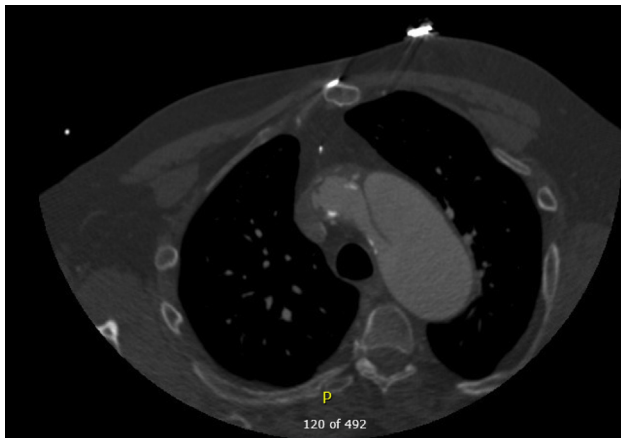


**FIGURE 1.** Asterisk indicates an intraoperative example of a proximal anastomosis new entry tear.

can contribute to the flow into and the pressurization of the FL, inducing negative remodeling if the relative flow through the FL exceeds that through the TL. In a study by Evangelista and colleagues,<sup>46</sup> the creation of a DANE occurred in 44.4% of those with a patent FL after hemiarach repair. The presence of a DANE with a diameter >10 mm was associated with worse outcomes, reflecting the importance of both the proximal location of the entry tear and the size of the entry tear on continued FL pressurization.<sup>46</sup> Similarly, Bing and colleagues<sup>48</sup> observed a DANE in 40.2% of hemiarach cases. Even without a DANE, patency



**FIGURE 2.** Graphical representation of a distal anastomotic new entry tear.



**FIGURE 3.** Axial contrast-enhanced computed tomography of a distal anastomotic new entry tear postoperatively.

of the FL and continued pressurization can occur due to the presence of re-entry tears, despite resolution of malperfusion. Zhang and colleagues<sup>49</sup> retrospectively analyzed >900 aortic dissections to evaluate the impact of re-entry tear size and location on FL pressurization. They found that more proximal and larger entry tears after surgical repair were correlated with greater FL pressurization, leading to a greater incidence of negative remodeling.<sup>49</sup>

### IMPACT OF DANES ON PATIENT OUTCOMES

In a study by Rylski and colleagues,<sup>45</sup> 95.6% of patients following standard hemiarch repair who showed negative remodeling and accelerated aortic growth had a DANE. Negative remodeling leads to expansion of the aorta, necessitating secondary aortic operations and mortality in up to 50% of patients. In 40% to 74% of the cases, the secondary operations involve the aortic arch.<sup>22-28</sup>

A patent FL has been shown to contribute to lower survival and greater reintervention rates after hemiarch repair.<sup>51</sup> Actuarial survival at 5 years in the presence of a patent FL was 76% compared with 95% with an obliterated FL. Similarly, event-free survival at 5 years was 63% in the presence of a patent FL compared with 84% with a thrombosed FL. It has been demonstrated that the average growth rate of both the aortic arch and proximal descending aorta is greater with a patent FL compared with a thrombosed FL.<sup>52</sup> Continued FL patency after hemiarch repair is associated with the presence of a DANE and is an independent predictor of reintervention at midterm follow-up.<sup>53</sup> Tamura and colleagues<sup>54</sup> demonstrated that patients in whom a DANE is not identified, despite a patent FL, have improved remodeling rates and survival as compared with those with a DANE. They found aortic growth was greatest in those with a patent FL with DANE whereas the presence of a DANE was a significant risk factor for distal aortic events, including reintervention and death.<sup>44</sup>

### TREATMENT STRATEGIES TO PREVENT DANE

Effective sealing of the DANE is difficult and inconsistent with the current standard surgical techniques. As such, a variety of strategies exist to prevent DANE formation with the goal of improving long-term survival and reducing aortic reintervention. All strategies have in common the goal of sealing the DANE and diminishing the antegrade pulsatile flow into the FL. With complete sealing of the DANE, there is increased rates of positive aortic remodeling<sup>53-55</sup> and reduced aortic growth over time.<sup>37</sup> Ultimately, closure of the DANE results in reduced rates of aortic reintervention and improvement in long-term survival.<sup>51</sup>

Total arch replacement (TAR) is indicated in patients with an aneurysmal aortic arch and those in whom the primary entry tear is in the arch,<sup>56</sup> but it may also be useful to prevent DANE. TAR with elephant trunk does not eliminate DANE, but it moves the DANE into the more distal aorta.<sup>57</sup> In fact, some surgeons advocate for TAR as initial surgical treatment to decrease the incidence of residual FL.<sup>58-60</sup> Tamura and colleagues<sup>54</sup> found that use of the elephant trunk technique was an effective solution to prevent DANE. Sealing the DANE with a frozen elephant trunk (FET), effectively moving the lesion from the ascending aorta to the mid-distal descending thoracic aorta, has demonstrated improved rates of positive remodeling.<sup>61</sup> In those patients in whom DANE still occurred, the ability to perform a second-stage thoracic endovascular aortic repair (TEVAR) was able to cover the DANE. The concept of conventional elephant trunk predates the introduction of FET and facilitates a 2-stage open technique with TEVAR for the surgical treatment of disease affecting the arch and the distal aorta.<sup>62</sup> The Canadian Thoracic Aortic Collaborative conducted a systemic review comparing FET with conventional elephant trunk and found that use of FET was associated with lower mortality without a significant increase in stroke or operative times, but the risk of spinal cord ischemia was greater with FET (5% vs 2.6% with conventional surgery).<sup>63</sup> The FET is a hybrid technique combining open and endovascular repair and is conducted in a single stage to replace the aortic arch and repair of the proximal part of the descending thoracic aorta.<sup>62</sup> However, the ability to perform FET is not available everywhere, primarily due to cost of the devices and need for surgical expertise at centers not familiar with the device. It is a technique that when used to treat acute aortic dissection can reduce distal aortic malperfusion, enhance FL thrombosis, and intuitively may prevent secondary aortic reinterventions and improve survival.<sup>62</sup>

To further elaborate antegrade TEVAR, conventional elephant trunk with or without TEVAR extension and FET are all examples of extended hybrid arch repair. Generally speaking, hybrid arch repair should be considered in

patients with (1) distal arch/proximal descending thoracic aortic aneurysm, (2) arch aneurysms with thoracoabdominal aortic aneurysm involved, and (3) acute type A aortic dissections, the focus of this review.<sup>64</sup> Conventional elephant trunk is used to facilitate a staged intervention with a retrograde deployment of a TEVAR by cannulating the elephant trunk is either planned or performed when indicated, ie, persistent, new malperfusion or continued aortic growth.<sup>57</sup> Antegrade deployment of a TEVAR graft was then used as a means to replace the elephant trunk. Conventional TEVAR grafts were, however, not designed for antegrade implantation and were not designed to facilitate a distal anastomosis with open repair.<sup>57</sup> This approach facilitated the single-stage repair for complex arch pathologies and the further development of custom-made prostheses. Two of the most commonly used FETs are the Thoraflex Hybrid graft (Vascutek, Glasgow, Scotland) and E-vita OPEN PLUS (Jotec, GmbH, Hechingen, Germany). A significant difference between the 2 devices is the Thoraflex can be deployed antegrade without a guidewire, whereas the E-Vita OPEN PLUS is designed to be deployed antegrade over a transfemoral wire.<sup>57,64</sup> In addition, the Thoraflex has the benefit of a 4-branched design for reimplantation of supra-aortic vessels and an additional side limb to allow for early distal reperfusion. In contrast, the E-Vita OPEN PLUS more closely resembles conventional TEVAR grafts, with the exception of the distal arch cuff to facilitate the distal anastomosis. There have been no randomized trials, but studies have shown FET is associated with lower rates of mortality and greater rates of spinal cord ischemia compared with conventional elephant trunk.<sup>63</sup>

An additional strategy is zone 2 partial TAR. The distal aortic anastomosis is placed in between the left common carotid and the left subclavian artery (LSCA). Zone 3 anastomosis is often more technically challenging, and a zone 2 anastomosis is felt to be less cumbersome and only marginally more difficult than a hemiarch.<sup>65</sup> The zone 2 partial TAR also allows for later TEVAR, either with covering the LSCA and landing before left common carotid or with the GORE TAG Thoracic Branch Endoprosthesis (W. L. Gore & Associates, Flagstaff, Ariz), a novel single branch stent graft extending into the LSCA.<sup>65</sup> This device, originally designed to treat aortic aneurysms, was successfully used in a small series of 5 patients with aortic dissection, with no perioperative mortalities, stroke, or spinal cord ischemia.<sup>65</sup> Similarly, to the previously mentioned distal arch repairs, on follow-up imaging all patients had a thrombosed FL.

Type II hybrid aortic arch repair is an alternative to conventional TAR.<sup>6,66</sup> In this technique, an ascending aorta replacement is performed with a short run of CPB and circulatory arrest, followed by debranching of all

supra-aortic vessels on cardiopulmonary bypass but without the crossclamp. This technique essentially moves the proximal landing zone forward.<sup>6,66</sup> The final step is to deploy a TEVAR antegrade. The major advantages of the type II hybrid aortic arch repair are avoidance of long periods of circulatory arrest.<sup>6,66</sup> A meta-analysis in 2018 of aneurysmal disease found that stroke rate was 2.5%, no permanent paraplegia, and late mortality was 12.5%.<sup>66</sup> This may be a preferable strategy in patients considered high risk.

The Ascyrus Medical Dissection Stent (AMDS) hybrid prosthesis is a novel device that can be used as an adjunct to standard surgical repair.<sup>67-69</sup> It is currently the only device available on the market. It is technically less cumbersome than the aforementioned techniques and can be used in adjunct to a hemiarch repair. It is designed to seal the FL at the distal anastomosis and to help pressurize the TL. It is deployed at the time of the index operation. The proximal portion of the bare metal stent is reinforced with a Teflon sewing cuff to attach to the distal anastomosis of the hemiarch. The bare metal stent lies in the arch and descending aorta. The initial midterm results of the stent recently published, and the investigators found that >95% of vessel malperfusions resolved due to the AMDS induced TL expansion. They found positive aortic remodeling occurred in all patients with ~75% of patients experiencing complete obliteration or thrombosis of the FL in the proximal aortic arch.

The concept of distal bare metal stent coverage is not novel with respect to management in type B aortic dissections. The use of TEVAR for both uncomplicated and complicated acute type B aortic dissection has resulted in improved positive remodeling, represented by stable or reduced aortic diameters and TL stabilization, and greater rates of FL thrombosis.<sup>70-72</sup> Induction of positive remodeling is dependent on a reduction in FL pressure. This is best achieved by sealing of the primary entry tear, thereby reducing the antegrade pulsatile flow into the FL.<sup>73,74</sup> Furthermore, rates of positive remodeling are greater with more stent-graft coverage, likely resulting from increased length of TL support, a reduction in FL size, and potentially increased coverage of distal re-entry tears.<sup>75-77</sup> This is referred to as the PETTICOAT (Provisional Extension to Induce Complete Attachment) technique, whereby a short segment of covered stent graft is used to seal the primary entry tear and then bare metal stents are placed to the level of aortic bifurcation.<sup>78,79</sup> Despite sealing of the primary entry tear, continued FL pressurization can occur in a retrograde fashion via distal re-entry tears. This may prevent complete thrombosis of the FL despite a reduction in FL pressurization.

## CONCLUSIONS

Standard hemiarch repair remains the gold standard for surgical repair of ATAAD despite the persistently high mortality and morbidity associated with the disease. This review article highlights the pathophysiologic aspects of ATAAD repair and the limitations of hemiarch repair. It is our belief that further consideration should be given to the initial intervention strategy. This review discusses DANE or failure to resect a large distal tear as being the primary mechanism for failure to manage malperfusion. The presence of a DANE and subsequent FL pressurization is a significant risk factor for poor long-term outcomes.

In conclusion, this review article has highlighted the following: (1) complications associated with ATAAD are often related to malperfusion and the presence of DANE; (2) standard hemiarch repair, although life-saving in select patients, may not be adequate to deal with the long-term complications and reintervention rates of ATAAD; and (3) consideration should be given to best management strategy for the persistent FL: TAR with FET, partial TAR, hybrid aortic arch repair, staged TEVAR with distal stent coverage, or the AMDS device.

## Conflict of Interest Statement

Drs Moon, Ouzounian, and Chu are all consultants for CryoLife, who currently owns the Ascyrus Medical Dissection Stent (AMDS). All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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