Innovations in Aortic Repair: Addressing Long-Term Efficacy and Procedural Safety

PhD thesis

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1 Introduction

1.1 Background to the saline flush trial

Stroke is a significant risk during TEVAR, caused primarily by debris and air embolization. Air emboli originate from the stent graft delivery system, where air trapped during manufacturing is released upon deployment. To counter this, delivery systems are flushed with saline per the instruction for use (IFU). However, the standard volume is often considered insufficient. A common practice is to use 120 ml of saline, four times the recommended amount, to more effectively displace the air and reduce the risk of air embolism. Alternative methods, such as using carbon dioxide or perfluorocarbon lavage, have also been explored and shown to be effective. Despite these advancements, completely deairing the system remains a challenge. Ongoing research focuses on improving delivery system designs and flushing protocols to enhance patient safety and outcomes, aiming to minimize embolic events during thoracic endovascular aortic repair (TEVAR).

1.2 Introduction of surgical refenestration study

The primary goal of treating acute type B aortic dissection (TBAD) is to manage malperfusion. While guidelines recommend TEVAR as the first-choice treatment for complicated TBAD (cTBAD), a lack of consensus suggests the disease's natural history is not fully understood. With the rise of TEVAR, open surgical techniques like open surgical suprarenal aortic fenestration (OSSAF) have been largely abandoned. OSSAF was previously used to address severe malperfusion but its invasive nature led to high morbidity and mortality, making it a last-resort option today. As a pioneering center, we are following patients who underwent OSSAF up to twenty years ago, when TEVAR was not widely available. By studying the long-term outcomes of these patients, we can gain valuable insights into the evolution of TBAD and inform future treatment strategies.

1.3 Background of covered stenting in CFA study

For large-bore endovascular procedures, the common femoral artery (CFA) is the most frequent access site. Effective closure of this site is critical for patient safety, and vascular closure devices (VCDs) are more effective than manual compression.

Despite advancements in delivery system diameters and operator experience, which have reduced vascular access site complications (VASC), these issues remain a frequent adverse event, with incidence rates up to 20% following procedures like TAVR and EVAR. Common complications include bleeding, stenosis, and occlusion, often resulting from vessel injury or incomplete closure. VASC is linked to increased morbidity and mortality, but a standardized treatment protocol is lacking. Treatment options vary, depending on operator experience and resource availability, and can include open surgical repair or endovascular techniques like balloon dilatation and stenting. Among these options, balloon-expandable covered stents (BECS) are increasingly being used. While balloon-expandable stents in flexible vessels like the CFA were traditionally avoided due to risks of kinking and fracture, BECSs have shown promising results in managing femoral access complications. However, long-term data on their safety and efficacy are still limited. Further research is needed to determine if BECS can become a standard treatment for these complications.

2 Objectives

2.1 Saline flush trial

The primary objective of this single-center, randomized trial was to compare two saline flushing protocols — standard (1x IFU) and increased volume (4x IFU) — in the context of standard EVAR. Specifically, we aimed to evaluate the efficacy of these flushing techniques in reducing the amount of air present in the aneurysm sac, as assessed through pre-discharge CT scans.

2.2 Surgical refenestration trial

This retrospective cohort study aimed to evaluate the long-term outcomes of OSSAF and examine the patterns of adverse remodeling in the repaired aorta.

2.3 Covered stenting in CFA study

In this multi-centric retrospective cohort study the aim was to assess the safety and efficacy of balloon-expandable covered stent implantation of CFA vascular-access related complications associated with a large-bore puncture.

3 Methods

3.1 Saline flush trial methodology

This study enrolled 30 consecutive patients undergoing standard EVAR between June 2021 and April 2022. Participants, aged over 18, were suitable for Terumo Treo and Anaconda and Cook Zenith Alpha EVAR devices, with complex cases excluded. Contrast media de-airing and injections followed IFU. Saline flushing volumes were 30 ml or 120 ml for Anaconda grafts, and 20 ml or 80 ml for other two grafts. Pre-discharge CTA measured trapped air volume in the aneurysm sac using a Hounsfield Unit-based algorithm, with manual exclusion of external air. A single blinded reader performed semi-automated measurements, and test-retest repeatability was assessed using the intraclass correlation coefficient. Patients were randomized into two groups: IFU saline volume (Group A) and quadrupled IFU volume (Group B). Block randomization ensured equal distribution within graft types.

3.2 Surgical refenestration study methodology

This study included 58 patients with cTBAD treated with OSSAF from January 1996 to November 2013. Preoperative

management involved heart rhythm, blood pressure and pain control. TBAD was considered complicated if rupture, malperfusion, intractable pain, refractory hypertension, or rapid aortic expansion was present, or if high-risk features existed. Clinical success was defined by the absence of major adverse events, aortic-related death or significant life-altering complications. Aortic diameters were measured on MRI or CTA scans. Early reoperation was defined as a second surgery within the hospital stay or in 30 days. OSSAF procedures were performed under general anesthesia without left heart bypass, via a left thoraco-abdominal incision. After heparin administration and supraceliac clamping, a posterolateral aortic incision was made, preserving intercostal or lumbar arteries. The dissected intima was resected from the aorta and the orifices of involved visceral branches, with false lumen thrombus removed. The remaining intimal membrane was then sutured, creating a dual-lumen aorta proximally and distally with a single-lumen visceral segment. The aortotomy was sealed. Follow-up visits were scheduled at 1, 3, 6, and 12 months post-surgery, and annually thereafter, including physical examination, clinical data, and imaging with CTA or MRA.

3.3 Covered stenting in CFA study methodology

This retrospective study enrolled all patients who underwent BECS implantation for CFA vascular access site complications at three major tertiary cardiovascular centers between January 2020 and May 2023. Demographic, risk factor, anatomical, procedural, and postoperative data were collected. Clinical status was assessed in-hospital and during follow-up visits (6/12 months, then annually). Follow-up included clinical examination and duplex ultrasound to assess stent patency and identify significant restenosis. The primary outcome was clinical success at two years, defined as lack of restenosis, freedom from target lesion reintervention or amputation, new claudication, or VASC-related mortality. Secondary outcomes included overall and VASC-related mortality, renal failure, myocardial infarction, stroke, respiratory failure, and technical success (successful blood flow restoration without significant extravasation or reintervention within 30 days). VASC severity was analyzed using VARC-3 criteria. Early and midterm outcomes were measured up to and from 30 days post-surgery. CFA calcification was evaluated on preoperative CTA or follow-up ultrasound.

4 Results

4.1 Results of Saline flush trial

Patients were divided equally between Group A (standard IFU volume) and Group B (quadruple volume), using three different EVAR devices. There were no significant baseline differences between the groups. The study found a significantly lower volume of trapped air in Group A (103.5 ± 210.4 mm^3) compared to Group B (175.5 ± 175.0 mm^3) ($p = 0.04$). The presence of trapped air was also significantly higher in Group B (87%) than in Group A (47%) ($p = 0.02$). Subgroup analysis by device type showed no significant differences in air kerma, trapped air volume, or Type II endoleaks. The Anaconda graft was identified as an independent risk factor for trapped air in multivariate regression analysis ($p = 0.039$). There were no clinically significant complications from air embolism, and the measurement repeatability was excellent (ICC = 1.0).

4.2 Results of Surgical refenestration study

58 patients with cTBAD were treated with open surgical suprarenal aortic fenestration and 67% presented with

symptoms of malperfusion upon admission. The in-hospital mortality was 27%, with an average hospital stay of 9.5 days.

Postoperative complications included acute kidney injury (20%) and transient spinal cord ischemia (4%), though neither became a permanent issue. At an average follow-up of 8.6 years, clinical success was achieved in 64% of cases. The 5-, 10-, and 20-year survival rates were 56.1%, 45.6%, and 21.6%, respectively. Approximately 47% of patients required reoperation over 18 years, primarily due to aneurysm formation. Follow-up measurements showed a significant increase in both thoracic ($p=.0001$) and visceral ($p=.028$) aortic diameters. However, the increase in the thoracic aortic diameter was significantly greater than that of the visceral aorta ($p=.0001$).

4.3 Results of Covered stenting in CFA study

This study evaluated the use of BECS in 23 high-risk patients with CFA VASC. Technical success was achieved in 91.3% of cases. In-hospital mortality was 4.2% due to recurrent bleeding. At a mean follow-up of 18 months, all-cause mortality was 37.5%, while VASC-related survival was 96.4%. Stent fractures occurred in 8.3% of patients without significant restenosis, and one patient experienced stent occlusion. Freedom from CFA

stent occlusion was 95.7% at one and two years. Clinical success throughout the study period was 90.5%, with a freedom from target limb revascularization of 95.7%.

5 Conclusions

5.1 Saline flush study

Stroke is a common and feared complication of TEVAR. A significant number of embolic events are believed to be gaseous, caused by air bubbles trapped in the delivery system. EVAR is increasingly used as a model to study this phenomenon because its delivery systems are nearly identical to those used in TEVAR, and any residual air can be easily detected on follow-up CT scans within the aneurysm sac. Various research groups have investigated methods to reduce residual air. Studies have explored the use of carbon dioxide (CO_2) or perfluorocarbon lavage, finding them to be effective. Our study is the first randomized controlled trial to directly compare different volumes of saline flush in an aortic prosthesis delivery system. Contrary to expectations and some previous in vitro findings, our results suggest that larger saline flush volumes do not reduce trapped air. This supports the idea that adhering to the device's IFU is critical for minimizing complication rates. The most likely cause of increased trapped air with larger flush volumes was the need for multiple syringe changes, which can introduce ambient air. Manual flushing, unlike automated injectors, does

not maintain constant pressure, further complicating the process. We observed significant differences in trapped air volumes across the three devices used. The Anaconda graft showed higher volumes, which could be attributed to its larger delivery system and a metal core that differs from the other devices. This finding has been reflected in the industry; for instance, the Zenith Alpha 2 (ZTA2) device now includes CO2 flushing as part of its approved protocol, highlighting a growing industry trend toward integrating advanced de-airing procedures into standard practice to minimize intravascular air embolism.

5.2 Surgical refenestration study

The treatment of cTBAD has shifted significantly from invasive open surgical techniques like OSSAF to less invasive endovascular interventions. While OSSAF was a leading approach in the early 2000s, it is now primarily reserved for patients who are not candidates for endovascular repair. Our experience with OSSAF for cTBAD provided several key insights. The operative mortality rate of 26.8% was a significant drawback compared to the lower rates reported in meta-analyses of TEVAR cases (3-13%). However, our long-term survival rates (56% at 5 years, 46% at 10 years) were comparable to those

reported for open surgical and TEVAR cohorts. This suggests that while open surgery has higher initial risks, it can offer durable long-term outcomes. Our analysis of aortic diameter changes over time revealed a significant increase in the thoracic aortic diameter, while the visceral segment's increment was not significant. We believe this protection against late dilation in the visceral segment is a direct benefit of the OSSAF procedure, which removed the intimal membrane. This finding suggests that our relatively high reoperation rate was likely due to the progression of thoracic aortic aneurysms rather than our surgical technique. Importantly, OSSAF preserved lumbar and intercostal arteries, resulting in no cases of permanent paraplegia.

5.3 Covered stenting in CFA study

Femoral vascular access site complications pose a significant risk in large-bore endovascular procedures. While traditional open surgery is a viable treatment, its associated mortality and morbidity rates have driven the search for less invasive alternatives. This study evaluated the use of BECS for treating CFA VASCs. In our cohort of 23 high-risk patients, BECS implantation achieved a technical success rate of 91.3%. We

observed an in-hospital mortality rate of 4.2% due to recurrent bleeding and a clinical success rate of 90.5%. The use of BECS offered advantages over open surgery, including reduced surgical burden and shorter hospital stays. Our technical success and CFA occlusion rates (4.3%) align with those of similar studies. Despite conventional contraindications for using balloon-expandable stents in the flexible CFA, our findings suggest that BECS can be a feasible and valuable option in frail, elderly patients where bending forces may be less impactful. The high-risk patient population and observed complication rates necessitate further study prior to the liberal application of BECS.

6 Bibliography

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