Physician Perspectives: AAA Trial Design in the Modern Era

Thoughtful discussion on the unmet clinical needs in treating abdominal aortic aneurysms and approaches to creating future endovascular aneurysm trials.

With Tim Resch, MD, PhD; Marc Schermerhorn, MD; and Bjoern D. Suckow, MD, MS, DFSCS, FACS, RPVI

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There is a significant unmet need in abdominal aortic aneurysm (AAA) treatment, as more than half of endovascular aneurysm repair (EVAR) patients experience failure of aneurysm regression, thus increasing their risk of reintervention, rupture, and higher mortality.[1] In this discussion, we explore the future of endovascular aneurysm clinical trials, particularly sac embolization trials, as a potential strategy to enhance sac regression and improve patient outcomes.

Dr. Resch, when monitoring patients post-EVAR, what metrics do you use to assess aneurysm regression? Do you primarily look at diameter, volume, or both?

Dr. Resch: Current protocols focus on diameter regression, but we're increasingly shifting toward volume measurements, as they provide a more sensitive assessment of sac changes. The challenge has been in simplifying volumetric measurement to make it practical for clinical use. However, we are now successfully implementing both CT-guided and ultrasound-guided imaging, allowing for more precise detection of issues in post-EVAR aortic endografts.

Dr. Schermerhorn, can you speak about the problem of aneurysm failure to regress?

Dr. Schermerhorn: This is a topic many of us have been studying for years. When EVAR was first introduced, our primary goal was simply to prevent aneurysm

sac expansion. However, we've since learned that even stable sacs carry some increased level of risk, and patient outcomes are significantly better when sac regression occurs after EVAR. Ours and other studies have shown that sac regression leads to better survival, greater freedom from rupture, and lower need for reintervention. Across the board, patients with sac regression fare significantly better than those with stability—and even more so compared to those with expansion, where outcomes worsen considerably.

We've also observed a clear trend: The greater the regression, the better the outcome, and conversely, the more expansion, the worse the prognosis. Currently, we use diameter thresholds of 5 to 10 mm to define major regression and expansion. However, perhaps we should be applying the same approach to volume measurements as well—what do you think, Tim?

Dr. Resch: I think that's likely a more sensitive approach, and it's something we should be prioritizing moving forward.

Dr. Suckow, what role does quality-of-life (QOL) assessment play in the follow-up of AAA patients after EVAR? Can you also describe the tool developed at Dartmouth for this purpose?

Dr. Suckow: I believe it's essential for modern clinical trials to incorporate at least some level of patient-reported outcome measures. Traditionally, outcomes have been defined by physicians, focusing on survival, graft durability, and device performance. However, particularly in aneurysmal disease, patients often struggle to fully grasp these clinical endpoints. Aneurysms are typically asymptomatic, and while patients understand they have one, they often know little about the condition itself. They recognize that treatment is purely preventative, but it doesn't necessarily change how they feel physically.

However, we've come to realize that simply knowing they have this "ticking time bomb" inside them can be a significant source of anxiety, fear, and worry. The prospect of undergoing a procedure—one that might not make them feel better and could even pose risks—adds another layer of emotional burden. To better understand and quantify this impact, we've developed a dichotomous QOL assessment tool. It evaluates a patient's QOL before their aneurysm is treated and again afterward, whether they undergo an endovascular or open procedure. This tool goes beyond just measuring worry and anxiety—it assesses how living with an aneurysm affects their daily function, mental well-being, and overall QOL.

Dr. Schermerhorn, please share some insights into the AAA-SHAPE feasibility trials conducted in New Zealand and the Netherlands and how they have led to the initiation of the AAA-SHAPE pivotal trial.

Dr. Schermerhorn: The initial AAA-SHAPE studies in New Zealand and the Netherlands, led by Dr. Andrew Holden and Prof. Michel Reijnen, focused on assessing the feasibility, safety, and outcomes of AAA sac embolization using shape memory polymer. These studies have now reached the 2-year follow-up mark.

With initial safety and feasibility established, the next research phase of this therapy starts with the pivotal AAA-SHAPE randomized controlled trial (RCT), which will evaluate both safety and effectiveness on a larger scale. We anticipate that the data from this trial will provide valuable insights to optimize patient selection and aneurysm sac management. We're optimistic that this research will play a key role in improving long-term outcomes for all EVAR patients.

How is the Dartmouth QOL tool currently being utilized in aortic trials, including AAA-SHAPE, Dr. Suckow?

Dr. Suckow: The Dartmouth QOL instrument is designed as both a preoperative assessment and a follow-up evaluation for patients who have undergone aneurysm repair, whether endovascular or open. It includes several key components that measure physical function, emotional impact, anxiety levels, and patient knowledge about their disease—helping us understand how this awareness influences their anxiety.

Currently, the QOL tool is being used in multiple clinical trials, including the AAA-SHAPE pivotal trial. We hope it will provide valuable insight into how much patients truly understand about their aneurysm at baseline and help address the fears and anxieties they experience, despite having "fixed" their aneurysm with EVAR. Beyond AAA-SHAPE, the QOL tool is also being utilized in the Nectero Medical stAAAble trial, which focuses on stabilizing small AAAs to prevent the need for future intervention. Our surveillance-specific version of the tool is particularly relevant for this patient cohort, allowing us to better understand the emotional and psychologic burden they carry. Additionally, the QOL assessment serves as a secondary outcome measure in our physician-sponsored investigational device exemption trial for fenestrated endografts. I've also been in discussions with endograft companies who plan to incorporate it into their upcoming complex AAA device clinical trials.

I'm pleased to see the growing adoption of this QOL tool and strongly believe that patient-reported

outcome measures should be a standard component of any AAA trial.

Finally, Dr. Resch, can you tell us about the PREVAR RCT and what specific outcomes you're evaluating for AAA patients?

Dr. Resch: The PREVAR trial—Preemptive Embolization of EVAR Patients—was designed to address a critical issue that Dr. Schermerhorn has highlighted: the persistence of type II endoleaks and the lack of sac regression after EVAR. Although type II endoleaks have been widely discussed and debated for years, their significance became even clearer when studies revealed that failure of sac regression is strongly linked to lower survival rates and higher reintervention rates. Previous trials have demonstrated that sac embolization can effectively reduce type II endoleaks and promote sac shrinkage. PREVAR aims to build on this evidence by evaluating whether a proactive approach to embolization can lead to better long-term outcomes for AAA patients.

One of the main challenges with previous sac coil embolization trials has been that the materials used interfered with follow-up imaging, making it difficult to accurately assess outcomes. When searching for a novel embolization agent that would allow us to conduct a prospective trial, I came across the IMPEDE-FX Embolization Plug (Shape Memory Medical). This device, made from a shape memory polymer, features a radiolucent, porous scaffold, making it a unique candidate for embolization without disrupting imaging.

We have since launched the randomized trial using a single stent graft (Endurant, Medtronic) within its anatomic instructions for use, combined with the IMPEDE-FX Embolization Plug for sac embolization. The protocol closely mirrors that of the AAA-SHAPE pivotal trial. Enrollment has progressed rapidly—we've already reached nearly 20% within a few months! The trial is going exceptionally well, and we're optimistic that this approach will enhance the known benefits of EVAR while addressing the persistent issue of nonregressing sacs. This problem is frustrating not only for physicians and surgeons during follow-up but also for patients who must undergo repeated imaging and multiple reinterventions to prevent further sac growth.

If these randomized trials confirm that this technique is both safe and effective, it will represent a huge step forward for endovascular AAA repair. It's also worth noting the growing enthusiasm for sac regression over the years. Although there was initial skepticism about whether it should be considered the ultimate outcome, I believe there is now widespread consensus. The next step is determining the most effective way to achieve it. ■

1. O'Donnell TFX, Deery SE, Boitano LA, et al. Aneurysm sac failure to regress after endovascular aneurysm repair is associated with lower long-term survival. J Vasc Surg. 2019;69:414-422. doi: 10.1016/j.jvs.2018.04.050

Disclosures
Dr. Resch: Received funding for PREVAR trial from Shape Memory Medical and Medtronic.
Dr. Schermerhorn: National Principal Investigator for AAA-SHAPE Pivotal RCT.
Dr. Suckow: Consultant to WL Gore, Cook Medical, Astute Imaging, GE, and Siemens.

Disclaimers: Not all devices discussed in this interview are available in all regions. The content contains information about the AAA-SHAPE Pivotal Trial, Shape Memory Medical's prospective, multicenter, randomized, open-label trial of the IMPEDE-FX RapidFill when used for prophylactic abdominal aortic aneurysm (AAA) sac filling during elective endovascular aneurysm repair (EVAR). For more information about the AAA-SHAPE Study, please visit https://clinicaltrials.gov/study/NCT06029660.

In countries recognizing CE Marking, the IMPEDE Embolization Plug, the IMPEDE-FX Embolization Plug, and IMPEDE-FX RapidFill are indicated to obstruct or reduce the rate of blood flow in the peripheral vasculature. In the USA, the IMPEDE Embolization Plug is indicated to obstruct or reduce the rate of blood flow in the peripheral vasculature and the IMPEDE-FX Embolization Plug is indicated for use with the IMPEDE Embolization Plug to obstruct or reduce the rate of blood flow in the peripheral vasculature.

The IMPEDE-FX RapidFill device is not approved for sale in the USA or Japan. Data on file at Shape Memory Medical.