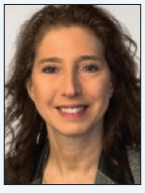
Abdominal Aortic Aneurysms in Women: Perspectives From AAA-SHAPE Investigators

Acknowledging the biological differences and advancing the standard of care.

With Linda Harris, MD; Caitlin Hicks, MD; and Eanas S. Yassa, MD



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It has long been established that meaningful sex-based differences exist in the presentation, treatment, and outcomes of abdominal aortic aneurysm (AAA).[1] Compared with men, women experience higher perioperative mortality, longer hospital stays, and a significantly higher risk of rupture at smaller aneurysm diameters. At the same time, women remain consistently underrepresented in AAA clinical trials, and their distinct anatomical and biological characteristics are often not reflected in device design or guideline development.[2]

Shape Memory Medical is dedicated to advancing new embolization-based therapies using its proprietary shape memory polymer platform and is actively exploring expanded clinical applications in aortic disease. The AAA-SHAPE trial (Abdominal Aortic Aneurysm Sac Healing and Prevention of Expansion) is a prospective, multicenter, randomized, open-label pivotal study evaluating the safety and effectiveness of the IMPEDE-FX RapidFill® device (Shape Memory Medical) in improving aneurysm sac behavior when used adjunctively with elective endovascular aneurysm repair (EVAR).[3]

We spoke with three Principal Investigators (PIs) from the AAA-SHAPE pivotal trial—Dr. Linda Harris, Dr. Caitlin Hicks, and Dr. Eanas Yassa—to explore how AAA differs in women and how care can be improved moving forward.

How and why does AAA behave differently in women?

Dr. Harris: We know that aneurysms in women don't behave the same way they do in men. They grow more

rapidly, they present with more challenging anatomy when we get to repair them, and biologically they don't form in the same way. Women's aortas also tend to be stiffer—particularly in the thoracic portion—and women are more likely than men to have thoracic aneurysms. There are a whole host of biological differences, so to assume aneurysms in men and women are the same and that the same devices will work equally well simply doesn't make sense.

Aneurysms are less common in women overall, but once women develop them, they tend to grow faster and rupture more frequently; it really is a different disease.

Dr. Hicks: Another important point is rupture risk. Women rupture at smaller aneurysm sizes, and that's something we see consistently. Right now, we use this half-centimeter adjustment for women, but it's really just a "guesstimate" because most of our data come from male patients. I suspect that the true threshold is quite a bit lower. The WARRIORS trial will help clarify this, but for now clinicians need to recognize that aneurysms in women don't behave the same way and that we need different thresholds and different markers of disease pathology.[4]

Dr. Yassa: When we repair aneurysms in women, we are often using guidelines that are extrapolated from studies that didn't include equal numbers of women. As I treat more women in my practice and pay closer attention to their native aortic diameter above the aneurysm, I begin to understand why these aneurysms surprise us—why they rupture earlier and why they behave differently. Looking at indexed aortic size rather than absolute diameter alone gives much better insight into the biology. It really is a different disease process that requires more nuance than a plug-and-play approach.

Despite progress, women remain underrepresented in clinical research. Why?

Dr. Hicks: This is not an aneurysm-specific problem—it's something we see across almost all clinical trials. Women are often caregivers, and many feel they don't have the time to participate. As a woman myself, I find it is much harder to enroll women in trials. Many feel they would be burdening the people around them if they agree to participate.

Dr. Harris: There are barriers at three levels: the patient, the PI, and the sponsor. On the sponsor side, are women included as PIs? Women are more likely to trust women physicians, just as underrepresented minorities are more likely to trust investigators who reflect their communities. That really does make a difference.

There are also unintended consequences in trial design. Something as simple as choosing a larger device size—even when size doesn't truly matter—can end up excluding women because we have smaller vessels. Transportation is another huge issue. Women are more often widowed and dependent on their children or social services to get to appointments, and they don't want to burden their families. In some cultures, women even need approval from a spouse or a male family member to participate.

Although it would be hard financially, one thing industry could do is to cap male enrollment. If you want 20% or 30% women in a study, you stop enrolling men once you reach the male threshold. That forces all of us to go find women. It's easier to enroll men—there's no question about it. So unless you do something deliberate, you'll never get balanced cohorts.

Dr. Yassa: Enrollment also depends on identifying disease in the first place. Women are often diagnosed with aortoiliac disease much later in its course. If you don't identify the pathology early, you can't include women when trial opportunities arise.

How can industry improve female representation among both patients and investigators?

Dr. Hicks: We need to move beyond the same small group of go-to investigators. One person doesn't need to be the PI on 10 studies. When you give different investigators, especially younger or more junior physicians, the opportunity to lead trials, you increase engagement and diversify the patient population. Diversifying the physician pool is one of the best ways to diversify the patients we enroll.

Dr. Harris: One issue is how people are identified to participate in studies. A lot of that happens through industry reps: who they know, who they interact with, etc. Women physicians often have less informal engagement with reps, so their names don't always get passed along, even when they are high-volume aneurysm surgeons. Partnering with professional societies and women's sections could help identify excellent female investigators whose names might otherwise be missed.

Dr. Yassa: Shape Memory Medical has done a very good job of being mindful about including women investigators. More broadly, junior surgeons need to seek allies and sponsors of either gender who will advocate for them and put their names forward. That's uncomfortable, but it's how the future of the field changes.

Dr. Harris: Imposter syndrome plays a big role.[5] Women are much less likely to self-nominate. There are

very few things in my career that I have ever self-nominated for, because I often felt I wasn't ready. I was lucky to have mentors who told me to put my name in and pushed me forward. Many women don't have that, even though they are exceptional surgeons.

Dr. Hicks: Industry has made real progress in the last 5 years in recognizing this problem, but they can't read our minds. If you want to be part of a trial, you need to say so—to your mentors and to sponsors. It might not be this study or the next one, but those opportunities will come.

Dr. Yassa: It's important to understand that imposter syndrome doesn't just hold back physicians; it also holds back patients. Representation matters. When patients feel understood by their physicians, they adhere to therapy, stay in surveillance, and report symptoms. That improves outcomes.

What do you hope AAA-SHAPE will reveal about women with AAA?

Dr. Hicks: I'm very excited about the sac regression data and whether it varies by sex. We don't have great sac regression data in general, so seeing what happens in both the control and treatment arms will be very informative.

Dr. Harris: Most studies are not powered to look at women separately, so we end up making assumptions based on very small cohorts. I hope we enroll enough women in AAA-SHAPE to see whether there truly are differences in how women respond, including differences in thrombotic and healing profiles with shape memory polymer embolization.

Dr. Yassa: Beyond sac regression, I'm focused on survival and durability. If we can achieve EVAR outcomes comparable to open repair, especially in women, that could change how we treat lower-risk patients and when endovascular repair is appropriate.

What unmet needs remain for women with AAA?

Dr. Hicks: We need female-specific devices—especially lower-profile access. Many of the exciting new technologies require 20- to 22-F sheaths that simply don't fit women. We need to translate innovation into smaller platforms so these devices are accessible to women, Asian populations, and others who don't fit the standard Caucasian male anatomy most devices are built around.

Dr. Harris: Women's vessels are more calcified, they don't stretch as easily, and there is more angulation and shorter necks. That makes low-profile, flexible systems even more critical.

Dr. Yassa: We also need better screening and earlier diagnosis so we can identify disease sooner and change the natural history before rupture risk becomes high.

FINAL THOUGHTS

As vascular care continues to evolve, it is becoming increasingly clear that a one-size-fits-all approach to AAA is no longer sufficient. Women represent a distinct biological and clinical population whose needs have too often been addressed through extrapolation rather than evidence. By pairing innovative sac-directed therapy with a deliberate focus on women's anatomy, biology, and representation in research, efforts such as AAA-SHAPE offer an opportunity to close that gap—ensuring that the next generation of endovascular advances is built on data that truly reflect the patients we treat. ■

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Disclosures
Dr. Harris: Site Principal Investigator for Gore, Shape Memory Medical, and Penumbra (no compensation received).
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