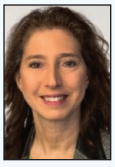
PANEL DISCUSSION

Women's Aortic Health: Are We Meeting the Need?

Discussing gender-based health inequities and how to address challenges.

Moderator: Linda M. Harris, MD, FACS, DFSVS
Panelists: Young Erben, MD; Javairiah Fatima, MD, FACS, DFSVS; Joseph V. Lombardi, MD; and Jessica P. Simons, MD, MPH



MODERATOR
Linda M. Harris, MD, FACS, DFSVS
Professor of Surgery
Program Director
Vascular Surgery Residency & Fellowship
Jacobs School of Medicine and Biomedical Sciences
State University of New York at Buffalo
Buffalo, New York
Disclosures: None.

Young Erben, MD
Associate Professor of Surgery
Division of Vascular and Endovascular Surgery
Mayo Clinic
Jacksonville, Florida
erben.young@mayo.edu
Disclosures: None.

Jessica P. Simons, MD, MPH
Associate Professor of Surgery
Division of Vascular and Endovascular Surgery
University of Massachusetts Medical School
Worcester, Massachusetts
jessica.simons@umassmemorial.org
Disclosures: None.

Javairiah Fatima, MD, FACS, DFSVS
Associate Professor of Surgery
Department of Vascular Surgery
Georgetown University School of Medicine
Co-Director, Complex Aortic Center
MedStar Heart and Vascular Institute
MedStar Washington Hospital Center
Washington, DC
javairiah.fatima@medstar.net
Disclosures: Consultant to Medtronic, Cook Medical, Endologix, and Terumo.

Joseph V. Lombardi, MD
Professor & Chief of Vascular Surgery
Cooper Medical School of Rowan University
Director, Cooper Aortic Center
Cooper University Health Care
Camden, New Jersey
lombardi-joseph@cooperhealth.edu
Disclosures: Consultant to Cook Medical, Shockwave, and Medtronic.

Current United States guidelines do not recommend screening for abdominal aortic aneurysm (AAA) in women, while societal guidelines do recommend screening. Should women be screened for AAA, and if so, what should the criteria be for screening?

Dr. Simons: I adhere to the Society for Vascular Surgery (SVS) guidelines regarding AAA screening in

women.[1] The United States Preventive Services Task Force (USPSTF) determined there was insufficient evidence to recommend for or against screening in women aged 65 to 75 years with a smoking or family history.[2] When evidence is insufficient, I believe it is reasonable to use expert consensus instead, such as the SVS document. To my knowledge, the recommendations against screening (ie, women who have never smoked and have no family history) do not differ between guidelines.

Dr. Lombardi: I do believe women should be screened for AAA. Relative to men, the poor outcomes of women undergoing AAA repair have been well documented. Women are challenged by more difficult anatomy, smaller vessels, and tendencies to rupture at lower size thresholds. Screening should give us time for earlier detection, affording female patients an opportunity for awareness, risk factor modification, and to establish the ever-important relationship with the vascular surgeon. Although it may not be a cost-effective strategy and the yield in diagnosis of AAA will be lower, I believe we should provide women with significant risk factors such as tobacco use and family history the same criteria we afford men.

Dr. Fatima: The USPSTF recommends against screening women who have never smoked and deem screening to be of questionable benefit and potential harm in women who have ever smoked or have a family history of AAA.[2] The American College of Cardiology and American Heart Association have made similar recommendations. However, these recommendations are based on population-based studies that were subject to selection and implicit bias. Most landmark studies, such as OVER, ADAM, DREAM, and EVAR 1, severely underrepresented women, leading to the thought that screening in women can lead to overdiagnosis and overtreatment. Additionally, treatment in these trials was with older-generation devices that were not designed for or suited to the known anatomic challenges encountered in women (eg, small access, tortuous/hostile necks). It is questionable as to whether the results of these trials can be generalized to women.

Despite a lower incidence of AAA compared to men, women have a higher risk of rupture.[3] The data extrapolated from the National Health Service AAA Screening Program demonstrated cost-effectiveness of screening in women, even more so in women who were smokers.[4] One may even argue that the lack of screening can actually lead to a delay in diagnosis, worsening of anatomic features, and worse outcomes secondary to the delay in repair. Based on this, SVS recommends screening in women > 65 years who have smoked or have a family history of AAA.[1]

Dr. Erben: Women should be screened for AAA. I would intentionally direct the attention to those women with prior smoking and/or family history, as the guidelines from the USPSTF recommend.[2] The data supporting this recommendation are deemed lacking/of poor quality/conflicting, and therefore the balance of benefits and harms cannot be determined. I believe that this is a multifaceted effect, including the lack of inclusion of women in many cardiovascular studies,[5] the lower prevalence of aortic aneurysmal disease in women,[6] the fact that women are less likely to be offered elective AAA repair and less likely to be eligible for endovascular aortic aneurysm repair (EVAR), and that they have a higher mortality and complication rates after both EVAR and open repair.[7]

Have endovascular aortic devices improved enough to allow for equal outcomes for men and women who undergo elective EVAR? If not, what else needs to be done to improve devices to eliminate gender differences in outcomes?

Dr. Erben: To a large degree, the devices have improved. However, there are a few women whose aneurysms will be challenging to treat due to tortuosity of their vessels and smaller common femoral artery access sites. It all comes down to surgical planning. If this is done correctly, the complication rates will be as low as those for the male patients. The key concepts are early detection, surveillance, and prioritizing women's cardiovascular health for best outcomes.

Dr. Simons: I think the industry has been trying hard since the introduction of EVAR to make devices as low profile as they possibly can be, while still providing a durable result. So, we can always strive to improve with respect to the poorer outcomes of women that relate to access site complications, but I think much of industry has its priorities aligned with that aspect of care for women with AAA. What could still be done to improve outcomes is additional study of the other mechanisms by which disparities exist. We should be asking questions such as "Are there hormonal differences in how the radial force of a seal stent impacts aortic degeneration?" and "Do women have fewer caretakers to help bring them to follow-up visits?"

Dr. Lombardi: Great question! Sweet et al reported significant anatomic differences in women compared to men, where women have decreased neck length, increased neck angulation, and smaller iliac access when adjusted for AAA size and age.[8] This does explain the finding that females are offered fewer endovascular repairs than males. Advances in fenestrated and branched technologies offer promise, yet profile and

access restrictions are still a significant obstacle for these devices with larger outer diameter. The ideal endograft will be a profile of 14 F that will thrive in hostile, short, angulated neck anatomy.

Dr. Fatima: It has been shown time and again that even elective EVAR is fraught with higher perioperative mortality in women (2%-3% vs 1%-1.5% in men) in the majority of the published studies. Pooled estimates of infrarenal EVAR suitability also differ significantly between men and women, and women are less likely than men to undergo EVAR electively for intact aneurysms. The principal morphologic criteria rendering women unsuitable for EVAR include both short and angulated proximal aneurysm necks and the dimensions of the access iliac arteries.

Successful partnership between industry and physicians spearheading on the aortic frontier has led to significant positive advances and improvements in technology to where they stand today. However, we still have a long way to go to design devices that address the anatomic limitations specific to female gender and thus increase eligibility of a larger proportion of women to EVAR while minimizing resulting complications, reinterventions, and readmissions. The LUCY study sponsored by Endologix (evaluating the Ovation abdominal stent graft platform) was a refreshing step in the right direction, with 34% EVAR eligibility in women, as are the attempts to address the need for more flexible and conformable devices to accommodate angulated necks and smaller access vessels by other aortic devices to reduce the gender gap in outcomes.

In women with hostile neck anatomy (short, angulated, reverse conical) and at higher risk of developing thoracic aneurysms, what is your preferred approach to intervention and why?

Dr. Lombardi: Patients may present with other mitigating factors that transcend morphology, such as pulmonary or cardiac comorbidities that drive a certain operation in the face of hostile anatomy. In my practice, these patients rarely get a more extensive repair for fear of thoracic degeneration. I do entertain endovascular considerations in all patients > 65 years, with younger patients afforded options of open and endovascular if feasible. With so many endovascular options now available using fenestrated devices, chimneys, and branched grafting, a solution usually presents itself in this category, particularly for those with prohibitive health risks and undesirable zone 5, 6, and 7 anatomies. However, occasionally, we see patients aged 70 to 75 years who are in good health and can undergo more traditional open repair.

Dr. Simons: Certainly, I have a bias toward extending the seal zone as proximally as I reasonably can, given the devices available here with the University of Massachusetts investigational device exemption trial of fenestrated and branched EVAR, and, fortunately, our outcomes to date support doing so. This is true for both men and women in my practice. The only difference relates to age at presentation; because women tend to present a bit older than men, I am even more likely to offer a complex endovascular strategy rather than a complex open repair that I might offer to a younger patient with hostile neck anatomy.

Dr. Fatima: In my practice, I follow the rule that the choice of repair, whether open or endovascular, should focus on the durability needed for each individual. If young and fit, patients with multiple hostile neck features (women have been shown to have a higher likelihood of having more complex aneurysms compared to men) may benefit from open repair; however, if endovascular repair is better suited based on physiology and/or anatomy, I believe it is necessary to build into healthy parallel aorta. This allows the option to build higher should the more proximal aorta demonstrate aneurysmal degeneration over time. For those with short and reverse conical necks, my approach is often a fenestrated repair, addressing the visceral and renal vessels to allow for a more durable repair, without burning any bridges for a future proximal extension. Long-term studies have shown more favorable sac regression and remodeling in women with this approach and long-term survival data comparable to men.[9] Assessment of interventional complexity and risk stratification based on anatomic and physiologic factors are critical in women undergoing these procedures. Aggressiveness of repair should be based on what durability means for each individual patient.

Dr. Erben: If the patient is a good surgical risk candidate, open repair should be considered. If this is not the case, assuring that there are parallel walls of normal aorta as the proximal endpoint of the repair is key, which includes extending proximally the seal zone for the aortic repair. Durability has been the question that we are all trying to answer for the endovascular repair, and I believe that providing an appropriate seal zone is the most important component.

Should aortic size index (ASI) be used instead of absolute aortic size in determining when to fix aneurysms in women?

Dr. Simons: We don't have adequate data to answer this question definitively. There are still many unanswered questions about how to best predict rupture

risk—maximum diameter, ASI, finite element analysis/wall stress. The concept of using ASI (rather than absolute diameter) is intuitively quite logical—even the basic definition of an aneurysm is relative to its adjacent normal segment. So, the next logical question is, if two people have the same ASI, is there still a sex disparity in rupture risk? A study of registry data was published in 2014, indicating that, yes, women were more likely to have been treated for a ruptured aneurysm than men even when ASI was the same.[10] This would indicate there may be even more than just size corrections that need to be made. Conversely, there are limitations to the study's retrospective nature and a cohort only of patients who underwent repair. In short, I don't use ASI, but I do consider repair for women at 5 cm rather than 5.5 cm for men. As always, it requires discussion of the benefits, risks, suitability for EVAR versus open repair, and overall surgical candidacy.

Dr. Fatima: Women consistently have been shown to have a higher risk of rupture compared to men at any given diameter and overall have been noted to rupture at smaller diameters. It has been shown that accounting for ASI reduced this discrepancy between men and women, attesting to the fact that even though overall diameter maybe small, it is large relative to their body size. ASI was noted to be a better predictor of adverse events, including ruptures in women. ASI may be a better decision-making tool for women with aneurysms < 5.5 cm.

Dr. Erben: The data have not been validated, but I believe that this should be an index rather than absolute aortic size. It is clear that the rupture risk of a 5-cm aorta in a woman who is 1.75 m in height is not the same as the risk in a woman who is 1.4 m in height.

Dr. Lombardi: Yes, but while size continues to be our best screening parameter, other criteria such as aneurysm morphology, rate of growth, and ratio along with health status should blend into the equation when considering repair. Size index makes complete sense, and I don't understand why it hasn't been adopted at society levels. The index considers the patient's individual stature and defines an abnormality in size accordingly. Perhaps over time it may help us better stratify female patients who should have treatment sooner.

Why do you believe outcomes for women remain worse than men when operated for ruptured aortic aneurysm, whether open or endovascular?

Dr. Fatima: Women tend to present for AAA repair at an older age, possibly due to lack of optimal screening guidelines. Studies have also shown that women tend to have worse cardiovascular optimization, such as use of statins, control of hypertension, and management of diabetes as compared with their male counterparts, which impacts perioperative outcomes. Women also tend to have more complex anatomic challenges compared to men; given their overall smaller body habitus and smaller access/iliac arteries, they are subject to lesser eligibility within the instructions for use (IFU) of any particular device and therefore subject to higher incidence of injuries, complications, and reintervention rates. Large real-world data such as the Vascular Quality Initiative show twice the rate of conduits and iliac injury in women compared to men, resulting in increased bleeding complications and need for transfusions, which has been shown as an independent risk factor for higher morbidity and mortality. The GREAT registry also demonstrated significantly higher rates of access-related complications in women. Finally, the delay in detection results in more challenging anatomy on presentation when ruptured, which directly impacts the outcome regardless of the chosen/eligible repair modality.

Dr. Simons: This disparity is undoubtedly multifactorial, with the literature identifying that women may present at an older age, have more undiagnosed comorbidities, experience more intraoperative complications related to iliac rupture or hostile neck anatomy, and several others. There could be other factors, such as delay in diagnosis, that result from poorer awareness of AAA in women. There could be disparities in threshold for withdrawing care postoperatively. But, I would not stop here with these potential explanations; I think further study is needed to mitigate the disparities and see what other factors might then be uncovered.

Dr. Lombardi: Overall, the prevalence of AAA in women is lower than that of men, and the development of AAA in women usually arises in the face of considerable comorbidity. A report by Lo et al showed that gender difference alone failed to show a difference in 30-day mortality for both open and endovascular repair.[11] Women who have poor outcomes after rupture present at an older age and tend to have more comorbidities, such as coronary artery disease, chronic obstructive pulmonary disease, and congestive heart failure. Women who presented with rupture also had smaller-sized aneurysms compared with men. This paints a picture of a more difficult group of patients who perhaps are not treated early enough and are burdened further by a lack of technology geared for their anatomy.

Dr. Erben: Again, the key concept here is early detection and intervention. We know that ruptured aneurysms will have a worse outcome no matter the sex of the patient. However, the attention is given in higher proportions to detect cardiovascular diseases in male patients rather than in female patients. Early detection, surveillance, and early repair are essential to obtain parity in terms of outcomes and prevent rupture.

Do you have the same or a different "preferred" endograft for women than men and why?

Dr. Simons: I do not have a different preferred endograft for women versus men. There are several commercially available devices that all perform well, even with challenging iliac anatomy. My primary consideration relates to the favorability of the neck; the decision isn't about which brand of device but about whether an infrarenal repair or complex repair is best.

Dr. Lombardi: Currently, I have similar anatomic preferences for endografts in women as I do men. I don't believe one endovascular device has universally separated itself as "better for women" than the others. One may preferentially use "the lowest-profile device" for women, but I have found this to be less of an issue with more infrarenal devices becoming lower profile. The female patient with a hostile neck may be a candidate for a fenestrated device but may have access issues that warrant an open approach.

Dr. Erben: Yes, I prefer to use less stiff devices for my female patients than for my male patients. Furthermore, hydrophilic coating and smaller French sizes are ideal for all patients but more so for my female patients.

Dr. Fatima: I am fortunate to have the ability to choose from amongst the many commercially available grafts. My choice of endograft is dependent on the anatomic needs of the individual patient, such as need for a lower-profile device in patients with smaller access vessels, use of a more flexible and conformable device in patients with angulated/tortuous necks, use of adjuncts to help fixate the device when necessary, and an FDA-approved investigational device exemption that allows me to build up with a fenestrated or branched endovascular device when complexity of the aneurysm demands a more extensive repair.

Why do you believe women with rupture are less likely to be offered repair than men, and what can be done to alter this?

Dr. Erben: I really wish I understood this bias. Personally, because of these biases, I tend to evaluate my female patients closer and pay attention to their symptoms. Again, recognizing these biases and understanding them is the first step to eliminating them and improving outcomes in our female patient population. I believe that culture change is what needs to be addressed in order to improve the outcomes in our female patient population. My hope is that with policies such as the one put forward by the National Institutes of Health,[12] more principal investigators are aware of the dire need to address health care disparities and thus automatically look to improve the outcomes of AAAs in women.

Dr. Fatima: Women have multiple factors that predispose them to do poorly when they present with ruptures, such as older age, poorly managed cardiovascular comorbidities, and worse anatomic challenges. To alter this, a culture change is necessary, starting with more conscientious screening of women with risk factors and a family history of AAA, better medical management of cardiovascular comorbidities, counselling on smoking cessation, and finally, access to devices that are better designed to improve anatomic eligibility for women within IFU for repair.

Dr. Simons: This remains a very interesting, multifaceted issue, starting with whether it's truly offered less versus offered at the same rate but declined more often. I'm not sure how easy it would be to tease that out of even a thorough chart review in many cases. However, if we assume all factors for surgical candidacy are equal, I would say, anecdotally, I have had more women decline repair or families of female patients decline repair. I don't even have data to back this up, so I certainly don't have data on why this would be true. I would note that a similar finding in some cancer literature (women declining treatment at higher rates) has been extensively studied without one clear reason.[13] It deserves far more study to ensure not necessarily that women undergo operation at equal rates but that they are offered at equal rates and that a decision to decline is truly consistent with the patient's wishes.

Dr. Lombardi: Although I am unsure of the data referenced for this question, a possible answer may be that women may present in extremis more often than men due to a lack of containment. Men are more likely to have more muscular abdominal and back confines with stronger connective tissue to delay free rupture.

Do we need additional endovascular device trials with better representation of women for AAA repair? For thoracic aortic aneurysm repair?

Dr. Lombardi: Absolutely. We have yet to understand our inability to match AAA repair outcomes in women

as compared with men. An all-inclusive yet dedicated female AAA trial, with all industry partners, would promise a large body of data that would be powered to answer where we are falling short and very likely help move the needle for this health disparity. I think the comparisons to male patients have allowed us to highlight the differences in female outcomes, but now we need to invest and dedicate a comprehensive study that will help distill information we have yet to uncover.

Dr. Erben: What we really need is inclusivity in the trials. Not necessarily additional trials, but an intentional attempt at recruiting women in the current and existing trials, including the dissection and thoracic aneurysm trials.

Dr. Simons: Yes, if it is at all possible. To me, this is as simple as scientific rigor—the study population needs to represent the patient population to which it will be applied to have the best generalizability. Especially as data have emerged that suggest there is a disparity, the scientific method would require that additional studies are conducted with the same rigor as the initial device approval studies. I recognize there are important real-world factors that can be prohibitive, but a strong effort should be made to attempt this. I fear that the use of registries or total product life cycle databases does not adequately answer these questions for many reasons, not the least of which is that it only includes cases where a device was implanted.

Dr. Fatima: Absolutely, in the ideal world, that is the way to bring about a change. Current available trial data are fraught with gender bias secondary to trial design favoring rapid enrollment of patients based on less challenging anatomic criteria. This has historically limited female enrollment numbers, reducing our ability to evaluate sex-based differences. We are still in the phase where we need to design EVAR and thoracic endovascular aortic repair devices that are better suited for anatomic needs in women and potentially power the study to truly assess for gender-based differences. ■

1. Chaikof EL, Dalman RL, Eskandari MK, e al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. J Vasc Surg. 2018;67:2-77.e2. doi: 10.1016/j.jvs.2017.10.044
2. US Preventive Services Task Force. Recommendation: abdominal aortic aneurysm: screening. Accessed November 5, 2021. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/abdominal-aortic-aneurysm-screening
3. United Kingdom Small Aneurysm Trial Participants, Powell JT, Brady AR, Brown LC, et al. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. N Engl J Med. 2002;346:1445-1452. doi: 10.1056/NEJMoa013527
4. Glover MJ, Kim LG, Sweeting MJ, et al. Cost-effectiveness of the National Health Service abdominal aortic aneurysm screening programme in England. Br J Surg. 2014;101:976-982. doi: 10.1002/bjs.9528
5. Napoli, N. Women underrepresented in CV clinical trials despite inclusivity requirements. Accessed December 1, 2021. https://www.acc.org/about-acc/press-releases/2021/08/06/14/45/women-underrepresented-in-cv-clinical-trials-despite-inclusivity-requirements
6. Lo RC, Schermerhorn ML. Abdominal aortic aneurysms in women. J Vasc Surg. 2016;63:839-844. doi: 10.1016/j.jvs.2015.10.087
7. Pouncey AL, Powell JT. Womens lives at stake: women suffer disproportionately after abdominal aortic aneurysm repair, so what can we do about it? Eur J Vasc Endovasc Surg. 2021;62:1-3. doi: 10.1016/j.ejvs.2021.04.025
8. Sweet MP, Fillinger MF, Morrison TM, Abel D. The influence of gender and aortic aneurysm size on eligibility for endovascular abdominal aortic aneurysm repair. J Vasc Surg. 2011;54:931-937. doi: 10.1016/j.jvs.2011.02.054
9. Witheford M, Chong DST, Martin-Gonzalez T, et al. Women undergoing endovascular thoracoabdominal aortic aneurysm repair differ significantly from their male counterparts preoperatively and postoperatively. J Vasc Surg. 2020;71:748-757. doi: 10.1016/j.jvs.2019.05.053
10. Lo RC, Lu B, Fokkema MT, et al. Relative importance of aneurysm diameter and body size for predicting abdominal aortic aneurysm rupture in men and women. J Vasc Surg. 2014;59:1209-1216. doi: 10.1016/j.jvs.2013.10.104
11. Lo RC, Bensley RP, Hamdan AD, et al. Gender differences in abdominal aortic aneurysm presentation, repair, and mortality in the Vascular Study Group of New England. J Vasc Surg. 2013;57:1261-1268.e12685. doi: 10.1016/j.jvs.2012.11.039
12. National Institutes of Health. NIH policy and guidelines on the inclusion of women and minorities as subjects in clinical research. Accessed December 14, 2021. https://grants.nih.gov/policy/inclusion/women-and-minorities/guidelines.htm
13. Moraes Dias L, Rebello Bezerra M, Fernandes Barra W, Rego F. Refusal of medical treatment by older adults with cancer: a systematic review. Ann Palliat Med. 2021;10:4868-4877. doi: 10.21037/apm-20-2439