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Key Takeaways From the SMART Trial's 3-Year Women's Subgroup Analysis

Announcer:
You're listening to GLC on ReachMD. This activity, titled 'Key Takeaways From the SMART Trial's 3-Year Women's Subgroup Analysis' is provided by Global Learning Collaborative.

Dr. Sweis:
I'm Ranya Sweis. I'm a structural interventional cardiologist in Chicago, and I'm happy to be here at the American Heart Association Scientific Sessions, also in Chicago. Earlier today, we had a poster presentation on some of the 3-year data from the subgroup analysis on women in the SMART trial, and I'm happy to go over that data with you today.

Before I get into the details of the SMART trial specifically, I just want to set the stage for why this is important. 70% to 80% of women have small aortic annuli, and this puts them at higher risk of worse hemodynamics after aortic valve replacement. We know from many studies that worse hemodynamics, specifically patient-prosthesis mismatch, is associated with worse outcomes long term for patients and especially women.

And we also know that in patients with small annuli who are treated with TAVR, studies have shown that hemodynamics using self-expanding valves compared to balloon-expandable valves are different The SMART trial stands for SMall Annuli Randomized to Evolut or SAPIEN Trial. This study was specifically designed to compare using a self-expanding valve versus a balloon-expandable valve for patients with small annuli. Interestingly, because women have mostly smaller annuli, 87% of this population for the study were women, even though the trial was not specifically designed as a study for women.

The SMART trial is a prospective randomized control post-market trial. 737 patients were enrolled overall. 637 of them were women and 100 were men. These patients were enrolled in 13 different countries at 81 different sites. 312 of the patients, of the women particularly, received the Medtronic Evolut, PRO, PRO+, or FX, and 309 of these patients received the Edwards SAPIEN 3 or SAPIEN 3 Ultra valve.

Of this population in general, the mean age was 80 years. The mean STS score was 3.4, and the mean aortic annulus was 378. In order to be enrolled in the trial, the patients had to have an aortic annulus less than 430 mm^2 by CT, and, of course, they had to have severe symptomatic aortic stenosis.

The design of the study included 2 co-primary endpoints. The first endpoint was a composite of mortality, disabling stroke, and heart failure rehospitalization through 12 months. The second co-primary endpoint was specifically related to valve function, specifically bioprosthetic valve dysfunction through 12 months in the implanted population.

So the primary analyses of this study were originally published in 2024 in *The New England Journal of Medicine*, and last year, the 2-year outcomes were presented, and we have the presentation of the 3-year outcomes this year. This was first presented in European meeting, and this morning, we had a poster presentation as well of the 3-year data from the subgroup analysis on women.

When we look at the results of the SMART trial, the first primary endpoint that included mortality, disabling stroke, or heart failure hospitalization has remained consistent with the initial presentations of this outcome. There is no significant difference in patients'

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outcome, whether they had a balloon-expandable valve or a self-expanding valve, and this showed basically that the Evolut valve was noninferior to the SAPIEN valve in this patient population.

When we look at the second outcome of bioprosthetic valve dysfunction, however, there was a significant difference. The Evolut valve had a rate of 16.4% bioprosthetic valve dysfunction in this population, whereas the SAPIEN valve had a rate of 55.3% bioprosthetic valve dysfunction.

When we look at the secondary outcomes that looked at prosthetic valve thrombosis, there was a significant difference between both valves as well, with a lower rate of bioprosthetic valve thrombosis by the VARC-2 criteria with Evolut compared to SAPIEN, and we also saw a higher rate of subclinical valve thrombosis with the SAPIEN valve.

When the analysis evaluated patient-prosthesis mismatch in the patients, there was also a significant difference between the valve systems between a patient-prosthesis mismatch where the self-expanding valve had a significantly lower rate of the VARC-3-defined patient-prosthesis mismatch compared to the balloon-expandable valve.

Other interesting analyses from the study looked at valve performance along the range of annuli sizes, and so the different valve sizes that were used in the study. The self-expanding valve had a very consistent large effective orifice area along the different valve sizes and annuli sizes with low mean aortic gradients that were pretty consistent throughout the study. Finally, when we looked at prosthetic valve thrombosis, the significant difference between the 2 groups was seen overall, but also there was significantly less VARC-3 clinical thrombosis.

So, in short, when we review the 3-year follow-up of these women, we continue to see that both self-expanding and balloon-expandable valve have similar rates for the composite of death, disabling stroke, and heart failure hospitalization. However, the self-expanding valve has a significantly lower rate of bioprosthetic valve dysfunction and significantly less VARC-3 clinical thrombosis. And as I mentioned in the exploratory analysis, the moderate and severe patient-prosthesis mismatch at 30 days seem to be associated with a high risk of cardiovascular mortality.

So putting this back into context where I started, that women are really underrepresented in clinical trials and patients, especially with small annuli, who are mostly women, are underrepresented and really not well understood. This is a large trial that looks specifically at this patient population that has been underrepresented and helps us understand what are some of the important things that we need to take into consideration when treating these patients.

TAVR has been a life-saving technology that has really changed the trajectory of medicine and taking care of patients with valvular heart disease. However, where we are now in the field is that we really need to individualize patient care and optimize it and think about the lifetime management of these patients.

So it's not just about saving their life with replacing their aortic valve and implanting a TAVR valve, but it's really about making sure that each patient gets the right valve for them that's going to improve their lifespan and their quality of life and make it a valve that has good longevity for them as well.

Thank you for joining me for this short and sweet review of the 3-year data from the subgroup analysis on women in the SMART trial.

Announcer:
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