radcliffe cardiology

# Title: EuroPCR 24: Ancillary SMART Trial Analyses
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## Dr Roxana Mehran

“Hi, I'm Roxanna Mehran. I'm an interventional cardiologist, professor of medicine, population health science, and policy at the ICAHN School of Medicine at Mount Sinai in New York.

### Overview of the SMART Trial

The SMART trial, the first pre-specified endpoint of the SMART trial, was to evaluate the outcomes in women for the first time. We are seeing very important data on women with a small annulus, which is actually quite a common finding in women who present with severe aortic stenosis. They often have a small aortic annulus, and the choice of valve matters. The SMART trial looked at an intra-annular balloon expandable valve versus a supra-annular self-expanding valve, Evolut versus Sapien, over a twelve-month period. There was a one-to-one randomization. We had 637 women, 90% of the population were women. This particular analysis was incredibly important and historic.

### Patient Population

The patient population were all women, average age of 80, with severe aortic stenosis, a small annulus, randomized to Sapien versus Evolut and followed through twelve months.

### Co-Primary Endpoints

We had two co-primary endpoints in the main SMART trial. For this sub-analysis, we similarly looked at the composite clinical outcomes of death, disabling stroke, and rehospitalization for heart failure. This was powered for non-inferiority, and we met that endpoint with no difference between the two groups.

## Hemodynamic Outcomes

The second co-primary endpoint, powered for the women enrolled in SMART, was the hemodynamic outcomes, specifically bioprosthetic valve dysfunction through twelve months. The key finding was a major statistically significant difference, a 33% difference in the incidence of bioprosthetic valve dysfunction, much lower in the Evolut group compared to the balloon expandable Sapien valve.

## Significance of Hemodynamic Changes

This is significant because hemodynamic changes and bioprosthetic valve dysfunction, specifically with prosthesis-patient mismatch as well as high gradients, are all associated with worse clinical outcomes. This is why we're following the patients out to five years. We expect to see a difference in clinical outcomes down the line. The choice of valve is incredibly important, especially in patients with a small annulus. The trial shows that valves are different and have different hemodynamic consequences. A small annulus is extremely predominant in women, and we now have a choice in choosing a valve that is hemodynamically superior over a twelve-month period. That valve is the self-expanding Evolut valve. It's supra-annular, providing a larger effective orifice area and lower mean gradient over twelve months.

## Clinical Implications

Whether these hemodynamic differences have important clinical implications remains to be seen. So far, through twelve months, no significant clinical implications have been observed, but this is early for valves, so we need to see longer-term data. We need to think deeply about our patients, their phenotype, how they present, what their anatomy is, and choose the right device for the right patient. My key takeaway is that we need to do a better job diagnosing aortic stenosis, especially in women. We need to ensure they receive proper evaluation and make important choices in terms of valve type, follow them through, and aim to improve their outcomes. Most importantly, it is possible to have women enrolled in clinical trials. Women are often underdiagnosed, underappreciated, and underrepresented in clinical trials. This trial showed that if you

enrich your trial with criteria more prominent in women, you will get women enrolled. In the SMART trial, 90% of the patients were women, and now we have answers for women. This is extremely significant for the care of women and improving their health outcomes.

**Future Directions**

The longer-term follow-up is essential, and we need to continue thinking smartly about designing clinical trials to be more inclusive. We should not just study a certain patient population that fits the criteria of our trials, but rather a population representative of our patients. More inclusiveness is necessary."