Title: TCT 23: 5 Trials That Will Change My Practice
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Date: 2 Nov 2023

Dr Mirvat Alasnag

" Hello, everybody. My name is Mirvat Alasnag, I'm an interventional cardiologist in Jeddah, Saudi Arabia, and I'm here to give you updates on the TCT conference and some of the most relevant late-breaking clinical trials in the intervention space. You know, the first one is the Agent IDE trial. Now, this is a pivotal randomized trial that compared the safety and efficacy of a drug-coated balloon compared with a conventional balloon angioplasty in patients who had in-stent restenosis.

It was a pragmatic design, prospective trial with a superiority design across about 40 US trial sites, and they included about 480 patients. The key inclusion was, as I mentioned, in-stent restenosis with patients who had previously been treated with bare metal stents and were symptomatic or drug-eluting stents with lesions that were anywhere from two in a vessel that was two to four millimeters diameter, stenosis 50% to 100%, and symptomatic individuals. Exclusion was left main disease, acute ST elevation, MI, thrombus.

And patients were really randomized, two to one after successful predilatation of the target lesion with either drug-coated balloon versus conventional angioplasty. And the primary endpoint was target lesion failure at one year, which was a composite of target lesion revascularization and target vessel myocardial infarction or cardiac death. And they were followed up for in hospital six months, 30 days, six months, one year and then annually between two and five-year intervals.

Initially, they were supposed to have 600 patients and then the primary analysis was done on 480 patients because it was evidently powered for events and this was recommended by the DCP board. The mean age was 67. 26% were women diabetics about 50%, but interestingly, about 77% had multi-vessel disease and over 50% had stable coronary disease, but 48% had lesions that were ten to 20 millimeters in length,

which rules this was quite diffuse long vessel disease and multiple stent layers were seen in 43% of the cohorts.

So this technical success was very high, 90%. And target lesion failure at one year occurred in 17.9% of those who got the drug-coated balloon and in about 28.7% in those with the angioplasty alone. The absolute risk reduction was 10.7, and the NNT was about ten. So overall, this was a positive trial where the results were consistent across all subgroups, whether they were looking at age, sex, diabetes, layers of stent and so on. So really helped with having this device available in the United States.

But other trials have already looked at drug-coated balloons and really compared them against drug-eluting stents, not just plain angioplasty. And perhaps that's the limitation of the Agent trial, the other trial that's also very, very important in structural space, really. And it's the ALIGN-AR. And this is a lot of the times patients who have Aortic regurgitation get off-label devices, which are the current Timbre Valve platforms, but in the ALIGN-AR, they actually looked at the Trilogy Valve, which is designed specifically for aortic regurgitation and it's meant to align with the native cusps and has locators which clip onto the native leaflets and conform to the annulus, allowing better alignment and deployment in the setting of Aortic regurgitation.

It's a single-arm prospective investigation device exemption study, and they look to add both safety and efficacy of the Jenavalve through the system in patients with symptomatic severe aortic regurgitation and were high risk for surgical aortic valve replacement. They included of course patients who are symptomatic with at least grade three plus aortic regurgitation and the Heart team had to decide on referring these patients. Exclusion criteria were uni or bicuspid valves or an aortic root that was more than five centimeters and of course a previous prosthetic valve in the aortic position or concomitant coronary disease.

Now, the primary safety endpoint was composite of all-cause death of stroke, life-threatening major bleeding or vascular complications and acute kidney injury and then primary efficacy endpoint whose all-cause mortality at twelve months. Some of the key secondary endpoints included cardiovascular mortality disabilities, stroke,

hemodynamic, valve performance and LP remodelling, as well as quality of life and NYHA functional class.

So the comparator for primary safety endpoint was performance goal, which was derived from contemporary high-risk TAVR cohorts reporting BARC two composite endpoints and this was set at 40.5. So they overall involved 108 patients, 177 of them under one successful implantation. 50% were women and the mean age was 75 years. Two-thirds had an NYHA class of three and four with a mean SDS about 4.1. The mean ejection fraction was 53.8%. The majority 91% of the procedures were carried out under general anaesthesia and a large valve was implanted in 7% patients. The procedural success was 92.8 with no procedural death, annual rupture or coronary obstruction.

So those are the most concerning potential complications. Valve embolization did occur in four cases. One ascending aortic section occurred. The primary safety endpoint at 30 days was 26.7%, meeting the non-inferiority criteria for the primary endpoint with the prespecified performance goal at the primary efficacy endpoint at all-cause mortality occurred in 7.8% of the cohort of one year, again meeting the non inferiority criteria primary efficacy endpoint. Important to note that this is really a first iteration of the device and operators are still in the learning curve and so is the Heart team.

In terms of imaging. At size one for aortic regurgitation secondary endpoints like pacemaker, implantation were reduced in the trial. 30% in the first 60 patients and then 14% in the next 60 patients. And so it kind of shows you that the learning curve does change in terms of implantation depth and so on. Quality of life. There was also a significant improvement in the surveys that were taken.

Now, the next thing is looking at important trials that were done for low-risk TAVR and because these are low-risk patients, it's important to get longer-term outcomes. The preliminary data that had come out from PARTNER 3 was one-year outcomes, but now the five-year outcomes were reported. Just as a reminder, the PARTNER 3 was a multicenter randomized trial. Randomization was one-to-one comparing TAVR using an expandable platform of Sapien 3 against SAVR in patients who had severe symptomatic

aortic stenosis and were at low-risk IE. The STS score was less than 4% and they had suitable anatomy.

The primary endpoint was a non-hierarchical composite death for any cause stroke, rehospitalization and secondary endpoints, again a hierarchical composite of death for any cause, disabling stroke, non-disabling stroke and rehospitalization. So at five years, follow-up was reached in 94.6% of those undergoing TAVR and 88% of those undergoing SAVR, perhaps prompting us to understand why these patients are lost to follow-up. In the surgical arm, the primary endpoint showed similar rates of both groups 22.8 to TAVR at 7.2 in the surgical arm and the secondary primary endpoint using the WIN method showed a total score of 22.1 for TAVI and 19% for SAVR.

So the mortality of five years was 10.2% versus 9% in TAVI versus surgery. Numerically the study reported five years at five years 48 stents in the TAVI group versus 34 in the surgical group. So numerically higher. But there's no difference in pacemakers and other parameters like stroke and so on. And from an echocardiogram point of view, which was also reported at TCT and simultaneously published, we see that the aortic valve gradient at five years was 12.8 in TAVR and 11.7 in the SAVR group. There was really no difference in the primary endpoint about size and valve hemodynamics and deterioration. It was not really significant.

Nevertheless, it is important to consider the TAVI choice in these patients, particularly that the mean age is actually pretty young in population. I think it is important to interpret this trial in the context of the evolutional risk where they reported the four-year results with the self-expanding valve, again at TCT and they looked at 1414 patients. The mean age here was 74 and mean STS was two for TAVI and 1.9 for SAVR. 94% of the patients, again in the TAVI group were available for follow-up and 89% in the SAVR group. And here it indicated that there was a continuing trend towards lower combined rates of all cost, mortality and disabling stroke. TAVR compared with aortic valve replacement and an absolute difference between the groups rose from 1.8 in favor of TAVR at two years to 3.4 at four years, demonstrating a very sustained benefit of transcatheter intervention for severe aortic stenosis. And so we wonder if the Heart

team really should be adopting a less conservative strategy in favor of Tabby, particularly in young low-risk patients.

But I think we still need ten-year outcomes because as I mentioned, this cohort was young, 74 years of age. So it is important that all factors considered in terms of anatomy and the totality of evidence, probably we need to be a little more selective. And finally, I want to end with an interesting trial, the TRISCEND trial, which looked at tricuspid regurgitation. Now, unfortunately, even in 2023 we don't have good options for transcatheter for tricuspid valve regurgitation. The surgical repair and replacement is not very durable. The current catheter repair options in terms of clipping have also not been very impressive.

And so the TRISCEND II trial, we looked at 400 patients and the first 150 pages were randomized and reported in this trial, mean age was 79 years, nearly 80% of women. The mean STS score where they used the risk estimate for mitral valve surgery in the absence of tricut regurgitation was roughly 10%. And all patients actually had AFib at baseline and about 35% to 40% had a pacemaker or a defibrillator implanted, which is really important because that means you can still implant a transcatheter valve with preexisting leads across the tricuspid valve. More than 77% patients had undergone replacement had secondary tricuspid regurgitation.

So the Evoque optimal medical therapy arm 43.8% had severe TR at baseline, 21.9% had massive TR at Torrential was about 34% and in the optimal medical therapy alone year, massive and Torrential represented about 40%, 27% and 31% respectively. Procedural total success was actually reasonable. Again, given that this was the first iteration of the divides and implanters were in their early learning curve, there were a couple of embolizations in this cohort and perhaps an RP perforation as well. Some required surgical intervention at 30 days.

The primary composite safety endpoint occurred in 27.4% of the 95 patients treated with the Evoque valve and so a rate compared favorably with the historic safety data of tricuspid valve surgery. At 43.8%, severe bleeding was 10.5%, the need for permanent pacemaker was 14.7% and as I mentioned, there was one actually, I haven't mentioned

it yet. There was a single case of device-related pulmonary embolism and cardiovascular mortality was 3.2%. So at six months there was a significant reduction in the tricuspid regurgitation. 98% of the patient, 8% of the patients had a moderate or less tricuspid regurgitation, 78% had none to trace and with medical therapy it was just 1.6 had moderate or less and 50% continue to have massive or torrential regurgitation in terms of quality of life. So the NYHA and the Kansas City Cardiomyopathy Questionnaire and six-minute walk were superior with the transcatheter tricuspid valve replacement compared with the optimal medical therapy. So it is promising, perhaps this is the first iteration. We're hoping that implantation technique and device refinements will improve these numbers, particularly in terms of acute procedural success. So thank you for hanging on here and listening to these important trials and I hope it was beneficial for you."