VIEWPOINT

Indication Creep in Transcatheter Aortic Valve Implantation—Data or Desire?

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Transcatheter aortic valve implantation (TAVI) has revolutionized treatment of symptomatic severe aortic stenosis (AS). Noninferiority or superiority of TAVI compared with surgical aortic valve replacement (SAVR) in 2 randomized clinical trials (RCTs) in low-risk patients[1,2] led to US Food and Drug Administration approval of TAVI in August 2019 to include all surgical risk levels. Current guidelines no longer recommend using SAVR risk alone in deciding between TAVI vs SAVR and instead focus on expected patient longevity, physiologic risk of SAVR, anatomic risks of TAVI, and patient wishes. This change led to TAVI becoming more common than SAVR.[3] Data from the Vizient Database for 2015 to 2021 show that among 17 487 patients younger than 65 years, TAVI use increased 2.7-fold such that in 2021, 47.5% of cases were TAVI and 52.5% were SAVR.[4]

We should ask, however, if this indication creep for TAVI in younger, low-risk patients is based on the data or just the desire (of both patients and physicians) for TAVI. To answer this question, we must remember that RCT results apply only to the populations tested and examine how we apply these findings to other populations.

Exclusion Criteria in Trials Among Low-risk Patients

The PARTNER 3[1] and Evolut[2] trials had several protocol exclusions. Patients better served with a mechanical valve, those needing additional cardiac surgery (eg, concomitant mitral or tricuspid valve surgery, ascending aortic replacement), and those with considerable coronary disease (CAD), bicuspid aortic valve (BAV), or anatomy unsuitable for TAVI were excluded. Based on these exclusions, is widespread use of TAVI supported by these data? In contemporary SAVR studies,[5] almost one-half of patients met at least 1 of these exclusion criteria and their clinical outcomes were better than or similar to those predicted by surgical scores in all groups except those requiring concomitant valve surgery.

The American Heart Association and American College of Cardiology (AHA/ACC) guidelines recommend SAVR (class 1) in asymptomatic patients with severe AS for an ejection fraction less than 50% and in those undergoing other cardiac surgery. A class 2a recommendation applies to asymptomatic severe AS in low-risk patients with positive findings on exercise stress test, B-type natriuretic peptide level more than 3 times normal, progression of peak velocity greater than 0.3 m/s/y, or a peak velocity greater than 5 m/s. No indication for TAVI in asymptomatic patients currently exists, although trials are addressing this population.

The AHA/ACC guidelines recommend SAVR (class 1) for patients younger than 65 years or with expected survival of at least 20 years. What do the 2 RCTs[1,2] tell us about TAVI in this age group? In both RCTs, fewer than 8% of the treated patients were younger than 65 years. Performing TAVI in this population raises questions related to lifetime management, coronary access, valve durability, and feasibility of repeat TAVI vs TAVI explant and SAVR. The use of TAVI for those younger than 65 years with anatomy suitable for SAVR and expected survival for age remains a knowledge gap that has yet to be adequately studied.

Patients with BAV were excluded from both of the RCTs.[1,2] With expanded use of TAVI in younger patients, the proportion of those with BAV will increase. The knowledge gap in this area is being addressed by a prospective trial[6] as well as national registry studies of TAVI in patients with BAVs. Studies are beginning to delineate the BAV anatomies that are high risk for TAVI complications and are well treated by SAVR. Most reports for BAVs remain retrospective and are highly selective. An RCT is the best way to study the use of TAVI in younger, low-risk patients with BAVs, but support for such a trial will likely need to come from outside of industry, which may have little incentive to study this.

The PARTNER 3[1] and Evolut[2] trials excluded patients with a Syntax score greater than 32 and 22, respectively. The prevalence of substantial CAD was 27% and 15%, respectively, in these trials; however, rates of concomitant revascularization were low in both at 10%. The Evolut trial[2] had a separate arm for those requiring revascularization, who had a mean Syntax score of 7. The use of TAVI in patients with symptomatic AS and substantial CAD is another knowledge gap requiring further RCTs.

Patients with symptomatic AS and concomitant conditions, such as ascending aortic dilatation or considerable mitral or tricuspid valve dysfunction, were also excluded from RCTs comparing TAVI with SAVR. Thus data about treating these patients are lacking as well.

In both RCTs,[1,2] all patients were certified by the local expert heart team to meet the inclusion and exclusion criteria, as well as to have anatomy appropriate for either SAVR or the transcatheter heart valve used in that trial. Both trials also required final approval of candidates by a national screening committee. Although occasional disagreements occur, one would expect the latter to approve most patients recommended by the former. Yet in the PARTNER 3 trial,[1] 34% of the cases were rejected at the national level and in the Evolut trial,[2] 14% were excluded. This disparity between the local heart team's decision and that of the national committee suggests that these cases were highly selected and thus the results were likely not applicable to all low-risk cases.

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Questions Regarding Durability in Younger Patients

Finally, with regard to younger patients with a longer life expectancy, what do RCTs tell us about durability? The longest durability data are from the NOTION RCT,[7] which shows good durability of both SAVR and TAVI at 8 years. As the number of TAVI procedures increase in patients younger than 65 years, it should be noted that the mean age in NOTION was 79.1 years. In 2 RCTs[8,9] of patients with intermediate risk, the mean age exceeded 80 years. It has been established that for biological valves replaced surgically, the younger the patient, the faster the valve tends to fail. In the RCTs involving low-risk patients, mean patient ages were greater than 73 years. Longer-term durability data in patients younger than 65 years should be obtained for TAVI if its use is to continue in this age group. Recent data on structural valve durability from the supra-annular self-expanding devices in high- or intermediate-risk patients suggest substantially better moderate to severe structural valve durability for TAVI vs SAVR, but these are early data in older patients.[10] It will be important to extend these data to low-risk patients as follow-up continues.

Conclusions

Data on valve durability should be included in shared decision-making when considering the downstream implications of choosing TAVI or SAVR. The choice of TAVI must also take into account a higher pacemaker rate, more patient prosthesis mismatch for SAVR after failed TAVR, and increased mortality risk for TAVI explant followed by SAVR vs repeat SAVR alone. The choice of SAVR must take into account implanting a surgical valve of adequate size to avoid mismatch. The implications of these choices will be magnified in younger patients with longer expected survival.

We are advocates for TAVI in appropriate cases. We urge our colleagues to consider and hopefully fill existing knowledge gaps to allow the continued rational expansion of indications for TAVI based on data that can support desire.

ARTICLE INFORMATION

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