

EDITORIAL COMMENT

Elevating Aortic Stenosis Treatment?*



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The last decade has seen revolutionary changes in the treatment of aortic stenosis through the inception and widespread adoption of transcatheter aortic valve replacement (TAVR). With this technological innovation has rightly come new curiosity about a disease state that might have previously felt staid. In fact, PubMed indexed publications for *aortic valve stenosis* increased 263% over the last 5 years compared with a decade before (5,317 from 2001 to 2006, 13,963 from 2011 to 2016). Where smaller, often single-center data had previously helped define guidelines (1), there are now large national and multinational registries of aortic valve replacement (AVR) and a raft of randomized clinical trials of aortic stenosis treatment from which to learn. Thus, it is an epistemological irony that returning to data predating TAVR may provide some of the most valuable information on how to approach valve replacement specifically because the data describe a natural history that may be less commonly seen in a new era of accessibility.

SEE PAGE 145

In this issue of *JACC: Cardiovascular Interventions*, Taniguchi et al. (2) and the CURRENT AS registry investigators describe the outcomes of 3,794 patients with severe aortic stenosis diagnosed in multiple Japanese medical centers between 2003 and 2011. In this observational analysis, patients were first stratified by their baseline left ventricular ejection fraction (LVEF) described in quartiles as <50%, 50% to 59%, 60% to 69% or $\geq 70\%$ and subsequently by initial

treatment strategy—AVR or medical management. A total of 2,603 patients were conservatively managed initially and 1,191 underwent early valve replacement. The authors ultimately found that patients with baseline LVEFs <50% and from 50% to 59% both did significantly worse than did those patients whose baseline LVEF was $>60\%$ if they did not proceed promptly to valve replacement, irrespective of symptom status. On the contrary, no statistically significant risk heterogeneity was seen per LVEF strata among patients who underwent an initial AVR strategy.

Current American guidelines recommend AVR for patients who have severe, high-gradient aortic stenosis and either symptoms attributable to aortic stenosis or LV dysfunction, defined as an LVEF <50% (3). Taniguchi et al. draw specific attention to their population of patients with a baseline LVEF of 50% to 59%, who, by current guidelines, are considered to have “normal” LV function but appear to have a 77% increased adjusted hazard for valve-related death or heart failure admission relative to patients with an LVEF of $\geq 70\%$ when managed conservatively. The implication being that perhaps the floor for “normal” LVEF in the setting of aortic stenosis has been set too low.

What makes these data from the CURRENT AS registry so unique—in fact almost curious—is how few patients underwent prompt surgical AVR. A total of 1,090 patients (29% of the registry population) had symptomatic, severe aortic stenosis at the time of enrollment (a Class I indication for valve replacement) but were conservatively managed originally, and ultimately only 46% of the total registry population ever received AVR over a median of ~ 3.5 years of follow-up. Thus, it is reasonable to wonder if significant unmeasured risks within the population deterred their surgeons from operating and ultimately limit the broad applicability of these data. The period of enrollment predated the routine use of frailty measures, and roughly 60% of the population did

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have a body mass index $<22 \text{ kg/m}^2$, which may be associated with frailty. However, this could also simply reflect the regional population. In any event, the potential value of not adhering strictly to current guidelines within this registry is the opportunity to demonstrate how well those same guidelines circumscribe the population most in jeopardy when managed conservatively.

The subsequent analyses regarding the definition of “normal” LVEF in an aortic stenosis population have far-reaching implications, but perhaps they may miss the broader question: Has the dominant paradigm for AVR—hemodynamically severe aortic valve stenosis plus attributable symptoms or left ventricular dysfunction—forever been a compromise born of (now) dated intraprocedural risks and a desire to limit repeat sternotomies for failing bioprostheses? The cost of such a bargain has been low, but meaningful, rates of adverse outcomes in the surveillance period. In the face of down trending procedural risks and increased opportunities to avoid some (if not most) difficult redo sternotomies, perhaps our tolerance for adverse events during the asymptomatic period of severe aortic stenosis should be reconsidered.

In a previous publication using this same CURRENT AS study population, conservatively managed asymptomatic patients demonstrated a 26.4% 5-year incidence of all-cause death compared with 15.4% for those who underwent valve replacement (4). A meta-analysis of severe asymptomatic aortic stenosis incorporating these data and others demonstrated a 71% unadjusted risk reduction in all-cause mortality among patients proceeding to early AVR (5). Aside from death, adverse LV remodeling and arrhythmias such as atrial fibrillation, features that appear to increase with worsening aortic stenosis, may significantly impact long-term quality

of life even after correction of the valve hemodynamics (5).

In light of these provocative observational data and radical secular changes in the treatment aortic stenosis over the last decade, the space is ripe for more definitive data. The investigator-sponsored, ongoing, EARLY TAVR (Evaluation of Transcatheter Aortic Valve Replacement Compared to Surveillance for Patients With Asymptomatic Severe Aortic Stenosis) trial (NCT03042104), which randomizes asymptomatic patients with severe aortic stenosis, an LVEF $>50\%$, and a negative exercise stress test to early TAVR or careful surveillance, should fill this gap and shed further light on whether we need to rethink delaying therapy for patients with hemodynamically severe aortic stenosis.

Keep in mind, this will not be the first time that technology has altered decision making and how we value aspects of a given choice. In the late 1800s the uppermost apartments in multifloor buildings were invariably domiciles for low-income workers or house servants. The value calculus of a room with a view was always weighed against the stairs one had to climb to get there. It was the elevator that turned top-floor apartments into penthouses and redefined their value. Whether our view toward earlier treatment of aortic stenosis changes commensurate with recent innovations and broader treatment options will need to be elevated through the ranks, but I would expect the point to be raised with increasing frequency in the years to come. Even the best bargain deserves reconsideration occasionally.

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