

Quantifying the Costs of Transcatheter Aortic Valve Replacement Hesitancy

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Aortic stenosis (AS) is one of the most common valvular heart diseases. It affects 5% of the adult population ≥ 65 years of age.¹ Current guidelines recommend surgical or transcatheter aortic valve replacement (AVR) for patients with severe and symptomatic AS.² Because there is no medical therapy that can halt disease progression or effectively treat symptoms, prognosis is dismal without AVR, with 1-year mortality of 25% to 50% in symptomatic patients with severe AS.³

The goal of informed consent is to provide patients and families with estimates of the risks and benefits of the procedure and to discuss alternative treatments, whether medical or procedural based, whenever available. In general, when the perceived benefits of the procedure exceed the potential risks, most patients decide to consent to the performance of the procedure. Given the safety of modern surgery and dismal prognosis of medical therapy, pursuit of transcatheter AVR (TAVR) is usually a straightforward proposition. Confronted with a 25% to 50% risk of dying without TAVR, most patients with symptomatic severe AS prefer to take the $<5\%$ risk of mortality associated with the procedure. Understanding the pros and cons of valve replacement is a hallmark of an effective shared decision-making process.

Variables associated with and outcome of initial TAVR refusal have not been previously studied in a systematic manner using a large national database, in part because most registries were designed to capture procedural outcomes, not refusals.

The study by Yamamoto et al in this issue of the *Journal of the American Heart Association (JAHA)* sheds light into this

subject by evaluating factors associated with and prognosis of initial refusal to a TAVR procedure in patients with symptomatic AS.⁴ How often do patients refuse TAVR? What are the reasons for TAVR refusal and why do patients change their mind? Finally, what are the outcomes of those patients who, having refused TAVR, change their mind and undergo the procedure at a later time?

Using a large ($n=1542$) Japanese TAVR registry (Optimized Catheter Valvular Intervention Transcatheter Aortic Valve Implantation), the authors make several interesting observations. First, TAVR refusal is uncommon (1.8%). Second, most patients who refuse a TAVR procedure do so out of fear (47%) or perception of clinical stability, despite a majority reporting class II or III New York Heart Association functional class symptoms. Third, 75% of patients who initially refused TAVR changed their mind after a heart failure exacerbation. Fourth, the median time from refusal to acceptance was 5 months. Finally, the short- and long-term outcomes of patients who initially refused TAVR were significantly worse than those of patients who initially accepted the procedure (30-day mortality, 7% versus 1.3%; 1-year mortality, 28% versus 10%).

The study has important limitations inherent to observational registries. First, the sample size of the refusal group is small ($n=28$), which tends to generate imprecise estimates of harm. Second, patients who initially refused TAVR were sicker than patients who accepted the procedure, because they were older (87 versus 84 years of age), were more likely to have a high-risk Society of Thoracic Surgeons score (67% versus 32%), and presented with comorbid conditions, such as clinical frailty, mitral regurgitation, and peripheral arterial disease at a much higher rate. The refusal group was also more likely to undergo nontransfemoral TAVR (32% versus 20%), which carries a higher risk of complications and prolonged length of stay.⁵ Are the poor outcomes of the refusal group attributable to treatment delay, comorbid conditions, or a combination of both? The authors attempted to adjust with statistical analysis, and TAVR refusal was independently associated with increased long-term mortality, with a hazard ratio of 3.37 (95% confidence interval, 1.52–7.48; $P=0.003$). It is well accepted that such adjustments are helpful but can never fully account for selection bias in retrospective analyses.

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Another limitation of observational registries is potential for immortal bias. Immortal time refers to the time period from the start of follow-up (in this case, the date of TAVR refusal) to the date of intervention (in this case, the date of TAVR performance) when the subject is not at risk of death by virtue of having lived to undergo the intervention.⁶ The overall effect of immortal bias is a false improvement in favor of the interventional group. Given our knowledge on the natural history of symptomatic AS, and the dismal prognosis without AVR, the effect of this type of bias is probably minimal.

Overall, the study reinforces the importance of prompt valve replacement after symptom onset in patients with severe and symptomatic AS. To put the study findings in perspective, TAVR came about because up to 40% of patients with severe AS who needed surgical AVR never underwent the procedure because of perceived or real risks associated with surgery.^{7,8} Assuming that patients with severe and symptomatic AS are in regular contact with the medical system and offered timely AVR, it is refreshing to see that the number of patients who currently refuse this minimally invasive procedure is in single digits. For this small minority, the current study suggests there is a price to pay for delaying TAVR. Increasing our efforts to educate patients and providers on the importance of timely AVR should remain a priority. Hesitancy is not without risks.

Disclosures

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consultant for Medtronic and Lake Regions Medical. Gössl has no conflicts to disclose.

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