Symptomatic Low-Gradient Severe Aortic Stenosis
With Preserved Left Ventricular Ejection Fraction
Now Less of a Clinical Conundrum
Susan E. Wiegers, MD

Accurate assessment of aortic stenosis (AS) severity is one of the more technically demanding studies in echocardiography. This is reflected in the Intersocietal Accreditation Commission for Echocardiography standards that specify that AS gradients must be measured from at least 3 different transducer positions and with a nonimaging, dedicated, continuous-wave Doppler transducer (Pedoff). The standards do not specify the measurement of any other valvular lesion. Submission and review of AS cases is required for laboratory accreditation by that body. Given the complexity in echocardiographic assessment, the determination that a patient has severe AS (defined as a valve area \( \leq 1 \) cm\(^2\)) but a mean gradient \(<40\) mm Hg despite a preserved left ventricular (LV) ejection fraction (LVEF) is often met with skepticism by our interventional colleagues. Low-gradient severe AS resulting from decreased LV systolic function can be assessed by dobutamine protocols intended to increase the flow across the valve and to distinguish true AS from pseudo-AS.\(^1\) Such is usually not the case in patients with preserved LVEF.

![Image](http://circ.ahajournals.org/)

The study group included both patients with low stroke volume indexes (SVIs; \(<35\) mL/m\(^2\)) and those with normal SVIs. In the entire group, there were 125 patients with normal SVI and 135 with low SVI. The low-SVI patients had slightly

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lower LVEF although still in the normal range, lower mid-wall fractional shortening (a measure of myocardial function), and smaller aortic valve areas, along with higher LV afterload. Surgical patients had a higher stroke volume on average, and there were more low-SVI patients in the medically treated group. After the PS analysis, it was shown that both low-flow and normal-flow patients treated medically had a 2-fold greater all-cause mortality compared with the AVR group. This is a very important finding. Although other studies have generally found a mortality benefit in AVR in patients with LGSAS with preserved LVEF, none accounted as carefully for the significant differences in baseline characteristic between the 2 groups. It is well known that medical therapy for symptomatic severe AS carries a terrible prognosis. The group of patients with LGSAS with preserved LVEF may have an even worse prognosis because the low gradient in general appears to reflect subclinical myocardial dysfunction. It is gratifying that this group can be offered AVR with an expectation of improvement in mortality. In this study, there was no difference in mortality for the medically treated patients with low or normal SVI. The recently released European guidelines rate AVR in the LGSAS group as a Class IIa indication (Level of Evidence, C). They caution that the diagnosis of severe AS should be carefully confirmed. Each laboratory is of course responsible for the quality of its assessments. Although catheterization is considered a Class III indication (should not be performed) for the assessment of AVA in patients with severe AS by echocardiography, this group of patients represents an exception to that rule.

PSs have been increasingly used to analyze observational data in an attempt to approximate a randomized trial. In the study by Ozkan et al, the differences between the surgical and medically treated groups were substantial. The surgical group was demonstrably healthier with fewer instances of diabetes mellitus, better renal function, fewer instances of hypotension, and less diuretic use. Because the healthier group of patients underwent surgery, on the face of it, it is not surprising that AVR was associated with lower mortality. Although there are several methods for PS, in a relatively small group with marked differences in characteristics, the usual way to determine the PS is to perform a logistic regression with treatment, in this case AVR, as the dependent variable. Because many of the clinical factors influence both treatment assignment and outcome, these clinical factors are all included in the logistic regression. The PS is then the likelihood of treatment assignment conditional on the baseline characteristics. The PS is entered into Cox multivariate models along with other clinical variables to estimate the treatment effect. As with all logistic regressions, there must be no unmeasured confounders, or the results will not be accurate. The authors rightly note that such unmeasured characteristics as frailty, severe chronic obstructive pulmonary disease, or dementia may have played a role in treatment selection and outcome.

How reliable is the method in general? In a recent analysis by Dahabreh et al, the results of observational studies using PS and randomized, clinical trials were compared in the studies of treatments in patients with acute coronary syndromes. They found that the estimates of treatment effect on mortality were consistent between randomized, clinical trials and PS studies. In only 2 of the 17 separate comparisons was there a statistically significant difference in treatment effect. However, the PS studies systematically overestimated the magnitude of the treatment effect found in the randomized, clinical trial of the same therapy. Thus, it must be cautioned that the finding that AVR substantially reduces mortality in the present article may be an overestimate of the true benefit.

In conclusion, this article is an important contribution to our growing understanding of the group of patients with severe AS and low transvalvular gradients despite preserved LVEF. It goes without saying that a randomized, controlled trial in this group of largely elderly patients with multiple comorbidities is unlikely to be conducted, particularly when medical therapy has been shown to have so dismal an outcome. Ozkan et al expand our understanding of the entity of LGSAS and make a powerful case for surgical intervention for symptomatic patients.

Disclosures

None.

References


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