

EDITORIAL COMMENT

Should We Reappraise Surgical Indications in Asymptomatic Severe High-Gradient Aortic Stenosis?*



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The optimal timing of aortic valve replacement in patients with severe aortic stenosis is not widely agreed upon. On the basis of retrospective autopsy data, it is generally believed that the prognosis of patients with no or minimal symptoms is relatively benign and that surgery can be safely delayed until symptoms develop (1). Accordingly, both the American Heart Association (AHA) and American College of Cardiology (ACC) and the European Society of Cardiology (ESC) guidelines consider symptomatic severe aortic stenosis as a class 1 indication for valve replacement but remain quite hesitant as to the optimal strategy to be adopted in asymptomatic patients (2,3).

Over the past decade, many investigators have tried, almost desperately, to substantiate the “wait for symptoms” strategy promoted by the guidelines. What have we learned from these studies? First, asymptomatic severe aortic stenosis is not a benign but a deadly disease. In a large natural history study involving 622 consecutive asymptomatic patients with severe aortic stenosis followed up at the Mayo Clinic, Pellikka et al. (4) reported a 5-year survival probability of <60%. In a similar study involving 239 initially asymptomatic patients with severe aortic stenosis, Pai et al. (5) reported an even lower 3-year overall survival rate of 38%. Importantly, when reported, the primary cause of death in these initially asymptomatic patients was not sudden cardiac death, as feared by most cardiologists, but rather acute heart failure. In a study by

Brown et al. (6), patients developing severe symptoms indeed entailed very high early mortality (40% at 2 months) if not promptly operated on. We also learned from these studies that the likelihood for an initially asymptomatic patient to remain asymptomatic is quite low and that most patients will develop symptoms and require surgery within the first 3 years after diagnosis. Finally, the few meta-analyses and propensity score-matched studies performed so far all concur in showing that performance of early aortic surgery compared with initial medical management is associated with greater long-term survival and a lower risk for heart failure (7,8).

SEE PAGE 43

In this context, the study of Zilberszac et al. (9) in this issue of *iJACC* provides additional support in favor of an earlier surgical strategy. The investigators investigated the 4-year outcomes of 103 older patients (mean age 77.3 ± 4.8 years) with asymptomatic severe aortic stenosis ($V_{max} \geq 4$ m/s) and preserved left ventricular ejection fractions. They observed that in this older population, the risk for either dying or developing an operative trigger, most often symptoms, was as high as 27% at 1 year, 57% at 2 years, 77% at 3 years, and 84% at 4 years. They also made 2 salient observations that could potentially change our practice. The first is that, despite being closely followed in a “heart valve clinic” program with clinical and echocardiographic follow-up examinations every 6 months, as many as 9 patients (8.7%) died before developing operative triggers. Second, they made the important observation that 43% of the patients developing symptoms had severe symptom onset (New York Heart Association functional classes III and IV) and that this mode of symptomatic presentation negatively affected their early and late post-operative outcomes, 4-year post-operative survival being only 46% in those who

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abruptly developed severe symptoms compared with 88% in those who developed mild symptoms before surgery. These findings are in line with those previously reported by our group (10). In a recent study, we indeed observed that about one-fifth of the patients operated on for New York Heart Association functional class III or IV symptoms were in class I 1 month before surgery, and this rapid clinical deterioration was associated with an increased operative mortality (17% vs. 3%; $p = 0.035$) and poorer long-term post-operative survival (69% vs. 90% at 4 years). All together, these results suggest that asymptomatic patients with severe aortic stenosis are being operated on too late and should probably be offered surgery before the onset of severe symptoms (i.e., at an asymptomatic or minimally symptomatic stage).

This raises the question of whether surgery should be offered to all asymptomatic patients with severe high-gradient aortic stenosis or if factors associated with worse post-operative outcomes can be identified. Currently, the AHA and ACC and the ESC guidelines consider the possibility of an earlier surgical approach only in patients who develop symptoms during exercise testing (Class 2A indication in the AHA and ACC guidelines, Class 1 indication in the ESC guidelines) or in those with either rapidly progressing aortic stenosis or very high transaortic flow velocities (Class 2A indication in both sets of guidelines). Whereas in the ESC guidelines, the threshold to define very high transaortic flow velocities has been set at 5.5 m/s, the AHA and ACC guidelines have chosen a lower threshold of 5 m/s. The results of the study of Zilberszac et al. (9) substantiate this lower threshold, as roughly 50% of the patients meeting this criterion developed symptoms within 1 year after diagnosis. In view of the guarded prognosis of those with initial transaortic flow velocities between 4 and 5 m/s, one may wonder whether an even lower threshold should not be considered in the future. Finally, the results of Zilberszac et al. (9) question the usefulness of exercise testing to risk-stratify asymptomatic patients with severe aortic stenosis, because about one-third of their older population was found to be unable to exercise.

Although the data of Zilberszac et al. (9) plead for an earlier surgical approach, particularly in patients whose transaortic flow velocities are in excess of 5 m/s, for such a strategy to be a reasonable option for asymptomatic patients, extremely low operative risks are essential. In the study of Zilberszac et al. (9), patients were operated on at a time when symptoms had developed, and their operative mortality was 7%. Although acceptable for older symptomatic patients, such operative mortality would probably be unacceptable if elective surgery had to be proposed before symptom onset, particularly in younger patients. Fortunately, large registries and databases indicate that in asymptomatic patients, operative mortality is quite low. In a recent work, we observed that operative mortality was as low as 1.4% among asymptomatic patients undergoing isolated elective aortic valve replacement in the presence of a normal left ventricular ejection fraction and normal pulmonary artery pressures (10). Operative mortality was even lower in the subgroup of patients who were operated on before the age of 75 years.

In conclusion, we believe that the time has come to reappraise the criteria used to indicate surgery in asymptomatic patients with severe aortic stenosis. Although exercise testing has been proposed to risk-stratify them, in daily clinical practice, it has a rather limited value in patients older than 70 years, as they frequently present with physical impairment, limiting their ability to exercise. One should therefore use alternative criteria to identify patients at high risk for symptomatic deterioration. In this regard, peak transaortic flow velocities appear to be among the strongest predictor of outcomes. In patients with low operative risk and a peak transaortic flow velocity >5 m/s, we believe it appropriate to propose elective surgery, in order to avoid mortality before the onset of symptoms and to improve post-operative outcomes.

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