EDITORIAL

The conundrum of watchful waiting versus pre-emptive surgery in asymptomatic aortic stenosis: are we any closer to an answer?

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Aortic stenosis (AS) is the most common valvular disease in Western countries. Its prevalence is expected to increase with population aging.[1] The most common etiology of AS in developed countries is calcific degeneration.[1] Severe AS poses a significant pressure load on the left ventricle and, once symptomatic, patients face a grim prognosis with a median survival of approximately 2 years, without an aortic valve replacement (AVR).[2] The current American College of Cardiology, American Heart Association, and European Society of Cardiology (ESC) guidelines recommend a class I indication for AVR in patients with severe AS with either symptoms or reduced ejection fraction.[3,4] However, the management of patients with asymptomatic severe AS with preserved ejection fraction remains controversial.[5] Earlier studies have proposed mortality rate in this population of 1% per year. However, recent observational and retrospective studies have reported a higher death rate.[6] In a recent registry by Tanigushi et al,[7] conservative management had a dismal prognosis in this population, with a cumulative 5-year incidence of heart failure hospitalization and all-cause mortality equal 26.4%. A major problem in this entity is to decide with certainty whether a patient is truly asymptomatic or not, as many patients downgrade their physical activity to avoid symptoms (pseudoasymptomatic). Exercise testing offers an excellent tool to delineate symptomatic status. Stress testing in patients with asymptomatic severe AS has a class IIA grade as a recommendation in the latest guidelines.[3,4]

In the current issue of the *Polish Archives of Internal Medicine* (*Pol Arch Med Wewn*), Dobrowolski et al[8] present their work regarding the utility of exercise N-terminal pro-B-type natriuretic peptide (NT-proBNP) in asymptomatic patients with severe AS. They compared a group of 50 patients with severe asymptomatic AS to a group of 20 healthy subjects. NT-proBNP levels at rest showed a significant correlation with a degree of left ventricular (LV) hypertrophy (LVH), as measured by LV mass index, as well as with severity of AS, as measured by aortic valve area and mean aortic pressure gradient. Exercise NT-proBNP levels showed a similar correlation with LV mass index and severity of AS. A degree of change from resting levels to exercise levels (ΔNT-proBNP) did not show a significant correlation with severity of AS or LVH. However, limitations of this study include a small number of patients (n = 50), and a heterogeneous sample including 62% of patients with a bicuspid aortic valve, which might explain the relatively young age of the AS group (mean, 38.4 years).

Indeed, a previous report suggested the use of different thresholds, based on age and sex.[9] A recent study[10] utilized brain natriuretic peptide (BNP) ratios generated on the basis of these thresholds. It demonstrated incremental prognostic utility of BNP in the setting of significant AS. Surprisingly, LVH was found only in 72% of the AS group, which raises questions about the severity and duration of AS in these patients. Another limitation is the lack of meaningful clinical data or endpoints, and lack of any follow-up. Nonetheless, this study confirms the fact that circulating biomarkers, such as BNP, offer a diagnostic tool in valvular heart disease, including AS. In a study by Goodman et al,[11] BNP added an incremental prognostic utility to known predictors of mortality, such as the Society of Thoracic Cardiovascular Surgeons score.[11]

Interestingly, in the study by Dobrowolski et al,[8] resting levels of NT-proBNP did not correlate with LV ejection fraction (LVEF) or indexed stroke volume, again confirming the already known fact that LVEF is a suboptimal parameter of true LV systolic function and usually is not affected until late in the course of the disease. In a study by Kafa et al,[12] patients with severe AS

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and normal LVEF before, who underwent AVR, showed significantly impaired LV global longitudinal strain (LV-GLS) preoperatively, indicating a subclinical myocardial damage and fibrosis despite having preserved LVEF. Furthermore, in intermediate-term follow-up postoperatively, patients showed adequate regression and recovery in LVH and LV remodeling but still had suboptimal recovery of LV-GLS. Indeed, previous reports have demonstrated incremental prognostic utility of LV-GLS in patients with severe AS and preserved LVEF.[13]

Exercise NT-proBNP levels in the study by Dobrowolski et al[8] did not add any benefit on top of resting levels. Nonetheless, exercise testing is still a very powerful tool in the management of asymptomatic patients with severe AS beyond symptomatic status assessment. In a recent study by Masri et al,[14] novel exercise testing parameters such as percentage of age-sex predicted metabolic equivalents and heart rate recovery predicted long-term mortality. Finally, it seems that more powerful tools, such as strain imaging, is needed to further risk stratify patients with asymptomatic valvular disease. The current controversy about the management of asymptomatic severe AS and whether to decide on early aortic valve replacement or on watchful waiting will be resolved soon, with the current AVATAR trial—the first ever randomized controlled trial randomizing patients with asymptomatic severe AS to both approaches.[15]

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