Repeat physical stress echocardiography in asymptomatic severe aortic stenosis

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In severe aortic stenosis (SAS), the presence of symptoms is associated with ominous prognosis with 5-year mortality of 15–50% [1], and is a well-established indication for valve replacement [2]. On the other hand, in asymptomatic SAS, case management requires clinical skills, and the timing of valve replacement is unclear. Holistic assessment of the clinical situation (including co-morbidities and frailty), risk stratification, and complementary tests are critical for managing asymptomatic SAS and determining optimal valve replacement timing.

In clinical practice, at the time of SAS diagnosis, approximately 50% of patients report being asymptomatic in their day-to-day life [1]. However, this may be due to an unconscious adaptive process causing them to limit the intensity of their physical activity. Thus, it can be difficult to determine whether a patient truly lacks symptoms, especially in elderly patients. Stress testing is useful for exposing symptoms, and is a safe technique for use in stable patients [3]; clinical practice guidelines recommend the use of stress testing when assessing asymptomatic SAS patients [2]. Valve replacement is indicated in patients who exhibit clinical signs during stress testing, or lower blood pressure during physical activity. However, it remains unclear whether it is of value to repeat a stress test to uncover symptoms in asymptomatic SAS.

The incidence of a positive stress test in SAS ranges from 15% to 65% [3]. Despite this variability, stress testing exhibits good negative predictive value for cardiovascular events [4]. Performing echocardiographic assessment before and after the stress test (physical stress echocardiography [PE]) provides additional physiological parameters that can help establish the cause of symptoms [5].

From June 2014 to August 2019, the value of PE and repeat PE during follow-up in 85 asymptomatic SAS patients who were prospectively enrolled in a specialized valve clinic (Table 1) was investigated. Baseline PE was the key indicator for aortic valve replacement in 23 (27%) patients: 8 (9.4%) had dyspnea, 2 (2.4%) angina, and 16 (18.8%) abnormal blood pressure response. Furthermore, 17 (20%) exhibited electric changes suggestive of ischemia, PE revealed a median gradient increase of > 20 mmHg during stress in 31 (36.9%) patients, ventricular dysfunction in 2 (2.4%) patients, and segmental disorders in 8 (9.5%) patients. Of the alterations observed during PE, those which were the reason to indicate valve replacement were only symptoms and abnormal blood pressure response. The rest of the information obtained helped to make the decision but it was not the main reason.

A second PE was performed in 27 patients (median time 16 months after the first PE), and a third PE was completed in 5 patients (median time 16 months after the second PE). The second PE was the key indication for aortic valve replacement in 9 (33.3%) patients; it was clinically positive by symptoms in 6 (22.2%) patients: 3 (12%) patients had dyspnea, and 4 (14.8%) angina and abnormal blood pressure response was found in 4 (14.8%) patients. Electric changes occurred in 9 (33.3%) patients, and a median gradient increase of > 20 mmHg...
in 15 (55.5%) patients. Finally the third PE was the key indicator for aortic valve replacement in 2 (40%) patients, because it was clinically positive by symptoms.

Present findings indicated that repeating PE during follow-up was useful for asymptomatic SAS management. Indeed, the key indication for valve replacement increased from 27% of cases at baseline PE to 33% in the second PE, and 40% in the third PE. This pilot study in patients with asymptomatic SAS demonstrated that PE at both the first visit and during follow-up was useful in indicating valve replacement. Further studies in larger cohorts are needed to confirm these findings, and to establish the optimal time-frames for serial PE in such patients.

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References

Table 1. Data of asymptomatic severe aortic stenosis patients undergoing physical stress echocardiography.

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>Women 32 (37.6)</th>
<th>Age [years] 74.1 ± 9.4</th>
<th>Smokers 9 (10.6)</th>
<th>High blood pressure 70 (82.3)</th>
<th>Diabetes mellitus 30 (35.3)</th>
<th>Dyslipidemia 65 (76.4)</th>
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</thead>
<tbody>
<tr>
<td>Echocardiographic data</td>
<td>Bicuspid aortic valve 22 (25.9)</td>
<td>Peak aortic velocity [m/s] 4.3 ± 0.3</td>
<td>Maximum aortic gradient [mmHg] 74.5 ± 11.1</td>
<td>Mean aortic gradient [mmHg] 47 ± 8</td>
<td>Aortic valve area [cm²] 0.77 ± 0.12</td>
<td>LVEF [%] 67.9 ± 0.12</td>
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<td>Blood count NT-proBNP [ng/L] 294.0 (148–661)</td>
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Data presented as number (%), mean ± standard deviation, or median and percentiles of 25–75 (Q1–Q3). LVEF — left ventricular ejection fraction; NT-proBNP — N-terminal pro-B-type natriuretic peptide