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iCONCEPTS

CONCEPTS ON THE VERGE OF TRANSLATION

Stress Echocardiography to Assess Stenosis Severity and Predict Outcome in Patients With Paradoxical Low-Flow, Low-Gradient Aortic Stenosis and Preserved LVEF

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The objective of this study was to examine the value of stress-echocardiography in patients with paradoxical low-flow, low-gradient (PLFLG) aortic stenosis (AS). The projected aortic valve area (AVA_{Proj}) at a normal flow rate was calculated in 55 patients with PLFLG AS. In the subset of patients (n = 13) who underwent an aortic valve replacement within 3 months after stress echocardiography, AVA_{Proj} correlated better with the valve weight compared to traditional resting and stress echocardiographic parameters of AS severity (AVA_{Proj}: r = −0.78 vs. other parameters: r = 0.46 to 0.56). In the whole group (N = 55), 18 (33%) patients had an AVA_{Proj} >1.0 cm^2, being consistent with the presence of pseudo severe AS. The AVA_{Proj} was also superior to traditional parameters of stenosis severity for predicting outcomes (hazard ratio: 1.32/0.1 cm^2 decrease in AVA_{Proj}). In patients with PLFLG AS, the measurement of AVA_{proj} derived from stress echocardiography is helpful to determine the actual severity of the stenosis and predict risk of adverse events. (J Am Coll Cardiol Img 2013;6:175–83) © 2013 by the American College of Cardiology Foundation

We previously reported that a significant proportion of patients with severe aortic stenosis (AS) on the basis of aortic valve area (i.e., AVA <1.0 cm^2 and indexed AVA <0.6 cm^2/m^2) may have a restrictive physiology resulting in lower left ventricular (LV) outflow (i.e., stroke volume index <35 ml/m^2) and lower than expected transvalvular gradients (i.e., <40 mm Hg)

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despite the presence of a preserved LV ejection fraction (i.e., LVEF ≥50%), and this clinical entity was labeled "paradoxical low-flow, low-gradient (PLFLG) AS" (1,2). Given that transvalvular flow rate is reduced in these patients, it cannot be excluded that, as in low LVEF, low-flow, low-gradient AS, some patients may have a pseudo severe AS due to incomplete opening of a moderately stenotic valve.

The distinction between true severe (TS) versus pseudo severe (PS) AS is essential because patients with TS AS and symptoms will generally benefit from aortic valve replacement (AVR), whereas patients with PS AS may not benefit from surgical intervention and may rather need intensive medical therapy and close follow-up. As recommended in the 2012 European Society of Cardiology/European Association for Cardiothoracic Surgery guidelines, AVR should be considered in symptomatic patients with PLFLG after careful confirmation of stenosis severity (Class IIa indication) (3). We previously reported that a new index of AS severity derived from dobutamine stress echocardiography (DSE), the projected aortic valve area (AVA_{proj}) at a normal transvalvular flow rate, is superior to traditional Doppler echocardiographic parameters (rest or peak stress gradient and AVA) to differentiate TS from PS AS and predict outcome in patients with low LVEF, low-flow, low-gradient AS (4). However, there are no published data about the utility of stress (dobutamine or exercise) echocardiography in patients with PLFLG AS. The objective of this study was to examine the diagnostic and prognostic value of stress echocardiography in patients with PLFLG AS.

ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

AVA = aortic valve area

AVA_{Proj} = projected aortic valve area

AVR = aortic valve replacement

CI = confidence interval

DSE = dobutamine stress echocardiography

HR = hazard ratio

LV = left ventricular

LVEF = left ventricular ejection fraction

PLFLG = paradoxical low flow low gradient

PS = pseudo severe

TS = true severe

Methods

Doppler echocardiographic and clinical data were prospectively collected in 55 patients with PLFLG AS defined as an AVA ≤1 cm^2, an indexed AVA ≤0.6 cm^2/m^2, a mean gradient ≤40 mm Hg, a preserved LVEF (>50%), and stroke volume indexed to body surface area ≤35 ml/m^2. These patients were recruited in the context of 2 prospective observational studies, TOPAS (True Or Pseudo-Severe Aortic Stenosis) and EXERSA (Exercise Stress Echocardiography in Aortic Stenosis) (4,5). Exclusion criteria for these studies were as follows: 1) moderate/severe aortic or mitral regurgitation or mitral stenosis; 2) atrial fibrillation or flutter; 3) paced rhythm; 4) unstable angina; 5) acute pulmonary edema; 6) end-stage renal disease; 7) pregnant or lactating women; and 8) unwillingness to provide informed consent.

All patients underwent stress echocardiography. Exercise stress echocardiography was performed in 37 patients with no or equivocal symptoms whereas DSE was performed in 18 patients who were symptomatic. The dobutamine infusion protocol consisted of 8-min increments of 2.5 or 5 μg/kg/min, starting at 2.5 μg/kg/min up to a maximum dosage of 20 μg/kg/min (4). The exercise test was a symptom-limited graded maximum bicycle exercise test, performed in the semisupine position on an ergometer table tilted to 20°, with an initial workload of 20 W to 25 W maintained for 3 min and subsequent increase in workload of 20 W to 25 W every 3 min (5). Doppler echocardiographic data were obtained at rest and at peak exercise/dobutamine stress.

The Doppler echocardiographic measurements included LV dimensions, LVEF determined by the modified biplane Simpson's method, stroke volume in the LV outflow tract, mean transvalvular flow rate (Q) by dividing stroke volume by LV ejection time, transvalvular gradients by the simplified Bernoulli equation, and AVA by the continuity equation. The LV outflow tract diameter was assumed to have remained constant during the stress test protocol. For each measurement, at least 3 cardiac cycles were averaged. The projected AVA (AVA_{proj}) was calculated, a posteriori, in each patient by the following equation, as previously described and validated (4):

$$AVA_{proj} = \frac{AVA_{peak} - AVA_{rest}}{Q_{peak} - Q_{rest}} \times (250 - Q_{rest}) + AVA_{rest}$$

where AVA_{rest} and Q_{rest} are AVA and Q at rest, and AVA_{peak} and Q_{peak} are AVA and Q measured at peak stress echocardiography. The treating cardiologists and cardiac surgeons were thus unaware of the results of $AVA_{Proj.}$

The endpoints for this study were as follows. 1) The severity of stenosis at the time of AVR as documented by macroscopic assessment of the explanted valve by the surgeon and pathologist with the use of standardized method and criteria (4); the weight of explanted valve was also measured with the use of a laboratory scale in a subset of patients. 2) The time to occurrence of the composite endpoint of death or need for AVR motivated by the development of severe AS with symptoms or LV systolic dysfunction.