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Resting Aortic Valve Area at Normal Transaortic Flow Rate Reflects True Valve Area in Suspected Low-Gradient Severe Aortic Stenosis

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ABSTRACT

OBJECTIVES This study sought to assess the diagnostic impact of stress echocardiography (SE) in patients with suspected low-flow, low-gradient aortic stenosis but normal resting transvalvular flow rate.

BACKGROUND SE may help to distinguish between true severe aortic stenosis and pseudosevere aortic stenosis in patients with low aortic valve area (AVA) and mean gradient. However, if rest flow rate is normal, then SE may not confer any additional diagnostic value, irrespective of resting left ventricular ejection fraction (LVEF) and indexed stroke volume (SVi).

METHODS Sixty-seven patients with suspected low-flow, low-gradient aortic stenosis who underwent SE were retrospectively studied. Following stratification by rest LVEF, SVi, and flow rate—using cutoffs of 50%, 35 ml/m^2, and 200 ml/s, respectively—we tested for significant changes in AVA during SE.

RESULTS Mean age was 77 ± 9 years and 60% of patients were male. Mean values for rest variables were as follows: AVA: 0.77 ± 0.12 cm^2; mean gradient: 27 ± 7 mm Hg; flow rate: 182 ± 37 ml/s; SVi: 32 ± 8 ml/m^2; and LVEF: 45 ± 15%. During SE, significant increases in AVA were observed regardless of resting LVEF and SVi state. In patients with rest flow rate ≥200 ml/s, AVA did not increase significantly during stress (rest AVA: 0.90 cm^2 vs. stress AVA: 0.97 cm^2; p = 0.11), and positive predictive value for confirming underlying true severe aortic stenosis was 84%. In adjusted analyses, rest flow rate was the only parameter associated with severe AS (odds ratio: 1.05, 95% confidence interval: 1.0 to 1.1; p = 0.002).

CONCLUSIONS Rest AVA measured under normal flow rate conditions is likely to reflect the true severity of AS and unlikely to change significantly with SE. Flow normalization may only be required in patients with AVA <1 cm^2 and mean gradient <40 mm Hg when the rest flow rate is <200 ml/s. (J Am Coll Cardiol Img 2015;8:1133–9)

The constellation of low cardiac output state, symptoms of aortic stenosis (AS), reduced aortic valve area (AVA), and transvalvular gradient on echocardiography represents the entity of low-flow, low-gradient aortic stenosis (LFLGAS) and challenges the clinician to discern between the presence of true severe aortic stenosis (TSAS) or pseudosevere aortic stenosis (PSAS). In the former, low transvalvular flow can result in a low gradient, potentially masking genuinely severe AS. In the latter, the diminished flow does not fully open moderately restricted leaflets, producing a spuriously low AVA (1,2).

Low-flow states can arise due to impairment of left ventricular ejection fraction (LVEF), or independently of LVEF, in the presence of restrictive

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ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

AVA = aortic valve area

EF = ejection fraction

LFLGAS = low-flow, low-gradient aortic stenosis

LV = left ventricle

LVEF = left ventricular ejection fraction

MG = mean gradient

PPV = positive predictive value(s)

PSAS = pseudosevere aortic stenosis

SE = stress echocardiography

SEP = systolic ejection period

SV = stroke volume

SVi = indexed stroke volume

TSAS = true severe aortic stenosis

physiology and/or reduced longitudinal function (3). LFLGAS is typically suspected in patients with a rest mean gradient (MG) <40 mm Hg, an AVA <1 cm^2, an LVEF <50%, and/or indexed stroke volume (SVi) <35 ml/m^2 (4). To help differentiate between true stenosis and pseudosevere disease, stress echocardiography (SE) is performed to normalize flow, permitting AVA and transaortic gradient to be remeasured at this juncture (4–6).

However, if flow is normal at rest, then there may be little incremental value in performing SE at all. Transvalvular ejection flow, or flow rate, is the principal determinant of both AVA and transvalvular gradient (1). Rather than quantifying ejection flow, much of the research to-date, and consequently clinical practice, has focused on surrogate measures during rest and SE. Impaired LVEF has been assumed to be a prerequisite to the existence of a low-flow state, and in routine clinical practice, an LVEF <40% to 50% remains the principal "red flag" for suspecting LFLGAS (4,7–9). However, LVEF is poorly correlated with flow state. Cardiac output, stroke volume (SV), and flow rate can all be preserved in patients with reduced LVEF and a dilated heart (10). Conversely, in patients with preserved LVEF, but advanced hypertrophic remodeling/restrictive physiology, the consequent reduction in SV has been used to define "low-flow" in these patients (11).

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Flow rate can be simply measured during rest and SE, by dividing the SV by the systolic ejection period (SEP), with a normal rate considered to be 200 ml/s (12). We hypothesized that transvalvular flow rate is superior to both SVi and LVEF in predicting the impact of flow correction on AVA in patients undergoing SE.

METHODS

STUDY POPULATION. From February 9, 2011 to November 20, 2014, echocardiographic data were retrospectively collected in 67 consecutive, symptomatic patients who were all candidates for valve intervention and who had been referred for SE to further assess severity of LFLGAS, which was defined as an AVA <1 cm^2, MG <40 mm Hg, and either LVEF <50% or SVi <35 ml/m^2. Of these, 18 patients (27%) and 49 (73%) underwent exercise and dobutamine SE, respectively.

Patients with other significant valve disease, prosthetic aortic valve, at least moderate aortic regurgitation, or who developed significant ischemia during stress imaging were excluded from the study. The study was approved by the local institutional review board.

PROTOCOL. The protocol included an echocardiogram at baseline followed by stress imaging. Exercise stress was performed either on a treadmill according to Bruce protocol or bicycle ergometer using the World Health Organization protocol. The test was interrupted when the patient developed symptoms of AS or when the patient reached the age-related maximum heart rate. Doppler echocardiographic data were collected at rest and peak- or post-exercise stress.

Dobutamine SE was performed according to a standard protocol. Dobutamine was infused at an initial dose of 5 μg/kg/min with 5-min increments up to a maximum dosage of 20 μg/kg/min depending on the severity of AS. Echocardiographic data were obtained at rest and intermediate dobutamine dose including pulse-wave Doppler-derived SV in the left ventricular (LV) outflow tract, mean and peak gradients by the simplified Bernoulli equation, AVA by the continuity equation, mean transvalvular flow rate, and LVEF determined by the modified biplane Simpson method. Flow rate was calculated by dividing SV by the SEP (ms). Twenty-four patients had suboptimal images for the assessment of LVEF and ultrasound contrast enhancement was used (Sonovue, Bracco, Milan, Italy). LV outflow tract diameter was assumed to have remained constant during the stress test protocol and was measured only at rest.

Patients with stress AVA remaining at <1 cm^2 and stress MG increasing to ≥40 mm Hg were classified as having TSAS (**Figure 1A**), with the remainder classified as having PSAS (**Figure 1B**), according to conventional criteria (4).

STATISTICS. Comparisons within groups were made using paired Student *t* test for continuous variables and McNemar test for categorical variables. To assess the impact of SE, paired Student *t* test was used to determine significant changes in AVA within groups and between groups using independent samples Student *t* test—following stratification by rest EF, SVi, and flow rate using cutoff values of 50%, 35 ml/m^2, and 200 ml/s, respectively. Positive predictive values (PPV) of normal rest flow rate and normal rest SVi for defining TSAS were calculated using conventional criteria as has already been mentioned; PPV was also calculated when only an increase in stress MG to ≥40 mm Hg was evident, irrespective of stress AVA.