JACC: CASE REPORTS VOL. 29, 2024


VALVULAR HEART DISEASE

CASE REPORT: CLINICAL CASE SERIES

# Exercise Cardiac Catheterization for Hemodynamic Evaluation of Paradoxical Low-Flow Low-Gradient Severe Aortic Stenosis

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## ABSTRACT

Patients with paradoxical low-flow low-gradient aortic stenosis pose a diagnostic challenge when it comes to assessing the severity of aortic stenosis (AS) noninvasively. We describe 2 patients who underwent exercise cardiac catheterization to augment their cardiac output and assess the severity of AS invasively to allow differentiation of true severe AS from pseudo-severe AS. (J Am Coll Cardiol Case Rep 2024;29:102306) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Severe aortic stenosis (AS) is a common valvular heart condition that accounts for most valve replacements in North America.[1] The diagnostic criteria for severe AS include a jet velocity of ≥4 m/s, a mean transvalvular pressure gradient ≥40 mm Hg, and an aortic valve area (AVA) <1.0 $cm^2$.[1,2] However, a subset of patients with AS have a valve area <1.0 $cm^2$ but with a mean transvalvular pressure gradient ≤40 mm Hg caused by low cardiac output (stroke volume index <35 $mL/m^2$). These patients with low-flow low-gradient (LFLG) severe AS can have either a low ejection fraction or a normal ejection fraction, of which the latter is labeled paradoxical LFLG severe AS.[1,3]

## LEARNING OBJECTIVES

- To understand the physiology of PLFLG AS and why it poses a diagnostic challenge.
- To understand how exercise cardiac catheterization can be used in patients with PLFLG AS to differentiate true severe AS from pseudo-severe AS.

Unlike classic LFLG severe AS with a low ejection fraction, differentiating true severe AS from pseudo-severe AS in PLFLG severe AS is challenging. For instance, the use of dobutamine to augment cardiac output is common in classic LFLG severe AS and can help differentiate severe from pseudo-severe AS. However, the use of dobutamine in PLFLG severe AS may pose a risk of hemodynamic collapse because these patients tend to have small left ventricles and may not tolerate dobutamine.[4] In this case series, we explore the utility of exercise cardiac catheterization in patients with PLFLG severe AS to augment their cardiac output and assess their aortic valve

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received December 10, 2023; revised manuscript received February 20, 2024, accepted February 21, 2024.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2024.102306

**ABBREVIATIONS AND ACRONYMS**

**AVC** = aortic valve calcium

**AS** = aortic stenosis

**AVA** = aortic valve area

**DSE** = dobutamine stress echocardiography

**LFLG AS** = low-flow low-gradient aortic stenosis

**LV** = left ventricle

**LVEF** = left ventricular ejection fraction

**LVOT** = left ventricular outflow tract

**MP** = multipurpose

**PLFLG AS** = paradoxical low-flow low-gradient aortic stenosis

hemodynamics invasively, with the purpose of discerning true severe from pseudo-severe AS.

## METHODS AND PROCEDURE DETAILS

Exercise cardiac catheterization was performed using the right radial artery and right internal jugular vein for access. Baseline oxygen consumption was measured using the Ultima Series Cardiorespiratory Diagnostic System (MCG Diagnostics). A balloon wedge catheter was placed in the right internal jugular vein. The aortic valve was crossed, and a 6-F multipurpose (MP) catheter was placed in the left ventricle (LV). An Abbott Pressure X wire was then advanced through a copilot connected to the MP catheter and positioned at the tip of the catheter in the LV. The pressure wire signal was normalized against the fluid-filled MP catheter. After that, the MP catheter was retracted into the aorta while the pressure wire remained in the LV, providing simultaneous aorta-LV pressures. Baseline pressures and cardiac output were measured, and the AVA was calculated using the Gorlin formula. Patients were then asked to perform a recumbent bike exercise to augment their stroke volume and flow rate. The same measures were then obtained with exercise. In this case series, we describe 2 patients with paradoxical low-flow (stroke volume index $<35$ mL/m$^2$), low-gradient ($\leq$40 mm Hg) severe AS diagnosed by transthoracic echocardiography who underwent exercise cardiac catheterization for further hemodynamic evaluation of their AS. Approval from the Institutional Review Board at the Mayo Clinic was obtained before this study.

## CASE 1

Patient 1 was an 85-year-old woman who presented with dyspnea and a diagnosis of PLFLG severe AS. She underwent exercise cardiac catheterization to evaluate the severity of her AS. Before exercise, she had had a baseline AVA of 0.9 cm$^2$ according to the Gorlin equation, with a mean gradient of 17 mm Hg, and a low cardiac index of 2 L/min/m$^2$ (Table 1, Figure 1). With exercise, her cardiac index increased to 4 L/min/m$^2$, the AVA increased to 1.5 cm$^2$, and the mean gradient increased to 19 mm Hg (Table 1, Figure 1). Given that these findings were consistent with pseudo-severe AS, aortic valve replacement was not performed, and the patient was treated for diastolic dysfunction.

**TABLE 1** Pre- and Post-Exercise Cardiac Catheterization Hemodynamic Data

| | Pre-Exercise | | | Post-Exercise | | |
|---|---|---|---|---|---|---|
| Patient # | AVA (cm$^2$) | Mean Pressure Gradient (mm Hg) | Cardiac Index (L/min/m$^2$) | AVA (cm$^2$) | Mean Pressure Gradient (mm Hg) | Cardiac Index (L/min/m$^2$) |
| 1 | 0.9 | 17 | 2.0 | 1.5 | 19 | 4.0 |
| 2 | 1.0 | 19 | 2.1 | 1.6 | 24 | 4.7 |

AVA = aortic valve area.

## CASE 2

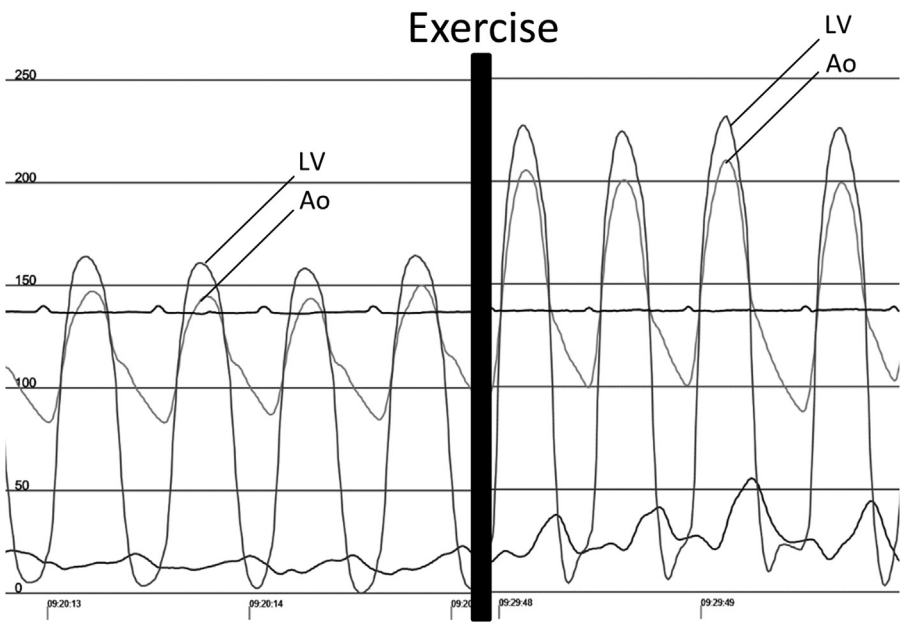
Patient 2 was a 78-year-old man who also presented with dyspnea and a diagnosis of PLFLG severe AS. He underwent exercise cardiac catheterization to evaluate his hemodynamics and to assess the severity of his AS. Before exercise, he had a baseline AVA of 1 cm$^2$, a mean gradient of 19 mm Hg, and a low cardiac index of 2.1 L/min/m$^2$ (Table 1, Figure 2). With exercise, his cardiac index increased to 4.7 L/min/m$^2$, the AVA increased to 1.6 cm$^2$, and the mean gradient increased to 24 mm Hg (Table 1, Figure 2). These findings were consistent with pseudo-severe AS, and therefore the patient did not undergo aortic valve replacement and was instead treated for diastolic dysfunction.

## DISCUSSION

In this study, we present a case series of 2 patients with PLFLG AS who underwent exercise cardiac catheterization for better characterization of their aortic valve hemodynamics. Our findings show that this method was feasible in these patients and assisted in differentiating true from pseudo-severe AS by augmenting cardiac output using exercise.

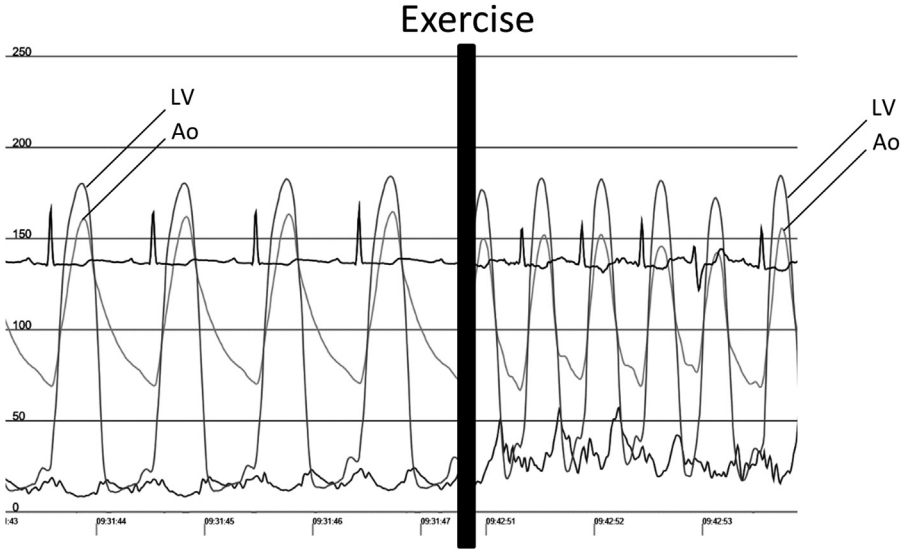
Assessment of AS severity and differentiation of pseudo-severe AS from true severe AS has been challenging in PLFLG AS patients. Noninvasive calculation of AVA is flow dependent, and reduced flow can lead to underestimation of AVA.[5] In cases of LFLG severe AS with low ejection fraction, stress echocardiography with dobutamine has been used to augment flow, leading to better assessment of the severity of the AS. However, in patients with PLFLG AS who have small LV cavities, dobutamine stress tests can lead to further decrease in LV filling and subsequent hemodynamic instability.[4,5] Moreover, before hemodynamic collapse, the use of dobutamine in patients with small LVs can lead to the development of LVOT obstruction and mitral regurgitation, which can confound the hemodynamic assessment across the aortic valve. Another adjunct noninvasive modality to help assess aortic valve severity in PLFLG

**FIGURE 1** **Pre- and Post-Exercise Cardiac Pressure Tracings for Patient 1**




The pre- and post-exercise pressure tracings for patient 1 do not show a significant increase in mean gradient pressure with exercise, suggesting that this patient has pseudo-severe aortic stenosis and that the primary driver of her cardiac dysfunction is her diastolic heart failure. Ao = aorta; LV = left ventricle.

**FIGURE 2** **Pre- and Post-Exercise Cardiac Pressure Tracings for Patient 2**




The pre- and post-exercise pressure tracings for patient 2 do not show a significant increase in mean gradient pressure with exercise, suggesting that this patient has pseudo-severe aortic stenosis and that the primary driver of his cardiac dysfunction is his diastolic heart failure. Ao = aorta; LV = left ventricle.

severe AS is the use of the aortic valve calcium (AVC) score. This can be obtained through multidetector computed tomography.[6,7] However, several limitations also exist for this modality in this patient population. AVC is an anatomical variable, not a direct hemodynamic surrogate. Although standard AVC thresholds for severe AS have been established, outcome studies have shown that there is more variability in thresholds for PLFLG and LFLG AS, making its application in these patients more challenging.[6]

Given the challenges with augmenting cardiac output in PLFLG severe AS, alternative modalities are necessary for the assessment of AS severity in these patients. In patients with PLFLG severe AS and hypertension, afterload reduction with sodium nitroprusside infusion in the cardiac catheterization laboratory has been shown to augment cardiac output and differentiate severe from pseudo-severe AS in these patients.[8] In this series, we evaluated the role of exercise for stroke volume and flow rate augmentation in normotensive patients with PLFLG severe AS. Noninvasive exercise stress testing can be challenging to perform, given the logistical difficulty with the echocardiographic evaluation of AS at peak exercise. Although a case report presented by Bandera et al[9] showed the utility of echocardiography in PLFLG AS, future studies are needed to determine whether exercise echocardiography is an accurate means of assessing hemodynamics and of differentiating true severe from pseudo-severe AS in a flow-augmented state. Therefore, we performed invasive hemodynamics with exercise to allow measurement of aortic valve hemodynamics at peak exercise. We found that exercise cardiac catheterization could lead to augmentation of flow, which allowed for discrimination of severe from pseudo-severe AS. Larger studies are needed to validate these findings and to assess treatment outcomes based on stratification after exercise cardiac catheterization.

## CONCLUSIONS

Exercise cardiac catheterization offers a potential novel diagnostic modality to help differentiate true severe AS from pseudo-severe AS in patients with PLFLG severe AS. Larger studies are needed to validate the use of this modality in this patient population.

## FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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**KEY WORDS** aortic stenosis, aortic valve replacement, exercise cardiac catheterization, paradoxical low flow low gradient