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CASE REPORT: CLINICAL CASE SERIES

Management of Intraventricular Gradient in Patients With Aortic Stenosis

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ABSTRACT

In patients with severe left ventricle hypertrophy and aortic stenosis, the presence of intraventricular gradient should always be investigated. Its prompt recognition enables a precise diagnosis and safe treatment of both conditions. We report 2 cases demonstrating a successful and novel approach to this clinical situation. (JACC Case Rep. 2024;29:102696) © 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/).

CASE 1

A 77-year-old woman with severe symptomatic aortic stenosis (AS) was admitted in ambulatory setting. Her functional status was classified as NYHA functional class III. On physical examination, peripheral edema was noted, and a 3/6 systolic heart murmur was heard in all auscultatory areas. Transthoracic echocardiography (TTE) revealed left ventricular (LV) hyperkinetic hypertrophy, with mid-cavity obliteration (Simpson's Biplane left ventricular ejection fraction [LVEF] 80%) (**Figure 1A**, Video 1). The aortic valve was calcified with a mean gradient of 46 mmHg at continuous wave (CW) Doppler (**Figure 1B**, Video 2). Mitral regurgitation was mild. Because of hourglass appearance, CW Doppler was also applied along the apical LV views to check for the presence of intraventricular gradient, showing a dagger-shaped waveform with a peak gradient of 68 mmHg (**Figure 1C**). Metoprolol was introduced and gradually increased to reach the maximum tolerated dosage of 100 mg/d. However, this adjustment did not result in any changes at TTE (Video 3). Consequently, disopyramide at a dosage of 200 mg per day was included. Following 1 week, there was a reduction in mid-cavity obliteration, with LVEF measuring 72% (**Figure 1D**). The mean gradient across the aorta remained consistent, whereas the peak intraventricular gradient decreased to 5 mm Hg (**Figures 1E and 1F**). At cardiac computed tomography (CT), extensive calcification of the aortic valve was

LEARNING OBJECTIVES

- To investigate the presence of intraventricular gradient in patients with AS and mid-cavity obliteration caused by severe hypertrophy.
- To effectively manage intraventricular gradient, thereby appropriately addressing aortic stenosis and preventing the risk of hemodynamic destabilization after TAVI.

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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.

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ABBREVIATIONS AND ACRONYMS

CT = computed tomography

CW = continuous wave

HCM = hypertrophic cardiomyopathy

LV = left ventricle

TAVI = transcatheter aortic valve implantation

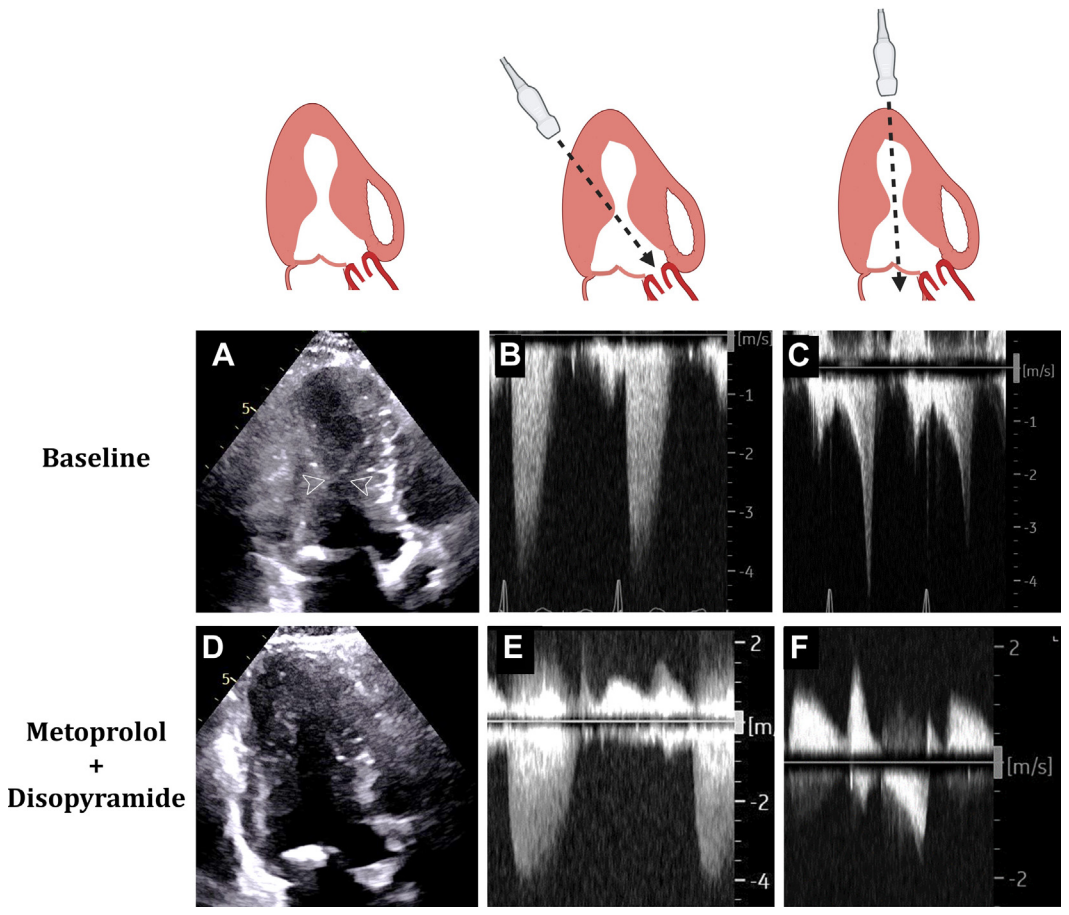
TTE = transthoracic echocardiography

observed, with a calcium score of 1,550 AU. Thus, the patient was hospitalized and underwent transcatheter aortic valve implantation (TAVI) successfully. Upon discharge, the patient's condition improved to NYHA functional class II, with less prominent LV mid-cavity obliteration and an ejection fraction of 73% (Video 4). The mean gradient across the prosthesis was 6 mmHg, with a negligible intraventricular gradient. Metoprolol and disopyramide were continued as part of the maintenance therapy regimen.

CASE 2

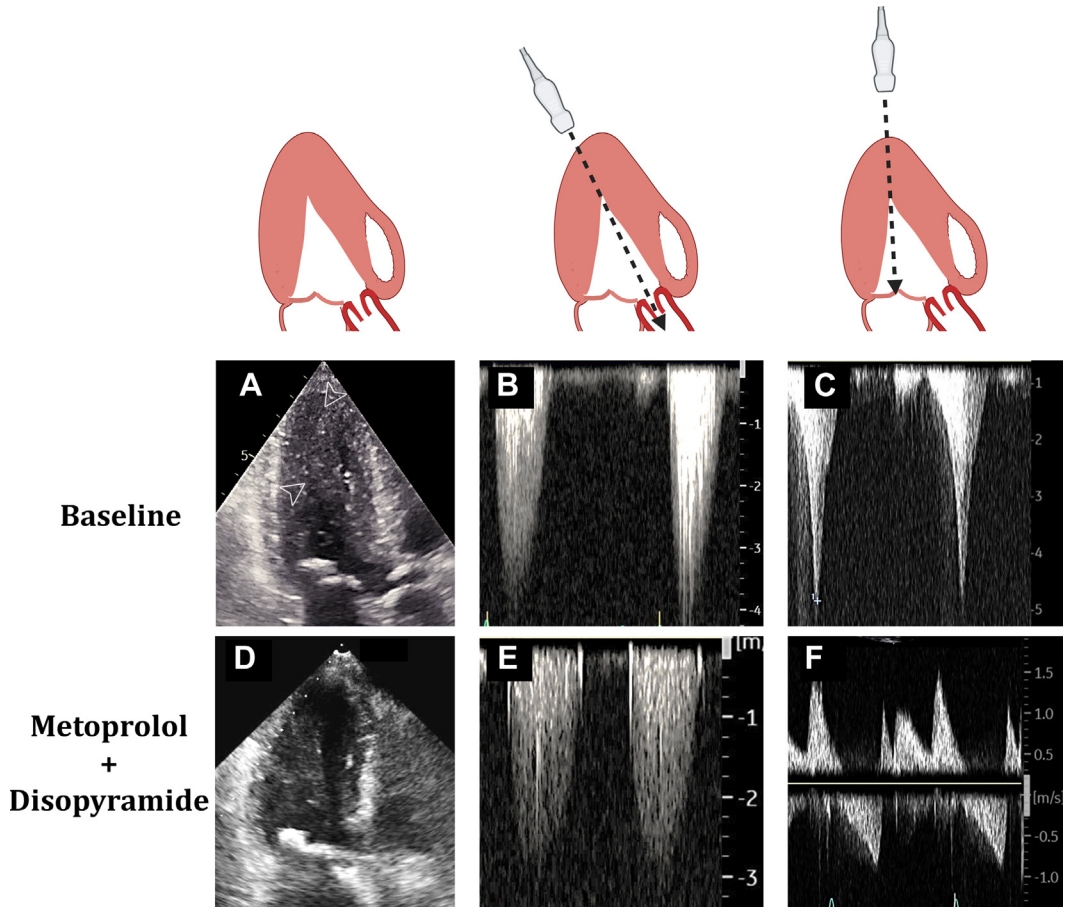
A 74-year-old woman was admitted in ambulatory setting with symptomatic severe AS. Physical examination revealed a 2/6 systolic heart murmur audible at the second right intercostal space, without signs of cardiac decompensation. TTE revealed hyperkinetic LV hypertrophy and cavity obliteration (**Figure 2A**, Video 5). Although the aortic valve appeared calcified with unclear delineation of CW, a diagnosis of severe stenosis was established (**Figure 2B**, Video 6). Mitral regurgitation was mild. Because of cavity obliteration, CW Doppler was also applied along the apical LV views to assess intraventricular gradient, showing a dagger-shaped waveform with a peak gradient of 100 mmHg (**Figure 2C**). Metoprolol initiation and titration up to a maximum tolerated dose of 100 mg every 12 hours did not substantially change the TTE findings (Video 7). Consequently, disopyramide at a dosage of 200 mg daily was introduced. After 1 week, the patient became asymptomatic, with a reduction in LV ejection fraction to 61%, and less pronounced LV cavity obliteration (**Figure 2D**). A well-delineated CW

FIGURE 1 Management of Intraventricular Gradient in Patients With Aortic Stenosis (Case 1)



(A) Baseline: left ventricular mid-cavity obliteration with hourglass appearance (white arrowheads). (B) Severe aortic stenosis at continuous Doppler. (C) Severe peak intraventricular gradient. (D) After therapy with metoprolol and disopyramide, less pronounced left ventricular cavity obliteration. (E) Severe aortic stenosis at continuous Doppler. (F) Negligible peak intraventricular gradient.

FIGURE 2 **Management of Intraventricular Gradient in Patients With Aortic Stenosis (Case 2)**



(A) Baseline: left ventricular mid- and apical cavity obliteration (white arrowheads). (B) Severe aortic stenosis at continuous Doppler. (C) Severe peak intraventricular gradient. (D) After therapy with metoprolol and disopyramide: less pronounced left ventricular cavity obliteration. (E) Moderate aortic stenosis at continuous Doppler. (F) Negligible peak intraventricular gradient.

was obtained, showing a mean aortic gradient of 28 mmHg, whereas the peak intraventricular gradient decreased to 16 mmHg (**Figures 2E and 2F**). A CT scan revealed moderate calcification of the aortic valve with a calcium score of 990 Agatston units. Therefore, TAVI was not pursued, and the patient was scheduled for follow-up, whereas metoprolol and disopyramide were confirmed (Video 8).

The study conformed to the Declaration of Helsinki on human research. Any information identifying the patients has not been included in the manuscript to respect the right to privacy.

DISCUSSION

LV outflow tract obstruction is a common finding in patients with hypertrophic cardiomyopathy (HCM), arising from a complex interplay of mitral valve abnormalities and septal hypertrophy. However, cavity obliteration (without systolic anterior motion [SAM] of the mitral valve) may also develop at mid or apical level and has been associated with adverse outcomes.[1] These 2 distinct conditions—LV outflow tract and mid-cavity obliteration—can be accompanied by the development of a similar dagger-shaped

intraventricular gradient.[2] Specifically, patients with AS and hyperdynamic, hypertrophic LV can develop mid-cavity obliteration and significant intraventricular gradient. Hemodynamically significant intraventricular gradient is defined as a peak gradient ≥30 mmHg.[3] We applied this well-established echocardiographic method—commonly employed in patients with HCM—with our patients with AS and mid-cavity obliteration. Our 2 cases illustrate that in patients with AS and mid-cavity obliteration, intraventricular gradients can coexist with the gradient across the aortic valve. Before scheduling patients for TAVI evaluation, we initiated medical treatment to reduce the intraventricular gradient. Metoprolol has been shown to reduce obstruction and symptoms in patients with obstructive HCM.[4] As a second-line approach, HCM guidelines recommend the addition of disopyramide, an antiarrhythmic class IA agent, which further reduces LV inotropism and obstruction with minimal risk of proarrhythmic effects.[3] Although their routine use in patients with AS is not established, the combination of metoprolol and disopyramide in our cases significantly reduced the intraventricular gradient, facilitating a more accurate diagnosis of the severity of AS and tailored therapeutic strategy.

Circulatory collapse, also referred to as suicide LV, is a documented phenomenon linked to heightened mortality after TAVI.[5] The sudden drop in LV pressure following TAVI, which leads to a reduced LV outflow tract area, has been described as the underlying mechanism behind this complication. In addition, the increased flow across the LV outflow tract creates a Venturi effect, pulling the anterior mitral valve leaflet into the outflow tract and causing dynamic obstruction. Intraventricular gradient has been shown to serve as a contributing factor for suicide LV.[5] It is important to note that although LV outflow tract obstruction has been associated with this complication, there is no evidence that mid-cavity obliteration may lead to the same outcome, as the latter is not linked to SAM. However, the immediate relief of the transvalvular gradient following TAVI exposes the LV to a sudden and substantial decrease in afterload, which—in the presence of hypercontractility and intraventricular gradients—we believe may still pose a risk of hemodynamic destabilization in patients with mid-cavity obliteration. The uncertainty surrounding the association between mid-cavity obliteration and suicide LV after TAVI should be carefully considered when making therapeutic decisions. Despite this lack of evidence, our approach aimed to mitigate potential risks of circulatory collapse post-TAVI. In the first case, TAVI could be performed under safer hemodynamic conditions, attenuating the risk of hemodynamic destabilization. In the second case, a more accurate assessment of AS led to deferral of TAVI. In conclusion, our cases highlight the importance of carefully investigating and managing intraventricular gradient in patients with AS and mid-cavity obliteration.

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KEY WORDS aortic stenosis, cavity obliteration, intraventricular gradient

APPENDIX For supplemental videos, please see the online version of this paper.