CASE REPORT

CLINICAL CASE

Mavacamten in Right Ventricular Outflow Tract Obstruction

Jasmine K. Malhi, MD,[a] Richard T. Carrick, MD, PhD,[a] Chloe Duvall, MD,[a] Faisal Rahman, BMBCh,[a]
Matthew W. Martinez, MD,[b] Jose Madrazo, MD,[a] Lili A. Barouch, MD[a]

ABSTRACT

Right ventricular outflow tract (RVOT) obstruction is a rare complication of ventricular hypertrophy in patients with hypertrophic cardiomyopathy (HCM). This study presents an unusual case of a patient with HCM with severe RVOT obstruction that was relieved successfully through the use of mavacamten. (J Am Coll Cardiol Case Rep 2024;29:102397) © 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/).

HISTORY OF PRESENTATION

A 23-year-old woman with hypertrophic cardiomyopathy (HCM) was referred to our clinic for progressive symptoms of chest pain, lightheadedness, and dyspnea on exertion. Her HCM was first diagnosed when she was 9 years of age during family screening evaluation. She remained asymptomatic for several years after her initial diagnosis. At the time of referral, she complained of dyspnea while walking to classes or going up stairs, particularly while carrying

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LEARNING OBJECTIVES

- To understand the pathophysiology of RVOT obstruction in HCM.
- To highlight the utility of invasive hemodynamic assessment for confirming or clarifying ambiguous causes of symptoms in HCM.
- To recognize possible therapeutic options available for treatment of symptomatic RVOT obstruction.

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her backpack. She had stopped participating in some of her favorite activities because of this shortness of breath, including no longer dancing with her regular church dance group. She denied edema, syncope, orthopnea, paroxysmal nocturnal dyspnea, or palpitations.

Vital signs were notable for blood pressure of 106/70 mm Hg and a regular pulse with rate of 79 beats/min. She had a height of 165 cm and weighed 77 kg (body mass index 28.3 kg/m^2). A 3/6 late-peaking systolic murmur that increased to 4/6 during Valsalva was appreciated on cardiac auscultation. She had no peripheral edema, and her jugular venous pressure was visualized at 7 cm above the sternal angle.

PAST MEDICAL HISTORY

She had undergone prior placement of a single chamber internal cardioverter-defibrillator 6 years earlier due to demonstration of extensive late gadolinium enhancement on cardiac magnetic resonance.

For medications, she reported adherence to metoprolol succinate 50 mg once daily and verapamil 40 mg as needed for chest pain. A pathogenic variant in *MYH7* was identified on genetic testing.

Pertinent family history included a mother with *MYH7*-associated HCM. There was no family history of sudden cardiac death.

DIFFERENTIAL DIAGNOSIS

Left ventricular outflow tract (LVOT) obstruction, systolic dysfunction, right ventricular outflow tract (RVOT) obstruction, atrial fibrillation, medication side effect, and noncardiac dyspnea.

INVESTIGATIONS

Initial electrocardiogram demonstrated sinus rhythm with right atrial enlargement, inferior Q-waves, and delayed R-wave transition (Figure 1). Echocardiogram revealed severe concentric hypertrophy of the left ventricle (LV) with maximal wall thickness of 24 mm in the mid-anterior septum and right ventricular (RV) hypertrophy with maximal RV free wall thickness of 11 mm. There was clear anterior motion of the mitral valve with septal contact and mid-to-distal cavity obliteration during systole. However, Doppler assessment (Figure 2) of hemodynamics revealed a resting LVOT gradient of only 12 mm Hg, increasing to 20 mm Hg with Valsalva. Mid-cavitary gradient was 41 mm Hg. There was flow acceleration noted in the RVOT, with RVOT peak gradient of 53 mm Hg and right ventricular systolic pressure (RVSP) of 95 mm Hg (estimated from tricuspid regurgitation jet). On stress echocardiography, she had limited exercise capacity completing only 3:27 on a Bruce protocol (5.1 METs).

Given these unexpectedly low LVOT gradients and suspicion for a hemodynamically significant RVOT gradient, right and left heart catheterization was pursued. Invasive hemodynamics are presented in Figure 3. Right heart catheterization revealed a mean right atrial pressure of 12 mm Hg, RV pressure of 92/12 mm Hg, pulmonary arterial pressure of 34/20 mm Hg, and mean pulmonary capillary wedge pressure of 19 mm Hg, confirming significant RVOT obstruction with peak-to-peak gradient of 58 mm Hg. Her cardiac index was severely reduced at 1.67 L/min/m². Invasive assessment of left-sided hemodynamics confirmed nonsignificant gradients at the basal LV

FIGURE 1 Electrocardiogram
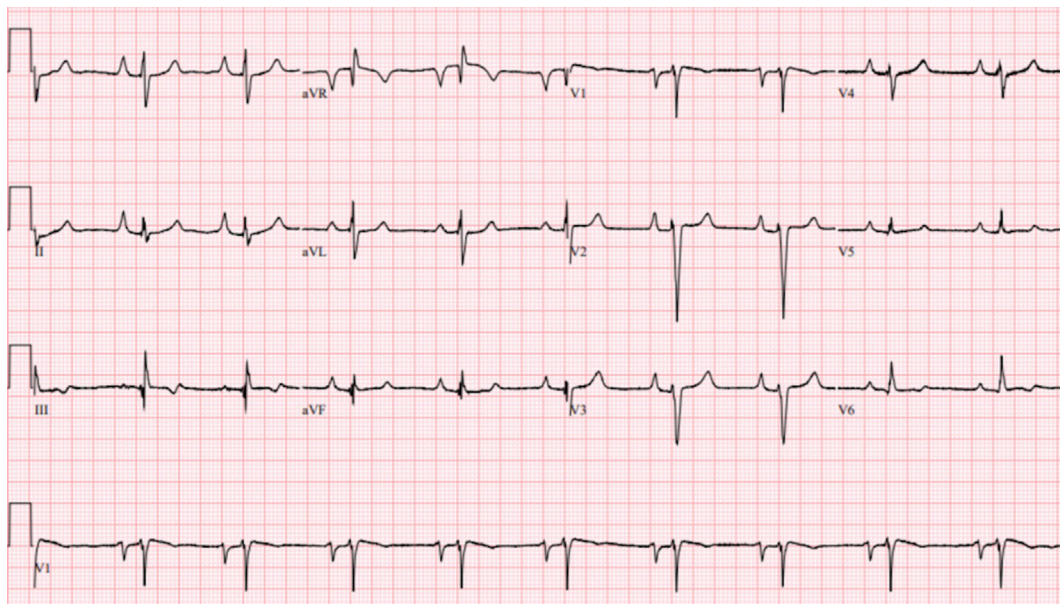
The patient's initial electrocardiogram.

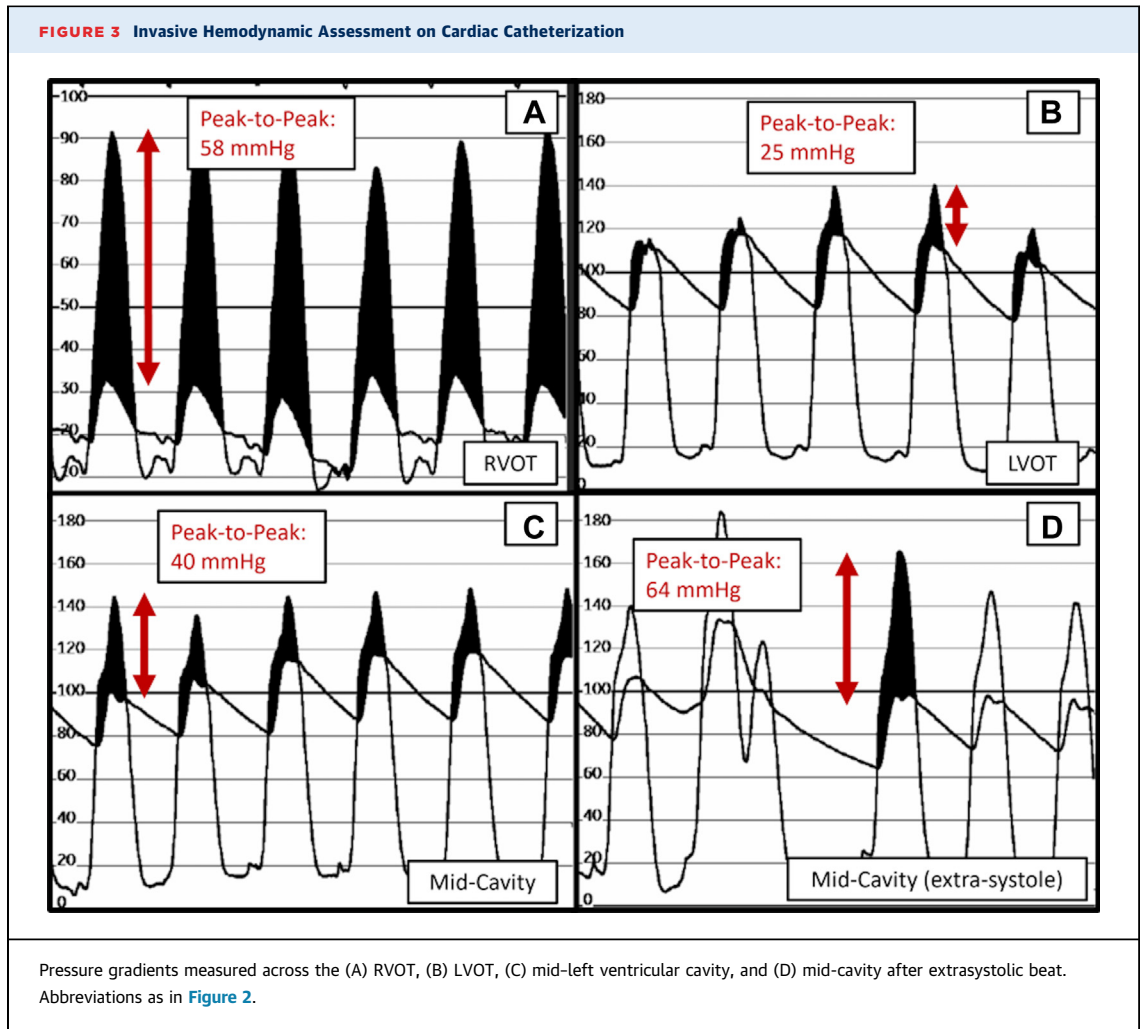**FIGURE 2 Initial Echocardiographic Assessment**
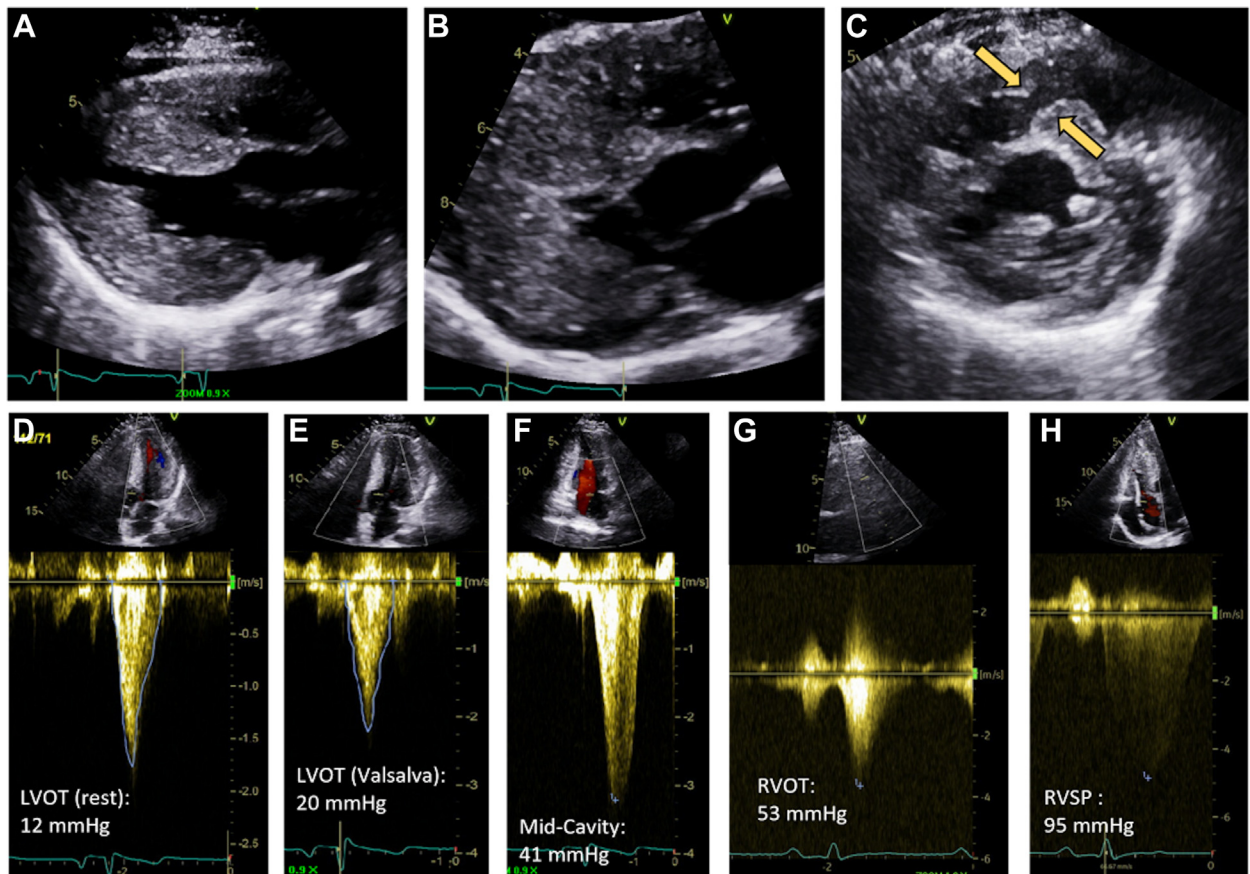
Parasternal long view showing severe left ventricular concentric hypertrophy and with right ventricular hypertrophy during diastole (A) and anterior motion of the mitral valve apparatus with septal contact and mid-to-distal cavity obliteration during systole (B). (C) The point of RVOT narrowing is highlighted by yellow arrows in this off-axis parasternal short view. Doppler-based pressure gradients are also shown for (D) LVOT at rest and (E) with Valsalva, (F) in the mid-left ventricular cavity, and (G) for the RVOT. (H) RVSP as estimated from tricuspid regurgitation jet was significantly elevated at rest. LVOT = left ventricular outflow tract; RVOT = right ventricular outflow tract; RVSP = right ventricular systolic pressure.

(peak-to-peak gradient 25 mm Hg) but identified significant mid-cavitary obstruction at rest (peak-to-peak gradient 40 mm Hg) that increased after extrasystolic beat (peak-to-peak gradient 64 mm Hg).

MANAGEMENT

Given persistent symptoms despite optimized traditional medical therapy, the evidence of biventricular, hemodynamically significant obstruction, and the patient's preference to defer cardiac surgery if possible, the decision was made to pursue therapy with the myosin inhibitor mavacamten in addition to her current therapy with metoprolol. Mavacamten was initiated at a dosage of 5 mg daily. Verapamil was discontinued. Mavacamten was uptitrated to 10 mg. Longitudinal echocardiographic assessments while on mavacamten are presented in **Table 1**. Over the first 28 weeks of treatment with mavacamten, left-sided gradients were mixed, with LVOT gradients stable to slightly increased (maximum gradient with Valsalva 38 mm Hg), whereas gradients in the mid-left ventricular cavity were relieved. On the other hand, right-sided pressures were significantly reduced by the 28-week echocardiogram, with final RVOT gradient of 13 mm Hg and final RVSP of 25 mm Hg (**Figure 4**). Left ventricular ejection fraction decreased from 85% to 65% (Video 1). She demonstrated dramatically improved exercise capacity on repeat stress echocardiography, completing 9:27 on a

FIGURE 3 Invasive Hemodynamic Assessment on Cardiac Catheterization

Pressure gradients measured across the (A) RVOT, (B) LVOT, (C) mid-left ventricular cavity, and (D) mid-cavity after extrasystolic beat. Abbreviations as in Figure 2.

TABLE 1 Longitudinal Echocardiographic Assessment

|	Initial Assessment	Mavacamten 4-Week Assessment (5 mg/d)	Mavacamten 8-Week Assessment (5 mg/d)	Mavacamten 28-Week Assessment (10 mg/d)
LV ejection fraction, %	85	75	75	65
LVOT gradient rest, mm Hg	12	31	12	4
LVOT gradient Valsalva, mm Hg	20	38	38	4
LV mid-cavity gradient, mm Hg	41	10	14	2
RVOT gradient, mm Hg	53	24	30	15
RVSP, mm Hg	95	40	Insufficient TR for assessment	25
Exercise duration on Bruce protocol, minutes	3:27	–	–	9:27
METs achieved	5.1	–	–	10.8

LV = left ventricular; LVOT = left ventricular outflow tract; MET = metabolic equivalent; RVOT = right ventricular outflow tract; RVSP = right ventricular systolic pressure; TR = tricuspid regurgitation.

Bruce protocol (10.8 METs). Importantly, she had significant symptomatic improvement and was able to exert herself without limitation (NYHA functional class I symptoms). She was able to resume moderate aerobic activities, including rejoining her dance group.

DISCUSSION

HCM is a genetic cardiomyopathy characterized by hyperdynamic systolic function and marked ventricular hypertrophy. Two-thirds of patients with HCM demonstrate dynamic mechanical obstruction of the LVOT. Pressure gradients exceeding 50 mm Hg are considered hemodynamically significant, at which point obstruction manifests clinically as symptoms of chest discomfort, dyspnea, or syncopal episodes. HCM may also result in right

FIGURE 4 Follow-Up Echocardiographic Assessment
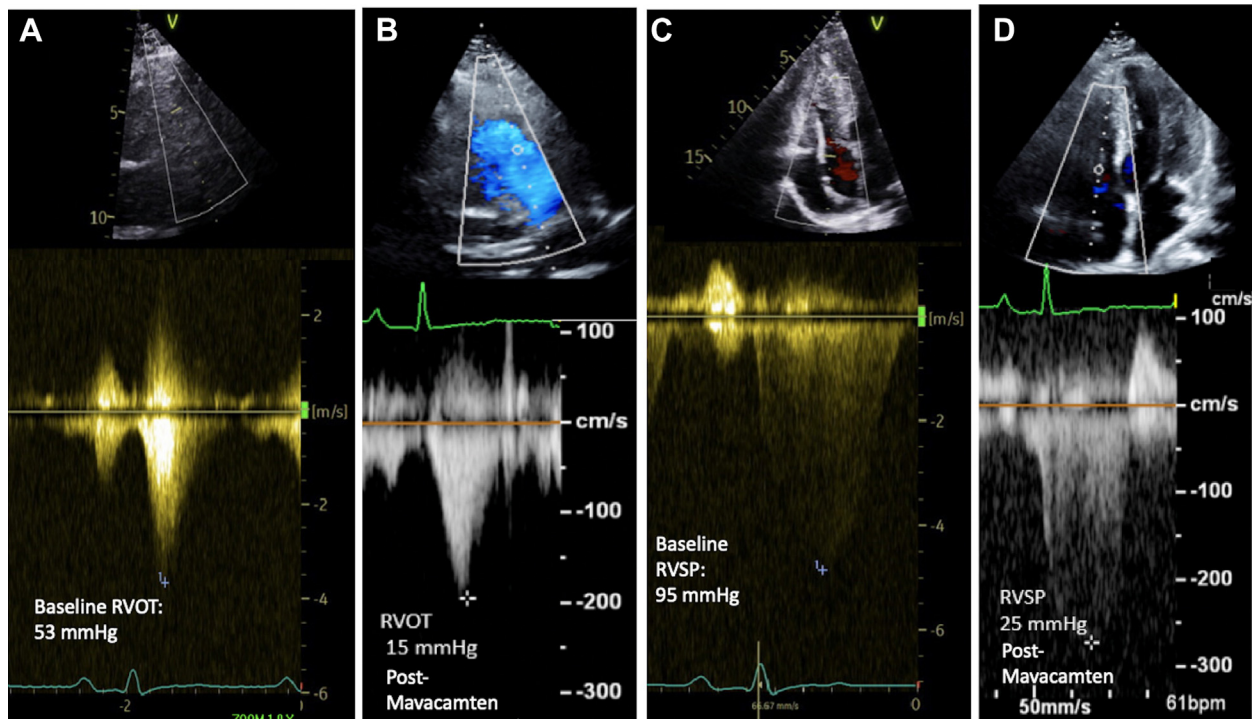
Baseline RVOT (A) and follow-up RVOT at 28 weeks (B) initial (C) and follow-up (D) RVSP as estimated from tricuspid regurgitation jet at rest. Note differences in scale. Abbreviations as in **Figure 2**.

ventricular hypertrophy (RVH), defined as RV wall thickness of greater than 5 mm. In rare cases, significant RVH can lead to symptomatic, mechanical obstruction of the RVOT.

Although RVH of at least 8 mm is found in approximately 33% of patients with HCM,[1] RVOT obstruction is rarer. Reports of right-sided obstruction have been largely limited to case studies or case series; thus, its exact incidence is unknown.[2-4] One small observational cohort of 34 patients with HCM with severe RVH (>10 mm) identified RVOT obstruction in 15% of patients.[5] Hypertrophy of the interventricular septum can contribute to right-sided obstruction through physical bulging into the septal aspect of the RVOT.[3] The specific genetic risk factors that determine patients with HCM with RVOT obstruction are largely unknown.[6] RVOT obstruction may represent a common downstream manifestation of a variety of genetic causes of severe RVH. Regardless of its cause, patients with HCM with severe RV involvement (maximal RV wall thickness >10 mm) seem to be at increased risk of syncope,

heart failure, and death compared with other patients with HCM.[6]

In part due to its rarity, management of RVOT obstruction in HCM is poorly defined and frequently requires a highly individualized treatment approach. Pharmacotherapeutics including beta blockers and non-dihydropyridine calcium channel blockers are indicated as first-line therapy in patients with HCM with NYHA functional class II or III symptoms, and are similarly reasonable in patients with symptomatic RVOT obstruction.[1] If medical therapy is insufficient, septal reduction therapy with surgical myectomy has been demonstrated to simultaneously relieve both LVOT and RVOT obstruction in some patients.[7] Targeted surgical interventions on the RVOT itself via patch enlargement or surgical resection of contributory muscle bundles have also shown efficacy for relief of RVOT obstruction in selected patients.[8] The use of myosin inhibitors for RVOT obstruction has not yet been evaluated because both initial studies demonstrating efficacy of mavacamten in patients with HCM (EXPLORER-HCM and VALOR-HCM)

focused on hemodynamically significant LVOT obstruction.[9] Although a study of mavacamten in patients with HCM without LVOT obstruction (OBSERVE-HCM) is ongoing, hemodynamically significant left-sided obstruction is currently required for mavacamten initiation.[9]

FOLLOW-UP

In this study, invasive hemodynamics were essential for clarifying the relative contributions of RVOT vs LVOT gradients to her symptoms. Disproportionate elevation in right-sided filling pressures strongly suggested that her right-sided obstruction was the primary driver of her reduced cardiac output and associated heart failure symptoms. Thus, relief of right-sided obstruction via the anti-inotropic effects of mavacamten offered the potential to reduce the patient's burden of symptoms and defer major cardiac surgery. Indeed, we found that her symptoms were significantly improved after starting mavacamten.

CONCLUSIONS

Although the novel myosin inhibitor mavacamten has recently demonstrated efficacy in reducing the severity of LVOT obstruction, no prior data exist regarding its use in patients with RVOT obstruction. Here, we present the first known case of relief of hemodynamically significant RVOT obstruction in a patient with HCM through use of mavacamten.

ADDRESS FOR CORRESPONDENCE: Dr Lili A. Barouch, Johns Hopkins University, Division of Cardiology, 5450 Knoll North Drive, Suite 170, Columbia, Maryland 21045, USA. E-mail: barouch@jhmi.edu.

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KEY WORDS cardiomyopathy, echocardiography, ejection fraction, left ventricle, murmur, right ventricle, treatment

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