Treatment of Severe Left Ventricular Outflow Tract Obstruction and Mitral Regurgitation With Alcohol Septal Ablation

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INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is a common genetic heart disease with varying genotypic and phenotypic characteristics.[1] The diagnosis and evaluation of HCM can be challenging as there are several mimickers of this morphology with or without obstruction (left ventricular [LV] hypertrophy in the setting of hypovolemic or hyperdynamic functional states, infiltrative diseases, glycogen storage disease, etc.).[2] There is a wide spectrum of clinical presentations from asymptomatic, to subclinical, to severely symptomatic patients, along with a variety of clinical manifestations including heart failure, atrial or ventricular arrhythmias, LV outflow tract (LVOT) obstruction, and mitral regurgitation (MR). While medical therapy is the first-line treatment for symptomatic HCM, many patients require invasive therapy with either alcohol septal ablation (ASA) or surgical interventions including septal myectomy and/or mitral valve (MV) repair/replacement.[1] While surgical intervention is often considered to be more durable and indicated for more severe symptoms, ASA can also be a highly successful invasive treatment strategy in appropriately selected individuals, even in patients with severe MR.[3]

CASE PRESENTATION

A 75-year-old woman with a history of hypertension, hyperlipidemia, and HCM presented with progressive dyspnea and chest pain on exertion refractory to medical therapy. The patient was previously trialed on calcium channel blockers and disopyramide; however, she developed intolerance due to side effects. Metoprolol succinate was well tolerated and uptitrated to a maximum dose (100 mg twice daily), but progressive dyspnea and chest pain continued. The workup included ambulatory electrographic event monitoring, which showed no significant atrial or ventricular arrhythmias. Cardiac magnetic resonance imaging demonstrated normal LV systolic function (without late gadolinium enhancement), asymmetric septal hypertrophy (16 mm), evidence of LVOT obstruction, severe left atrial enlargement, and moderate-to-severe MR (as evaluated by volumetric analysis). Coronary angiogram demonstrated mild luminal coronary artery disease and large, branching first septal perforating vessel (Video 1). Echocardiogram demonstrated asymmetric LV septal hypertrophy, severe LVOT obstruction with a peak gradient of at least 100 mm Hg at rest and 130 mm Hg with Valsalva, and severe MR with a mildly elongated anterior mitral leaflet and only mild systolic anterior motion (SAM) of the MV apparatus. After a lengthy, multidisciplinary care team discussion with the patient, she elected to pursue ASA rather than septal reduction surgery with possible MV repair/replacement.

Intraprocedural hemodynamics were obtained preablation, which correlated well with echocardiographic assessments. At baseline, echocardiography confirmed the presence of asymmetric LV septal hypertrophy, mildly elongated anterior mitral leaflet with severe MR (Videos 2-4), and mild SAM (Figure 1). By echocardiography, LVOT gradient was estimated to be 150 mm Hg at rest and as high as 293 mm Hg following premature ventricular contraction (PVC; Figure 2A, B). Continuous-wave Doppler of the MR waveform demonstrated an LV to left atrial gradient of 256 mm Hg (Figure 3). Invasive hemodynamics prior to ablation demonstrated an aortic pressure of 136/51 mm Hg and an LV systolic pressure of 267 mm Hg at rest and near 300 mm Hg following PVC (Figure 4A, B).

VIDEO HIGHLIGHTS

Video 1: Coronary angiogram of the left coronary system demonstrating mild luminal irregularities and large, branching first septal perforating vessel.
Video 2: Parasternal long-axis view demonstrating asymmetric LV hypertrophy with elongated anterior mitral leaflet.
Video 3: Parasternal long-axis view with color Doppler demonstrating severe MR.
Video 4: Apical 4-chamber view with color Doppler demonstrating severe MR.
Video 5: Modified parasternal long-axis view following injection of intracoronary ultrasound-enhancing agent into septal perforating vessel with enhancement of the proximal interventricular septum.
Video 6: Apical 4-chamber view with color Doppler following ASA demonstrating only mild MR.
Video 7: Three-month follow-up echocardiogram of parasternal long-axis view with color Doppler demonstrating only mild MR.

View the video content online at www.cvcasejournal.com.

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Keywords: Hypertrophic cardiomyopathy, Left ventricular outflow obstruction, Alcohol septal ablation, Mitral regurgitation

Conflicts of interest: The authors reported no actual or potential conflicts of interest relative to this document.

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2468-6441
https://doi.org/10.1016/j.case.2022.06.006

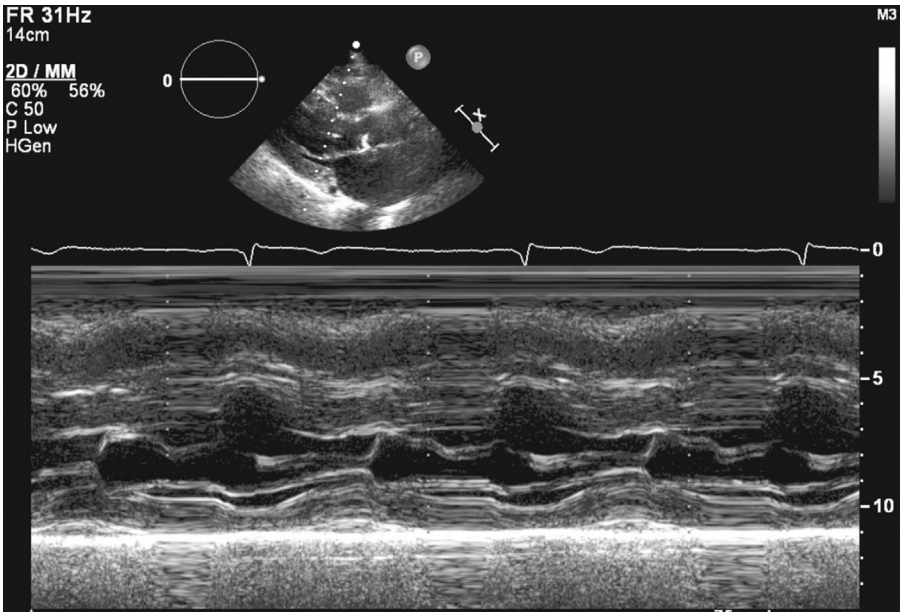

Figure 1 M mode through MV demonstrating SAM of MV apparatus.

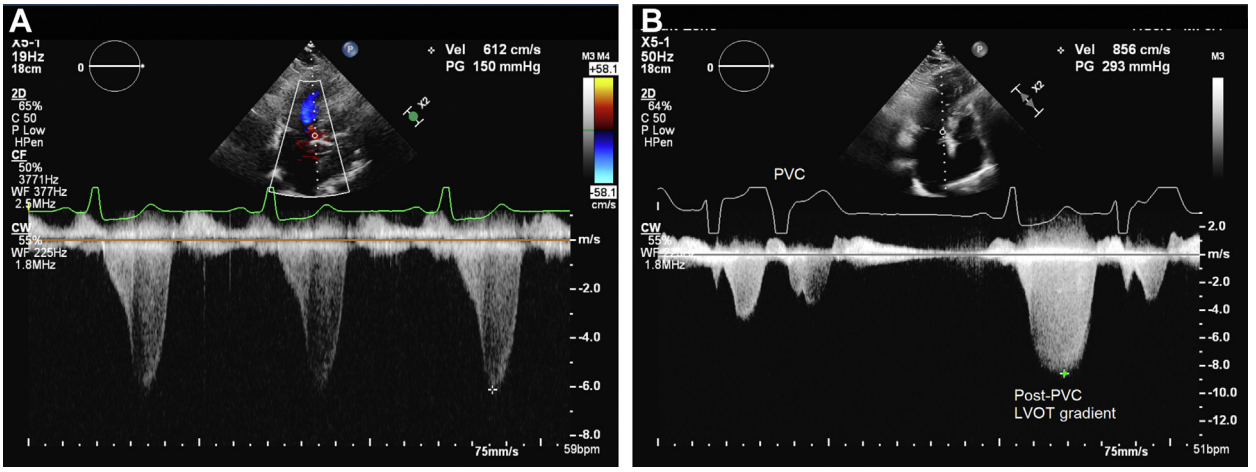

Figure 2 **(A)** Continuous-wave Doppler through the LVOT demonstrating a resting gradient of 150 mm Hg. **(B)** Continuous-wave Doppler through the LVOT demonstrating a gradient of 293 mm Hg following a PVC.

Ultrasound-enhancing agent was administered to the first septal perforating vessel that showed adequate treatment zone in the proximal interventricular septum (Video 5). Following a total of 1.5 mL of intracoronary ethanol delivered to the first septal perforating vessel, hemodynamics significantly improved. After alcohol ablation, the resting LVOT gradient was roughly 13 mm Hg by echocardiography (Figure 5A), with a 27 mm Hg gradient following PVC (Figure 5B) and a 10 mm Hg LVOT gradient by invasive hemodynamic assessment (Figure 6). The resting LV systolic pressure improved from 267 to 178 mm Hg following ablation. Furthermore, there was significant reduction in MR (Video 6) following ablation. Follow-up echocardiography 3 months after the procedure demonstrated continued improvement in the LVOT gradient (Figure 7) and MR (Video 7), and the patient's symptoms drastically improved.

DISCUSSION

The invasive management of symptomatic patients with HCM is complex, with many patient-specific and anatomical considerations. More specifically, after failing medical therapy, many patients will require septal reduction therapy (SRT) to manage overall symptom burden. As a result of a variety of anatomical features (thickened interventricular septum, hypercontractile states, relative low preload states, abnormal MV pathology, and apically displaced papillary muscles),

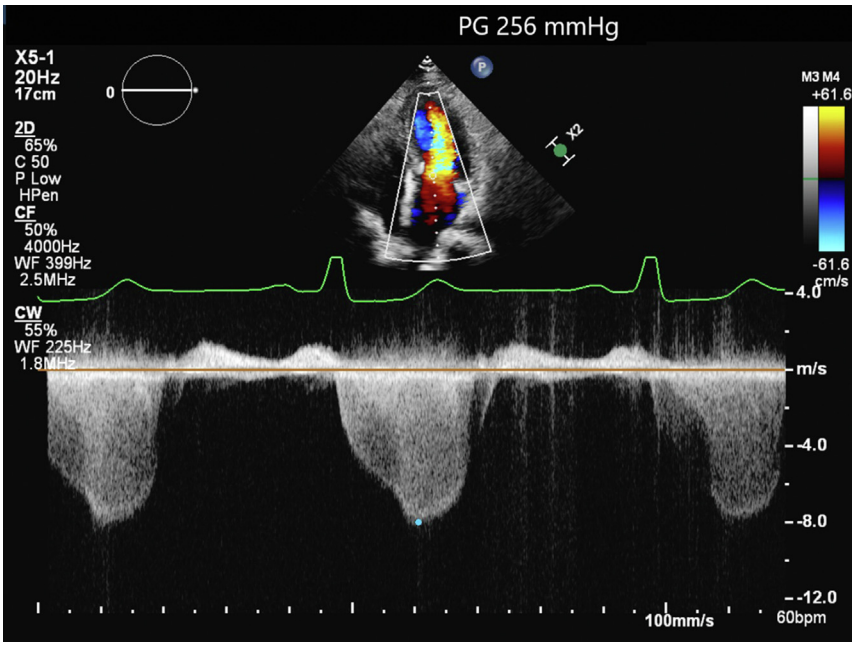

Figure 3 Continuous-wave Doppler through the MV demonstrating significantly higher peak gradient (256 mm Hg) and different waveform morphology than LVOT gradient.

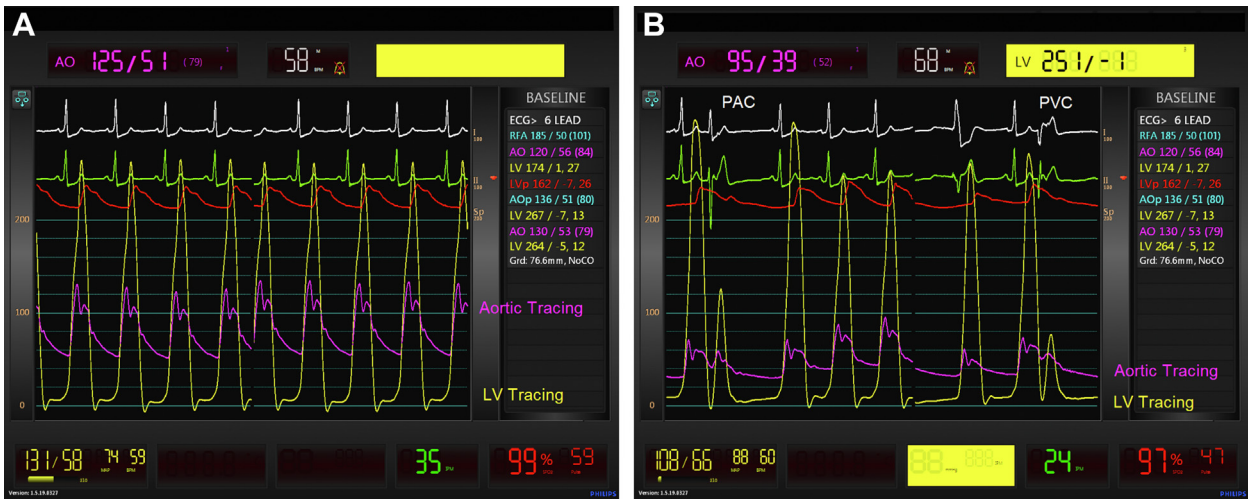

Figure 4 **(A)** Invasive hemodynamics demonstrating a resting LV systolic pressure of 267 mm Hg and an aortic pressure of 130/53 mm Hg (137 mm Hg systolic gradient). **(B)** Invasive hemodynamics demonstrating classic "Brockenbrough-Braunwald-Morrow" sign following premature atrial contraction with an increased LV outflow gradient and a decrease in pulse pressure.

LVOT obstruction may be multifactorial in nature.[4,5] Similarly, the mechanism of MR in patients with HCM is also multifactorial and can be in part attributed to LVOT obstruction with elevated LV systolic pressures, abnormal MV pathology with elongated anterior leaflets, and papillary muscle displacement.[1] As a result, patients with severe LVOT obstruction and concomitant severe MR have historically been referred for surgical management due to evidence that suggests more successful and durable outcomes with SRT as well as the ability to address MV pathology.[6,7]

There is, nonetheless, increasing evidence that surgical SRT alone may help to improve the severity of MR in the absence of severe underlying MV pathology.[8,9] While it is common for patients with HCM to have MR attributable to both primary and secondary causes, it is important to differentiate those patients with significantly abnormal MV pathology leading to MR and those patients who have significant MR despite relatively normal pathology. While not fully understood, the reduction of MR with SRT is believed, in part, to be a result of improving the underlying LVOT gradient (by reducing rapid ejection of blood through the LV and limiting the Venturi drag forces on MV apparatus) as well as reduction of LV systolic pressures and subsequent offloading of the pressure gradients between the left ventricle and left atrium.[8,10,11] Yu *et al*[8] describe a strong relationship between

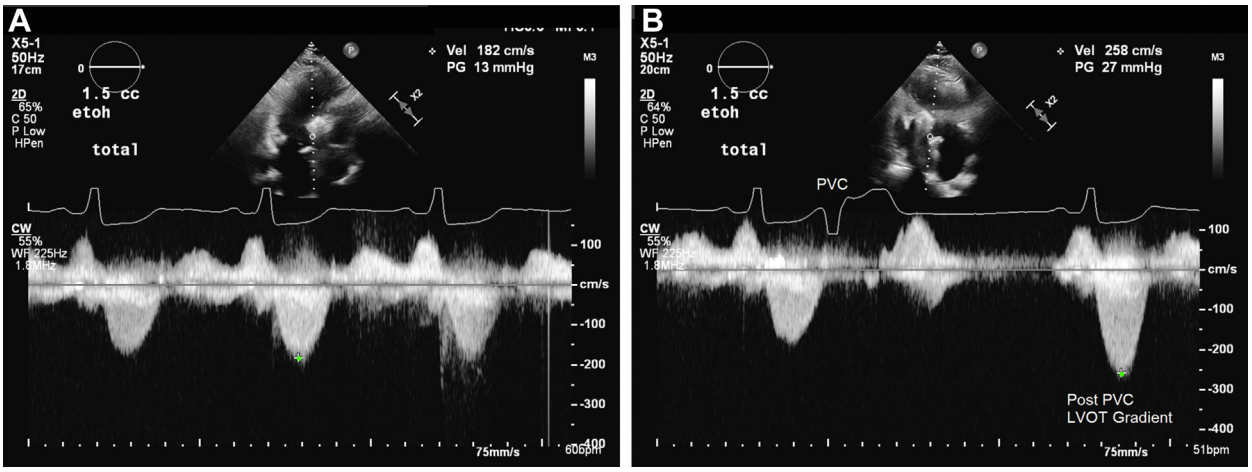

Figure 5 **(A)** Following ASA, continuous-wave Doppler through the LVOT now only demonstrates a resting gradient of 13 mm Hg. **(B)** Following ASA, continuous-wave Doppler through the LVOT now only demonstrates a 27 mm Hg gradient following a PVC.

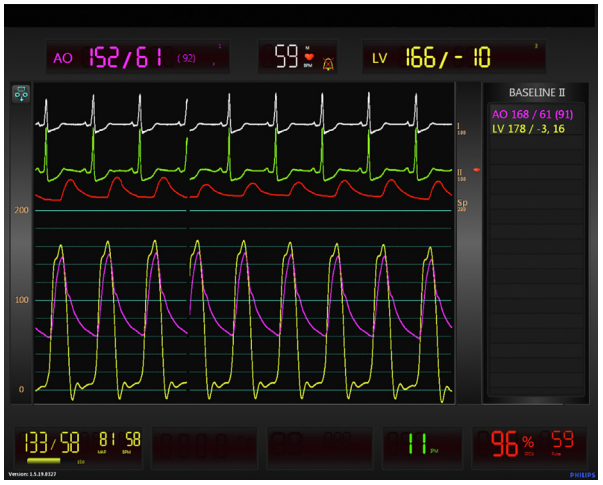

Figure 6 Following ASA, invasive hemodynamics demonstrating a 10 mm Hg resting LV systolic gradient.

LVOT peak gradient and MR severity (as measured by jet area) as well as improvement in the severity of MR following septal myectomy in patients without significant intrinsic MV pathology.[8] There may also be regional and functional differences following SRT that can impact the LVOT and MV geometry and impact the severity of MR.[12] While all of these findings have not been as well established in those undergoing ASA, the underlying physiology remains similar.

We present a case of severe LVOT obstruction and MR, in the absence of significant MV pathology, which was successfully treated with ASA. We hypothesized that the severity of the patient's MR was attributable to a variety of factors, including the significant LVOT gradient and elevated LV systolic pressures, not only the MV pathology alone. In conjunction with patient-specific wishes, this provided the opportunity to perform ASA as the initial invasive strategy aimed at addressing the severe LVOT obstruction and concomitant severe MR.

CONCLUSION

Alcohol septal ablation remains an important invasive treatment strategy in patients with HCM and severe LVOT obstruction, even in the setting of significant MR. While there are no large, randomized trials that directly compare invasive treatment strategies, the decision to pursue various invasive treatment options should be based on patient preference, multidisciplinary care team recommendations, and appropriate and suitable anatomy. The presence of significant MR, without significantly abnormal MV pathology, in conjunction with a thorough risk and benefit discussion with the patient, should not specifically preclude attempts at ASA; however, more dedicated research would help clarify the role of ASA in the management of patients with HCM-related MR and LVOT obstruction.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2022.06.006.

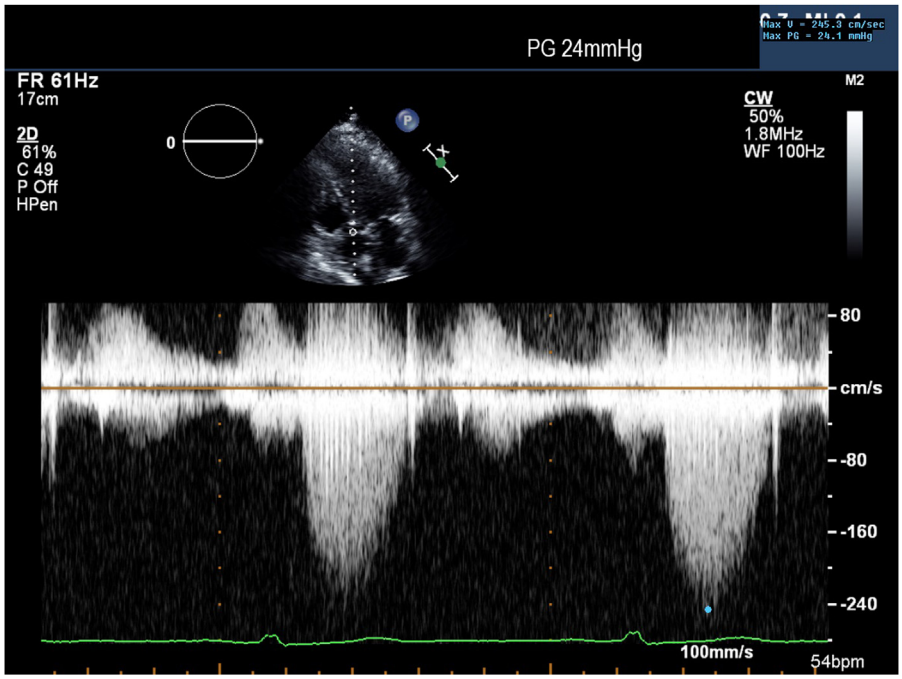

Figure 7 Three-month follow-up echocardiogram demonstrating LVOT gradient of 24 mm Hg.

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