

Percutaneous Septal Reduction Therapy in a Patient with Severely Symptomatic Hypertrophic Obstructive Cardiomyopathy

An experience from a tertiary care centre

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HYPERTROPHIC CARDIOMYOPATHY (HCM) IS a heterogeneous group of genetically-transmitted diseases characterised by abnormal hypertrophy and disarray of the cardiomyocytes.¹ The hypertrophy is usually asymmetrically affecting the basal septum, though other morphological variants such as apical or mid-septal which are also not uncommon. Although the global prevalence of HCM is reported to be around 0.16–0.29% (approximately 1 in 344–625) of the general adult population.¹ The true prevalence is likely higher as many patients with HCM are asymptomatic and diagnosed during family screening or late in adult life once symptoms begin.^{2,3} With increased awareness of the disease, improved cardiac imaging modalities and increased availability of genetic screening of families, the reported prevalence appears to be increasing and it is now estimated that around 0.6% of the population carry HCM-related genes.⁴

Patients usually present with symptoms late in adult life. The more severe forms may present in early childhood or the teenage years. The symptoms include dyspnoea related to the diastolic dysfunction or left ventricular outflow tract (LVOT) obstruction, angina-like chest pain due to oxygen demand supply mismatch caused by the severe hypertrophy or light-headedness, syncope or palpitations due to the LVOT obstruction or arrhythmias. LVOT obstruction at rest occurs in around a third of patients with HCM while another third has provokable obstruction. The remaining third have hypertrophy without obstruction.¹

Management of patients with HCM can be challenging and depends on the symptoms experienced by the patient. Pharmacological management with negative inotropic and negative chronotropic agents such as beta-blockers, calcium channel blockers and disopyramide helps alleviate symptoms by improving left ventricular diastolic filling and systolic stroke volume, but is achieved in only 50% of the cases.⁵ Additional interventional treatment strategies should be considered early during the course of the disease. Outcomes of randomised studies on dual-chamber

electrosystolic stimulation with a dual chamber pacemaker have been disappointing.⁶ Implantable cardioverter-defibrillators should be considered for those at high risk for sudden cardiac death.

For patients with significant LVOT obstruction, septal reduction strategies in the form of surgical septal myectomy (SM) or alcohol septal ablation (ASA) should be considered. These alternative therapeutic modalities are supported by a large body of evidence confirming positive short- and long-term outcomes in symptomatic patients.¹ The open-heart surgical approach was the only treatment option available until the early 90s. This commentary offers a description of the authors' experience with treating a severely symptomatic middle-aged female patient with obstructive HCM. The patient did not respond to medical therapy and successfully underwent ASA at a tertiary care hospital in Muscat, Oman in 2017. To the best of the authors' knowledge, this is the first such experience from the country.

An Exemplary Case From The Authors' Service

A 51-year-old active, obese female patient (BMI 36.8 kg/m²) with Sjögren's syndrome, dyslipidaemia, fatty liver and obstructive sleep apnoea presented to a tertiary care hospital in Muscat, Oman, in 2017 with worsening exertional dyspnoea. She had been investigated previously and had an echocardiogram a few years earlier which was reported as good left ventricular function with concentric left ventricular hypertrophy (LVH). A 12-lead electrocardiogram (ECG) revealed sinus rhythm with LVH and secondary repolarisation abnormalities [Figure 1A]. A gated cardiac computed tomographic study showed normal coronary arteries. The investigations for a possible respiratory cause were unremarkable.

In view of the worsening dyspnoea and possible pulmonary hypertension, the patient underwent a repeat

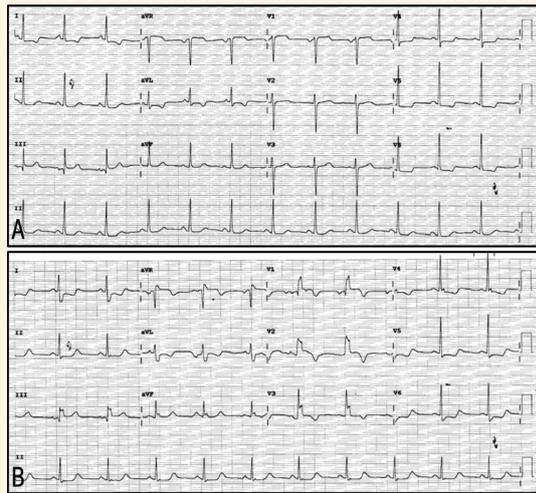


Figure 1: Baseline standard 12-lead electrocardiogram of a 51-year-old female patient showing (A) normal sinus rhythm and voltage criteria for left ventricular hypertrophy with secondary repolarisation abnormalities seen in the lateral leads and (B) complete right bundle branch with ST elevation in V1/V2 consistent with a septal infarction taken after alcohol septal ablation. The atrio-ventricular conduction time is also normal.

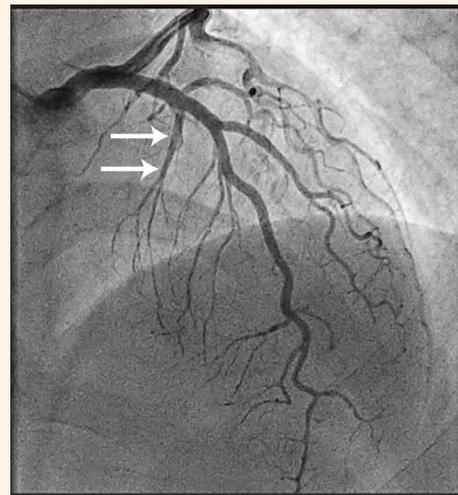


Figure 2: Selective coronary angiogram of the left coronary system in the cranial projection laying out the course of the left anterior descending coronary artery of a 51-year-old female patient. The dominant septal perforator branch (arrows) arising from the proximal segment, which was the target for balloon occlusion and subsequent alcohol injection, can also be seen.

echocardiogram. The echocardiogram revealed moderate asymmetrical septal hypertrophy (ASH) with an interventricular septal (IVS) diastolic dimension of 21 mm (normal: <11 mm) and a posterior left ventricular wall diastolic dimension of 10 mm (normal: <11 mm; IVS/posterior wall ratio: 2.1). Systolic anterior motion (SAM) of the anterior mitral valve leaflet was noted with a resting left ventricular mid-cavitary gradient of 42 mmHg that accentuated to 51 mmHg with the Valsalva manoeuvre. There was mild concomitant mitral regurgitation with a normal-appearing mitral valve apparatus. There was no evidence of pulmonary hypertension. The patient's previous echocardiogram,

from approximately five years earlier, was reviewed and confirmed the absence of ASH or SAM.

The patient was started on oral bisoprolol up to a dose of 10 mg once daily, with modest symptomatic improvement. An exercise-stress echocardiogram was performed while on maximum treatment. She was only able to exercise for 5.02 minutes on the standard Bruce protocol attaining a total of seven metabolic equivalents (METs). Her blood pressure dropped from 146/68 mmHg to 135/37 mmHg at peak stress. The test was stopped due to severe dyspnoea. No significant arrhythmias were documented. However, the echocardiogram at peak exercise recorded a significant gradient of 80 mmHg across the mid-

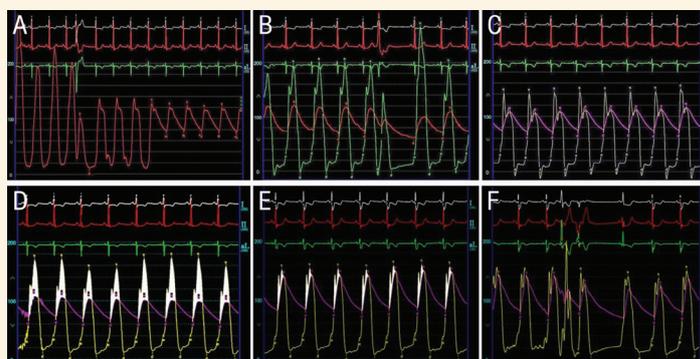


Figure 3: Haemodynamics obtained at the time of first, left heart catheterisation showing (A) a significant pressure gradient between the left ventricular (LV) apex and LV outflow tract with no gradient between the outflow tract and the aorta, (B) the classic Brockenbrough-Braunwald-Morrow sign with a marked post-extra systolic accentuation of the peak to peak pressure and mean gradients, (C) septal ischaemia resulting from balloon-occlusion of the septal perforator branch, (D) a significant 100 mmHg gradient measured between the LV and aorta using simultaneous pressure tracings from both chambers (E) marked reduction in the resting pressure gradient after injection of 100% ethanol into the target septal perforator and (F) complete elimination of post-extra-systolic accentuation after alcohol injection.

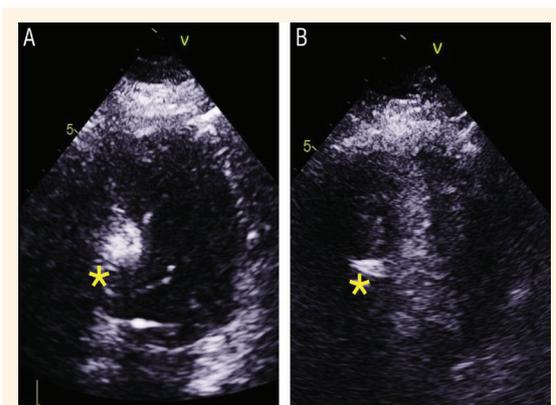


Figure 4: Echocardiographic scans of the 51-year-old female patient obtained during alcohol septal ablation (A) with agitated saline and iodinated contrast mixture and (B) with ultrasound-enhancing agent. Note the focal opacification in the target area in the mid-interventricular septum (asterisk) without right ventricular extension or involvement of the papillary muscle.

left ventricular cavity with mild mitral regurgitation and normal pulmonary artery pressure. A detailed discussion was undertaken about the patient's options for septal reduction therapy in view of the failure of medical therapy and the worsening of symptoms and the presence of severe LVOT obstruction at rest which was accentuated on provocation. The patient consented to ASA.

An initial coronary angiogram demonstrated angiographically normal coronary arteries and delineated one dominant septal perforator (SP) branch in the proximal left anterior descending (LAD) coronary artery [Figure 2]. The initial resting left-ventricular-aortic mean pressure gradient was measured at 38 mmHg through a gradual pull-back performed using an end-hole catheter [Figure 3A]. The post-extra-systolic beat showed a dramatic accentuation of the peak pressure gradient to 160 mmHg and the mean pressure gradient to 100 mmHg indicating severe dynamic mid-cavity obstruction, which is the classic Brockenbrough-Braunwald-Morrow sign of dynamic LVOT obstruction [Figure 3B]. Balloon occlusion of the dominant SP for two minutes resulted in a remarkable diminution of the LV gradient down to 22 mmHg [Figure 3C]. A contrast-enhanced echocardiogram was performed using agitated saline and iodinated contrast mixture and Definity® [Lantheus Medical Imaging, Billerica, USA] ultrasound contrast administered through a microcatheter in the target SP branch, revealed a very focal area of opacification in the septum at the point of anterior mitral valve leaflet-septal contact and the aliasing zone on colour Doppler images [Figure 4].

A standard coronary guide wire was secured into the distal LAD and a stiffer support-type coronary guide wire, in the dominant SP branch. A coronary microcatheter was advanced into the side branch. This was intended for local alcohol delivery. After excluding the SP from the LAD with a 2.5 × 9.0 mm semi-compliant balloon, 100% ethanol was injected into the SP in 0.5 mL aliquots to a total amount of 2 mL. The resting mean pressure gradient eventually decreased to 21 mmHg with no post-extra-systolic accentuation [Figures 3D–F].

The procedure was well-tolerated and no significant arrhythmias or heart blocks were encountered [Figure 1B]. She experienced mild, manageable chest pain and transient complete heart block that resolved with an otherwise unremarkable hospital stay. The immediate post ablation transthoracic echocardiogram demonstrated only a 5 mmHg gradient across the mid-LV cavity both at rest and post Valsalva. There was now an absence of SAM of the anterior mitral valve leaflet and only trivial mitral regurgitation. Similar findings were documented on an echocardiographic study done 10 days later, at which point the patient had already resumed her daily activities without any symptoms. A stress echocardiogram was repeated eight weeks after the intervention (off bisoprolol). At this time the patient's exercise duration had increased significantly to 8.1 minutes attaining 10 METs with a normal blood pressure response. Both the resting and immediate post-exercise echocardiogram revealed no mid-cavitary gradient. At two-year follow up, the patient was off-treatment and remained asymptomatic with a good exercise tolerance.

The authors confirm that written consent for submission and publication of this work, including images and associated tests, has been obtained from the patient. The patient had no objection to the publication, provided her identifying details were anonymised.

Author Reflections

ASA has been gaining favour worldwide as the procedure of choice in managing patients with HCM and LVOT obstruction, who fail medical therapy. The first septal ablation was performed by Ulrich Sigwart in 1994.⁷ He described three patients with severe dynamic subaortic obstruction. All three patients responded to a trial of balloon occlusion of the target SP branch, following which injection of absolute alcohol completely abolished the outflow tract gradient within seconds of alcohol delivery and remained eliminated

even at 12 months of follow-up. The procedure aims to induce a controlled chemical infarction of left ventricular septal myocardium at the point of septal-mitral leaflet contact. It is not uncommon to see a resurgence in gradient after days or weeks due to local myocardial oedema. Once necrosis and fibrosis set in, thinning and fibrotic retraction of the basal septum results in a more gradual reduction in outflow gradient.⁸ The effect is augmented by mild left ventricular dilatation and regression of hypertrophy due to afterload reduction.

Clinical and echocardiographic outcomes after ASA appear comparable to SM. Early observational studies comparing outcomes after ASA and SM, showed a significant reduction in LV gradient and a marked improvement in functional status without a significant difference in in-hospital mortality.⁹ In a meta-analysis of twelve observational studies, investigators from the Cleveland clinic showed no difference in short term (3-month) and long term (5-year) mortality.¹⁰ ASA produced a significant improvement in New York Heart Association functional class, post-procedural reduction in septal thickness and LVOT gradient. There was no difference in post-procedural LV ejection fraction and degree of mitral regurgitation. Patients undergoing ASA very commonly developed right bundle branch block after septal ablation and were more likely to require permanent pacemaker implantation (odds ratio [OR] = 2.57, 95% confidence interval [CI]: 1.68–3.93; $P < 0.001$) and had higher residual gradients.⁹

Another concern about ASA was the hypothetical risk of scar-related ventricular arrhythmias and increased risk of sudden cardiac death. One systematic review addressing this concern, reported similar rates of all-cause mortality and sudden cardiac death in patients treated with ASA and SM.¹¹ Furthermore, when adjusted for baseline characteristics, the odds ratio for treatment effect on all-cause mortality was 12.5% lower in the ASA-treated patients (OR = 0.28, 95% CI: 0.16–0.46) compared to those who underwent SM (OR = 0.32, 95% CI: 0.11–0.97).¹¹ The annual risk of sudden cardiac death after ASA is reported to be 0.5% per year, which is comparable to the general population.^{12–14}

Conclusion

ASA is a viable alternative to surgical myectomy in symptomatic patients with hypertrophic obstructive cardiomyopathy. The procedure results in a significant improvement in functional status and carries favourable short-term and long-term outcomes. The current authors' experience has shown a favourable

immediate and long-term outcome for this condition in the first case treated with ASA in Oman at a tertiary care hospital. Extant literature suggests that it is relatively safe, less invasive and cheaper than open heart myectomy which should be performed by experienced surgeons in specialised centres capable of performing high risk procedures. The successful outcome of this endeavour opens up a treatment option to patients in Oman that was not previously readily available to them.

AUTHOR CONTRIBUTIONS

All authors have contributed equally in writing the manuscript, verifying the scientific contents and preparing its final version after review for publication. All authors approved the final version of the manuscript.

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