Alcohol Septal Ablation to Reduce Heart Failure

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KEYWORDS

• Hypertrophic cardiomyopathy • Alcohol septal ablation • Heart failure

KEY POINTS

- Hypertrophic cardiomyopathy (HCM) is the most common inheritable cardiac disorder with variable phenotypic expression.
- HCM can induce heart failure via left ventricular outflow tract obstruction, mitral regurgitation, diastolic dysfunction, and systolic dysfunction, as well as secondary pulmonary hypertension and atrial fibrillation.
- Severely symptomatic patients, despite optimal medical therapy, should be considered for invasive septal reduction techniques.
- Alcohol septal ablation can reverse the various mechanisms of heart failure in HCM and lead to clinical improvement with excellent short and intermediate results. Long-term results are promising but lacking in number, so more work is needed to describe the sustainability of the results in various patient populations.

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is the most common inheritable cardiac disorder, with an estimated prevalence of 0.2%, or 1 case in 500 individuals[1,2]. Most of these patients have no or mild symptoms, but around 10% will develop heart failure symptoms refractory to medical therapy.[3] These patients are frequently considered for invasive septal reduction techniques: either surgical septal myectomy or alcohol septal ablation (ASA).[4] This article discusses the various mechanisms through which HCM induces heart failure, how ASA can reverse each of these mechanisms, and the evidence for clinical improvement and sustainability after the procedure.

MECHANISMS OF HEART FAILURE IN HYPERTROPHIC CARDIOMYOPATHY

Left Ventricular Outflow Tract Obstruction

The hallmark finding of symptomatic obstructive HCM is the presence of left ventricular outflow tract (LVOT) dynamic obstruction. About one-third of patients will have a significant LVOT gradient (defined as a gradient $\geq$30 mm Hg) at rest; one-third will have a significant gradient only with provocation, and the final one-third will not have a significant gradient at rest or with provocation.[5] Systolic contraction of the hypertrophied basal septal segment was initially thought to be the cause of this dynamic obstruction, but further studies have shown that drag forces imposed on an abnormal mitral apparatus leading to systolic anterior motion (SAM) of the anterior mitral leaflet are the cause of LVOT obstruction.[6–9] Mitral apparatus abnormalities that have been correlated with LVOT obstruction include mitral valve leaflet elongation, abnormal chordal attachment, anterior displacement of the papillary muscles, and bifid papillary muscle.[9,10] This helps explain the presence of severe LVOT obstruction in some patients in the absence of severe septal hypertrophy.

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Mitral Regurgitation

Mitral regurgitation has long been correlated with obstructive HCM. In the majority of cases, the regurgitation is a secondary process directly related to the SAM of the mitral leaflet. This has been described in angiographic studies with an eject-obstruct-leak timing of events.[9,11] Thus, the onset of mitral leaflet–septal contact is one of the determinants of the severity of obstruction as well as the prolongation of ejection time and the extent of mitral regurgitation.[9,11–13] Hemodynamic conditions that affect LVOT obstruction often have a similar effect on mitral regurgitation severity. Given the link between obstruction and mitral regurgitation, afterload reduction and diuretics can lead to worsening of mitral regurgitation in this setting. The mitral regurgitation jet is directed posteriorly and laterally and occurs in mid to late systole. Centrally or anteriorly located regurgitant jets, or holosystolic regurgitation, should be further investigated for primary mitral valve disease.

Diastolic Dysfunction

Diastolic dysfunction represents a significant and largely misunderstood cause of heart failure in HCM. Observational studies have shown that diastolic dysfunction starts early and will progress in HCM patients over time, and that advanced diastolic dysfunction (defined as a restrictive filling pattern on echo-Doppler interrogation) is an independent predictor of death and need of heart transplantation.[14] HCM can affect diastolic filling via increased left ventricular (LV) chamber stiffness, impaired relaxation and/or diminished residual chamber dimensions from massive hypertrophy (the latter works through increased LV chamber stiffness). It was initially believed that increased chamber stiffness due to hypertrophy and myocardial fibrosis was the cause of diastolic dysfunction in HCM patients. Although this does play a role, it has become increasingly evident that impaired relaxation also plays a large and more complex role. The systolic load from outflow tract obstruction, delayed inactivation from increased sarcoplasmic calcium, and nonuniformity of systolic and diastolic ventricular loads cause the impairment in ventricular relaxation.[4,9,12,15–18] Already a difficult to treat condition, diastolic dysfunction in HCM can be exceedingly challenging, as diuretics are the baseline for therapy but can actually worsen symptoms via increased outflow tract obstruction.

Systolic Dysfunction

LV ejection fraction (EF) is usually normal to hyperdynamic in patients with HCM, but in end-stage or "burnt-out" HCM, depressed EF occurs.[19,20] Replacement fibrosis is usually present in these patients and may be related to the underlying myocardial fiber disarray, myocardial ischemia and/or infarction due to micro or macrovascular disease, or some combination of these components. At this stage of the disease, LVOT obstruction is usually absent despite a progression in clinical symptoms and worsened prognosis. LV systolic dysfunction represents a minority of cases, but with a grave prognosis, with a hazard ratio for death or cardiac transplantation reported as high as 25.[14,21] At this end stage, limited therapeutic options are available, so patients should be considered for V_{O_2} testing in preparation for heart transplantation.

Pulmonary hypertension

It is not uncommon for HCM patients to have pulmonary hypertension. This is due to the elevated LA pressure because of LV diastolic dysfunction, and in the setting of dynamic obstruction, mitral regurgitation. Mean PA pressure usually decreases as LA pressure decreases after successful septal reduction therapy, and there are several examples of patients having a dramatic decline in PA pressure after alcohol septal ablation.

Notwithstanding, it is important to carefully consider the etiology of pulmonary hypertension in HCM patients and determine the actual contribution of elevated LA pressure. This is possible with right heart catheterization where the transpulmonary gradient is measured along with pulmonary vascular resistance. Pulmonary hypertension (not type II), in and of itself, is not a reason to withhold septal reduction therapy, even if it were due to pulmonary parenchymal or vascular disease. This is due to the contribution of increased LA pressure to the elevated PA pressures. Thus, some decline in mean PA pressure occurs, albeit the elevated PA pressures are not normalized in these patients. Conversely, if HCM patients have pulmonary hypertension largely due to elevated LA pressure, it is not advisable to use pulmonary vasodilators, as they can lead to pulmonary edema in this setting.

Atrial fibrillation

HCM patients with LA enlargement (due to diastolic dysfunction and mitral regurgitation) have a higher risk of atrial fibrillation. The arrhythmia in turn increases the risk for systemic embolic events and for the development of acute heart failure. Given the presence of LV diastolic