



EDITORIAL COMMENT

Alcohol septal ablation for the treatment of obstructive hypertrophic cardiomyopathy: A demanding option[☆]



Ablação septal alcoólica no tratamento da miocardiopatia hipertrófica obstrutiva: uma opção exigente

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The management of patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM) has, over the years, generated considerable controversy.

A subaortic gradient, at rest or with provocation, which demonstrates the presence of obstruction, is found in a significant number of patients. It frequently causes symptoms and is associated with worse prognosis, including higher risk of heart failure, atrial fibrillation and cardiovascular death.¹ Although there is currently no evidence that abolishing the gradient in asymptomatic patients improves prognosis, in symptomatic patients, reducing the gradient (at rest and particularly during exertion) results in symptomatic improvement in many cases.

Current guidelines recommend negative inotropic drugs (beta-blockers, verapamil and disopyramide) for the initial treatment of such cases.² However, for patients with persistent symptoms or intolerance to drug therapy, mechanical removal of the obstruction should be considered. There are two options: surgical septal myectomy, in which the basal portion of the interventricular septum is resected, and alcohol septal ablation (ASA), which induces necrosis in the proximal septum.

Septal myectomy, first developed in the 1960s and still considered the gold standard by which other techniques are evaluated,³ is effective in most patients when performed in experienced centers, reducing or abolishing the gradient and producing lasting symptomatic improvement,^{2,4–6} and with low operative mortality (1–2%) when performed in isolation.

ASA was introduced in 1995⁷ and rapidly developed into an attractive alternative to surgery, being less invasive, effective in gradient reduction and apparently simple to perform. There are, however, three main areas of concern associated with this treatment: the safety of the procedure, inappropriate use (there are fears that it could be seen as an easy option to be applied even when not justified by symptoms), and lack of knowledge of its long-term consequences and prognostic impact.

With regard to the safety of the procedure, careful patient selection, the use of smaller quantities of alcohol and contrast echocardiographic monitoring are important developments that have reduced the risk of damage to atrioventricular conduction tissue and hence the need for permanent pacing and the danger of the myocardial necrosis spreading to areas other than the target tissue, with potential short- and long-term consequences.

Concerns that ASA would be used inappropriately have abated with the increasing maturity of the technique in experienced centers where the fundamental factor is the careful characterization of candidates, with particular emphasis on the mechanism of obstruction and how

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this relates to symptoms. The underlying mechanism is not the same in all patients. In most cases, changes in LV geometry caused by asymmetric septal hypertrophy and anterior displacement of the papillary muscles result in contact between the mitral leaflet(s) and the septum during ventricular ejection, which creates the subaortic gradient. However, in some patients the dominant mechanism is abnormalities of the mitral valve and/or of papillary muscle insertion, in which case surgery is the better option. Furthermore, a subaortic gradient is not uncommon in elderly hypertensive patients even in the absence of significant septal hypertrophy.

The degree and extent of hypertrophy is an important factor in deciding between the treatment options and in guiding the actual procedure. In situations of extensive septal hypertrophy there may also be mid-ventricular obstruction that is mainly responsible for symptoms, rather than a subaortic gradient; in such cases the best option may be surgery, although ASA may be possible if the alcohol is administered in arteries that irrigate more distal myocardial segments.⁸

Concerns arising from the lack of knowledge of the long-term consequences and prognostic impact of ASA have lessened. Although there have been no randomized trials directly comparing septal myectomy and ASA, meta-analyses and comparative studies have not shown significant differences in survival between the two techniques,^{4-6,9} though ASA is associated with higher residual subaortic gradients and more frequent need for permanent pacemaker implantation.^{4,9} There thus appears to be good reason to consider ASA a safe and effective alternative to surgical myectomy in carefully selected and well-characterized patients.

In this issue of the *Journal*, Fiarresga et al. report the experience of their center with ASA over a four-year period,¹⁰ the first results on this technique in Portugal. As well as presenting their results, they describe their protocol in detail with regard to patient selection and the actual procedure, focusing on its risks and possible complications, together with ways to avoid or minimize them.

Their series includes 40 patients with HCM, significant obstruction (gradient >50 mmHg at rest or with provocation) and symptoms refractory to medical therapy (beta-blockers and/or calcium channel blockers).

Selection of candidates for the technique is crucial, as the authors point out, and great care was taken in this regard. As seen in other studies of patients undergoing ASA,⁹ the population was mainly female, with a mean age of around 60 – although 15 patients (37.5%) were aged 75 or over – and most had a history of hypertension. Two points merit special mention. The first is that older patients with HCM, who will naturally tend to have more comorbidities, may benefit from ASA, since they can thus avoid the risks of surgery, for which they may already have been deemed unsuitable. The second is that the presence of hypertension, possibly due to its high prevalence, is no longer seen as precluding a diagnosis of HCM. In a series by Sorajja et al.,⁹ comparing the outcomes of ASA and myectomy (177 patients in each group), the prevalence of hypertension was significantly higher in the ASA group, even though the mean age of the two groups was similar (63±13 vs. 62±12 years); the prevalence of a family history of

HCM and of HCM-related sudden death was similar in both groups.

The rate of major procedure-related complications was low (two patients), and two patients required permanent pacing due to atrioventricular block. There were no in-hospital deaths. These results reflect the care taken to ensure the safety of the procedure, including correct identification of the target vessel, which was changed in 10% of cases, and the decision to implant permanent pacemakers based on risk scores. Although the immediate goal of reducing the subaortic gradient has been abandoned in favor of assessing the result after healing of the septum, a more logical and safer approach that avoids repeated alcohol injections, it would be interesting to know the evolution of the gradient following the procedure, since this appears to be a predictor of mortality and need for reintervention.⁹

In a follow-up of 22±14 months, the success rate was 84% (improvement in functional class as indicated by exertional dyspnea or angina, together with a reduction of >50% in gradients at rest or with provocation); the gradient was reduced in 33 patients (89%) and there were no procedure-related complications.

In a critical assessment of the outcomes of ASA in both the long and short term, and its impact on prognosis beyond gradient reduction in and symptomatic improvement, it is important to have the most detailed possible characterization of the population undergoing the procedure. This means excluding phenocopies such as sarcomeric HCM that may also benefit from a similar invasive treatment but can have a very different medium-term prognosis. It also requires thorough characterization of the type of hypertrophy (whether confined to the septum or extending to other walls) and consideration of any family history of the disease or of HCM-related sudden death, possibly complemented by genetic testing. In a disease as complex as HCM, in which so many factors can affect prognosis, such data will shed light on the disease's course after successful invasive treatment, particularly ASA.

There is agreement that not all HCM patients with subaortic obstruction and significant symptoms are candidates for or will benefit from ASA and that the decision to perform the procedure should be based on careful patient assessment by clinicians experienced in the diagnosis and management of the disease. Moreover, ASA is technically demanding and requires appropriate training and experience. Nevertheless, although its long-term consequences and benefits remain to be clarified, the excellent results of the initial experience of a reference center demonstrate that ASA is a promising therapeutic option for many Portuguese patients with HCM.

Conflicts of interest

The author has no conflicts of interest to declare.

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