Editorial
Alcohol septal ablation in the management of obstructive hypertrophic cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is a genetic cardiac disorder characterized by a particularly complex pathophysiology with diastolic dysfunction, myocardial ischemia and, in about 20% of patients, a dynamic obstruction to the left ventricular outflow[1-3]. Malignant ventricular tachyarrhythmias and atrial fibrillation are also part of the clinical picture of HCM[1-3]. The disease course and prognosis are extremely heterogeneous. Some patients develop severe symptoms of heart failure, others die suddenly often at a young age and in the absence of previous symptoms, while many have few or no symptoms and a normal longevity[4]. Therefore, patient management is challenging and application of new treatment strategies requires great caution, as well as particular expertise with this disorder. We will examine the results and discuss the potential therapeutic role of percutaneous alcohol septal ablation, a technique introduced in 1995 for the treatment of patients with the obstructive form of HCM.

Management of patients with obstructive hypertrophic cardiomyopathy

Not uncommonly, the presence of a significant left ventricular outflow gradient is compatible with mild or no symptoms and normal or near normal longevity in patients with HCM[3,4]. Therefore, the presence of the outflow gradient should not be the sole or main justification for invasive treatment in this disease. Also, surgery (a resection of 3 to 4 g of cardiac muscle from the basal ventricular septum, or myotomy-myectomy operation) has not been shown to prolong life, and thus, is justified only for the purpose of improving symptoms in patients with a marked outflow gradient in basal conditions and severe symptoms of heart failure (New York Heart Association functional class III-IV) refractory to medical therapy[1-3].

At referral centers with large experience in the myotomy-myectomy operation, surgery has an operative mortality of about 3%, abolishes or markedly reduces the outflow gradient in more than 90% of patients and is associated with a substantial and long lasting (more than 5 years) improvement in symptoms in more than 70% of patients[5-8]. However, substantial experience with surgical treatment of HCM is available only at a small number of centers. Therefore, there is interest in potential alternatives to surgery.

Percutaneous alcohol septal ablation

During the past few years, percutaneous alcohol septal ablation has been proposed as an alternative to the myotomy-myectomy operation for HCM patients otherwise considered candidates for surgery. The technique has been applied in a rapidly increasing number of patients with HCM at two referral centers in Germany and one in the United States[9-12]. At present, the total number of HCM patients who have undergone the procedure at these three centers is in excess of 600 (oral presentations). A fourth center that has used alcohol septal ablation since 1995, has shown a more conservative approach and has performed the procedure in a smaller number of patients[13,14].

In brief, alcohol septal ablation consists of the following: an angioplasty balloon catheter is introduced into a proximal septal perforator branch of the left anterior descending artery. The balloon is then inflated to prevent spilling of alcohol into the anterior descending artery. Alcohol is injected through the catheter into the myocardium to cause a localized necrosis of the basal portion of the septum. The purpose of the procedure is to decrease systolic excursion of the ventricular septum and septal thickness in the area of systolic contact between the septum and mitral valve and, by this mechanism, to increase left ventricular outflow tract size, reduce or abolish mitral-septal contact and the outflow gradient, and improve symptoms.

Immediately after alcohol injection, and due to the reduced systolic thickening of the septum, a substantial decrease in the outflow gradient has been reported in the majority of patients[9-14]. A further decrease in the gradient may result from thinning and remodeling of the septum in the weeks and months following the procedure[12]. Symptomatic improvement has also been reported in most patients, although systematic long-term evaluation of objective measures of cardiovascular function is still lacking.

The image of this new technique projected in the literature by the most experienced centers has been particularly positive regarding the short-to-mid term results and reassuring about the potential risks[9-14]. We strongly believe, however, that a note of caution is necessary and a close look at the limitations and risks associated with percutaneous alcohol septal ablation is required at this time.

Risks and limitations of percutaneous alcohol septal ablation

A list of acute complications associated with percutaneous alcohol septal ablation is reported in table I. A major source of concern and a potential lethal complication of this procedure is extensive myocardial damage beyond the target area. The interventricular septum is the most densely vascularized portion of the heart. The septal perforator branches of the left anterior descending artery interconnect among themselves, and with similar septal branches from the right coronary artery, to produce a network of collateral channels. Therefore, alcohol injected into a septal perforator branch of the anterior descending artery may reach areas of the myocardium far from the apparent anatomic territory of distribution of the branch and cause a larger than expected myocardial necrosis. Most of the centers that perform alcohol septal ablation inject an echocardiographic contrast agent into the selected septal perforator, under transthoracic echocardiographic monitoring, to assess the distribution of flow to the myocardium and reduce the risk of extensive myocardial damage[11,12] (Fig. 1). This methodology has shown that alcohol injected into a septal perforator branch may reach anatomically distant areas of the myocardium such as the apex of the left ventricle, the right ventricular free wall, or a papillary muscle, resulting in systolic dysfunction or acute and severe mitral valve regurgitation[12,15] (Fig. 2).

Table I. Reported acute complications of alcohol septal ablation.

Complete atrioventricular block
Dissection of the LAD
Anterior myocardial infarction due to spilling of alcohol in the LAD
Rupture of the ventricular septum
Left or right ventricular free wall infarction
Papillary muscle infarction with severe mitral valve regurgitation
Ventricular fibrillation within days after the procedure
Death

LAD = left anterior descending coronary artery.

An important limitation of alcohol septal ablation has been somewhat overlooked by the current literature on this technique. As the septal perforator branches vary greatly in size, number and distribution, and in their functional interconnections, not all patients have a septal branch that allows selective delivery of alcohol to the area of systolic contact between the septum and mitral valve. Therefore, the presence of optimal anatomical-functional conditions for the procedure can only be assessed at the time of the coronary arteriography-echocontrast evaluation. When the distribution of flow through each of the probed septal branches clearly extends beyond the basal septum, alcohol should not be injected. However, in selected patients, it may be useful to inject alcohol into a small perforator branch that perfuses only a portion of the myocardium within the target area. While this approach may not reduce the outflow gradient acutely, it may lead to an increase in the outflow tract size and a decrease in the gradient over a period of weeks or months, through a process of progressive remodeling of the damaged area of the septum[12].

A pro-arrhythmic effect of the alcohol-induced myocardial scar is a potential complication of alcohol septal ablation that should not be ignored. It is well known that, in HCM, the left ventricle is electrically unstable and sudden and unexpected death is part of the natural history of the disease[1-3]. Indeed, the risk of sudden death in HCM is essentially life-long and is higher in young patients. However, follow-up data after alcohol septal ablation are available only in a relatively small number of patients and cover a short period of time[10,12]. Therefore, the possibility exists that, in the long term, the procedure may increase the rate of sudden death.

Since the atrioventricular conduction system passes through the posterior septum, complete atrioventricular block necessitating permanent pacemaker implantation is probably the most common complication of alcohol septal ablation, with a reported occurrence that varies

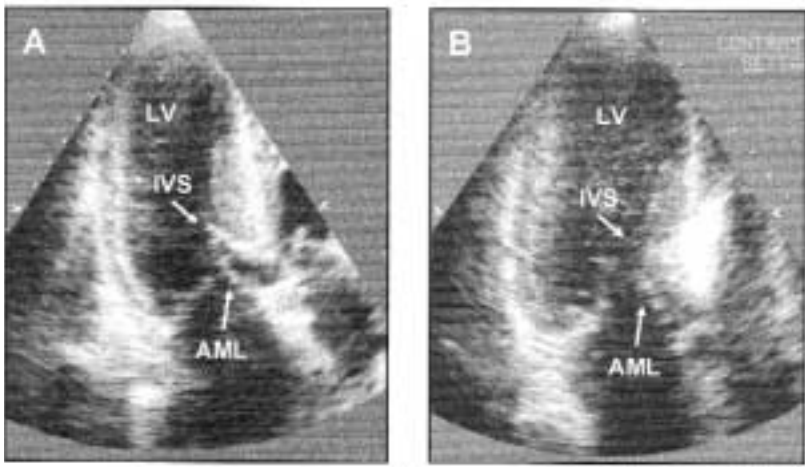

Figure 1. A: *echocardiographic apical 4-chamber view in a patient with hypertrophic cardiomyopathy.* B: *injection of myocardial echocontrast into a septal perforator branch shows distribution of contrast confined to the target area, i.e. the area of contact, during systole, between mitral valve leaflets and the interventricular septum (IVS). AML = anterior mitral leaflet; LV = left ventricle.*

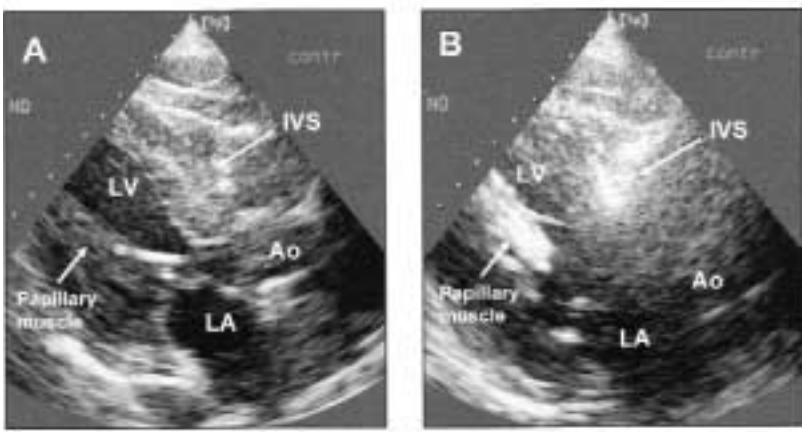

Figure 2. A: *echocardiographic apical 4-chamber view in a patient with hypertrophic cardiomyopathy.* B: *injection of myocardial echocontrast into the first septal perforator branch opacifies the basal portion of the interventricular septum (IVS), but also a hypertrophied papillary muscle. Ao = aorta; LA = left atrium; LV = left ventricle.*

greatly in different centers (7 to 33% of patients)[9-14]. This risk of pacemaker dependence for life should raise additional concern, and suggests great caution in advising the procedure to young patients.

Present role of alcohol septal ablation

Considering the potential complications of alcohol septal ablation summarized above, and the fact that the sole purpose of this therapy is to improve symptoms (not to prolong life), we must be prudent in adopting this treatment strategy, especially in young patients. Also, the reported acute mortality for alcohol septal ablation does not appear to differ from surgical mortality at centers with particular experience in either of the two procedures (about 3%)[6-14] while long-term follow-up is available only for surgery. Therefore, there is no reason why patient selection criteria for septal ablation should differ from those used for surgery, i.e., presence of a marked outflow gradient under basal conditions and severe symptoms (New York Heart Association functional class III or IV) unresponsive to drug treatment[1-3,16]. Patients with this clinical presentation are exceedingly uncommon and probably represent less than 5% of the overall HCM population[3,16]. Indeed, surgery has only a minor role in the management of patients with this disease, as it is also indicated by the fact that two major referral institutions for surgical treatment of HCM in the United States have performed a combined total of less than 350 myotomy-myectomy operations over a period of 20 years[6,7]. Since the three centers with particular interest in septal ablation have performed this procedure in more than 600 patients with HCM during a period of about 4 years, selection criteria have probably been expanded to include patients with mild symptoms. In addition, an augmented risk for sudden death or syncope appears to have been included among the indications to septal ablation[10-12]. During the last 30 years, however, surgery has not been proven to reduce the risk of sud-

den death or prevent syncope in this disease[1-3], and we have recently shown that the presence of the left ventricular outflow gradient is not associated with an increase in the rate of sudden death in HCM[17]. Therefore, prevention of either sudden death or recurrent syncope should not be considered an indication to invasive treatment focused on reducing the outflow gradient.

Over a period of about 1.5 years, and despite the relatively high number of patients with HCM who are referred to us and to other HCM referral centers collaborating with us[18], we have performed alcohol septal ablation in only 7 patients. Each of these patients had an outflow gradient ≥ 50 mmHg in basal conditions and was in advanced New York Heart Association functional class III or IV despite treatment with beta-blockers or verapamil at high dosages and diuretics. Five of these patients showed a definite symptomatic improvement to functional class II, with a substantial decrease in the gradient and in the associated mitral valve regurgitation (Fig. 3). Two patients did not show any symptomatic improvement. This patient population is obviously too small to draw conclusions regarding the efficacy of this technique. However, it underlines once more the point that those patients who fulfill the correct selection criteria for either surgery or septal ablation constitute only a small proportion of the overall HCM population. Therefore, although we do not wish in any way to diminish the current interest in alcohol septal ablation, it would seem unlikely that there will ever be a patient cohort large enough to justify the existence of more than a few referral centers for this technique in a country of the size of Italy.

Conclusions

Alcohol septal ablation appears to be a promising treatment option for HCM patients with a marked outflow gradient in basal conditions and severe symptoms of heart failure unresponsive to medical treatment. Experience with this technique, however, remains limited to a few centers, major complications are possible, and the long-term impact on prognosis is still undefined. Also, the proportion of patients with HCM who meet the selection criteria for invasive treatment is small. Therefore, it would appear prudent at this time to refrain from initiating a program of alcohol septal ablation in centers unlikely to see an HCM population large enough to generate a subgroup of appropriate candidates for this procedure.

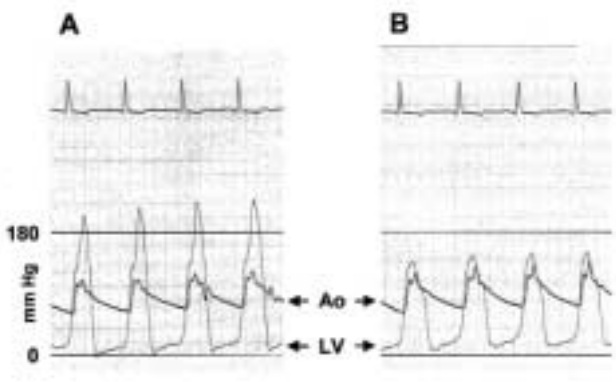

Figure 3. A: *left ventricular outflow tract gradient of 100 mmHg in basal conditions in a patient with hypertrophic cardiomyopathy.* B: *the outflow gradient is reduced to 16 mmHg after injection of alcohol into a septal perforator branch. Ao = aorta; LV = left ventricle.*

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