ORIGINAL ARTICLE

Clinical and Echocardiographic Follow-Up of Patients With Hypertrophic Obstructive Cardiomyopathy Treated With Percutaneous Septal Ablation

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Introduction and objectives. Alcohol septal ablation is a therapeutic option for patients with hypertrophic obstructive cardiomyopathy who remain symptomatic despite medical treatment. Our aim was to monitor clinical and echocardiographic progression in patients with hypertrophic obstructive cardiomyopathy treated by septal ablation at our center.

Methods. Thirty-five septal ablations were performed in 34 patients (79% male) who had symptomatic hypertrophic obstructive cardiomyopathy despite optimum medical treatment. The procedure was successful in 32 (i.e., the reduction in left ventricular outflow tract pressure gradient, or LVOTPG, was >50%). During clinical and echocardiographic follow-up, New York Heart Association (NYHA) functional class and LVOTPG were monitored.

Results. The patients' mean age was 63 (12) years. The mean follow-up period was 9 (3) months. Immediately after septal ablation, LVOTPG decreased significantly, from 74.2 (25.3) mm Hg to 26 (25) mm Hg (*P*<.001), and remained low throughout follow-up. Moreover, echocardiography showed that the interventricular septum thickness also decreased during follow-up, from 19 (3) mm to 15 (2) mm (*P*<.0001). A significant improvement in NYHA functional class (from 93% in class III-IV to 84% in class I-II) was also observed. Two deaths occurred within 48 hours after the procedure. The most frequent complication was complete heart block (20%; n=6).

Conclusions. Alcohol septal ablation is effective in patients with hypertrophic obstructive cardiomyopathy who remain symptomatic despite medical treatment. However, the procedure is associated with a significant rate of complications and should, therefore, be reserved for selected patients, in particular for elderly patients and those with comorbid conditions.

Key words: *Hypertrophic obstructive cardiomyopathy. Septal ablation. Subaortic stenosis.*

Seguimiento clínico y ecocardiográfico de pacientes con miocardiopatía hipertrófica obstructiva tratados con ablación septal percutánea

Introducción y objetivos. La ablación septal percutánea (ASP) es una opción terapéutica para pacientes con miocardiopatía hipertrófica obstructiva (MCHO) con mala respuesta al tratamiento médico. El objetivo fue evaluar de forma prospectiva la evolución clínica y ecocardiográfica de los pacientes con MCHO tratados con ASP en nuestro centro.

Métodos. Se practicaron 35 ASP en 34 pacientes (79% varones) con MCHO sintomática pese a que recibían un tratamiento médico optimizado. Se consideró eficaz en 32 (reducción del gradiente de presión en el tracto de salida del ventrículo izquierdo [GPTSVI] > 50%). Se realizó un seguimiento clínico y ecocardiográfico, y se evaluaron la clase funcional (CF) y el GPTSVI.

Resultados. La edad media fue de 63 ± 12 años. El seguimiento medio fue de 9 ± 3 meses. Inmediatamente después de la ASP se redujo de manera significativa el GPTSVI (74,2 ± 25,3 a 26 ± 25 mmHg; p < 0,001) y se mantuvo así durante todo el seguimiento. Asimismo, se redujo el grosor del septo interventricular (de 19 ± 3 a 15 ± 2 mm; p < 0,0001). La CF de los pacientes mejoró (desde un 93% en CF III-IV de la NYHA hasta un 84% en CF I-II). Dos pacientes fallecieron en las primeras 48 h posprocedimiento y la complicación más frecuente fue el bloqueo auriculoventricular completo (n = 6, 20%).

Conclusiones. La ASP es una terapia eficaz en pacientes con MCHO sintomática refractaria al tratamiento médico. Sin embargo, se asocia con un riesgo significativo de complicaciones, por lo que se reserva para pacientes seleccionados, especialmente para los de mayor edad o con alguna comorbilidad asociada.

Palabras clave: *Miocardiopatía hipertrófica obstructiva. Ablación septal. Estenosis subaórtica.*

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Received October 24, 2005
Accepted for publication March 30, 2006

ABBREVIATIONS

HOCM: hypertrophic obstructive cardiomyopathy.
LVOT: left ventricular outflow tract.
PSA: percutaneous septal ablation.

INTRODUCTION

Hypertrophic obstructive cardiomyopathy (HOCM) is characterized by a narrowing of the left ventricular outflow tract (LVOT) caused by hypertrophy of the interventricular septum and systolic anterior motion of the mitral valve.[1] Obstruction in the LVOT reduces cardiac output thus contributing to the dyspnea and syncope symptoms presented by these patients. Although from the prognostic viewpoint its impact is less understood, in fact treatment succeeds in improving the symptoms in most subjects.[2] Negative inotropic drugs are the first therapeutic choice when aiming to reduce the obstruction in the LVOT and succeed in improving functional capacity and symptomatology in a high percentage of patients. However, approximately 5% of them remain symptomatic despite using the maximum tolerated doses.[3] More aggressive treatments are proposed for these patients, such as dual-chamber pacemaker implantation (whose clinical benefit remains controversial), surgical myectomy, and percutaneous septal ablation (PSA) with alcohol.[2,3] This technique, which was more recently introduced, has been used in a few studies conducted with short- and medium-term follow-up with good outcomes and which in many cases are comparable to those of myectomy.[4-7] The great majority of these studies were carried out in populations less than 60 years old on average. There are fewer studies with older populations where hypertrophic cardiomyopathy associated with hypertension prevails.[8] This type of hypertrophic cardiomyopathy has characteristics different to that found in young individuals where the origin is genetic.

The aim of our study was to evaluate prospectively the clinical and echocardiographic evolution of the patients with HOCM treated with PSA with alcohol in our center, paying special attention to those patients over 65 years old.

METHODS

All patients diagnosed with HOCM with persistent symptoms, despite optimized medical treatment and an LVOT gradient higher than 50 mm Hg at rest or provocable, were candidates for PSA. Furthermore, the first 24 patients who were candidate for PSA were also carriers of dual-chamber pacemakers that did not improve their functional class. The average period from pacemaker implantation to PSA and inclusion in the study was 21±15 months. All patients presented ventricular hypertrophy with septal thickness greater than or equal to 15 mm and obstruction in the LVOT with systolic anterior motion of the mitral valve. We excluded patients with valvular structural anomalies due to repair or surgical replacement, anomalous papillary muscle insertion or systolic dysfunction of the left ventricle.

Percutaneous Septal Ablation With Alcohol

The procedure was done via introduction and inflation of a catheter balloon in a septal perforator branch of the left anterior descending coronary artery. The distal vessel was opacified with angiographic contrast material (Urografin®; Schering AG, Berlin, Germany) to verify the absence of the passage of contrast agent to the anterior descending coronary artery. By means of transthoracic bidimensional echocardiography and injection of echo-contrast material (Levograf®; Juste, SAQF, Madrid) through the catheter, it was confirmed that the territory irrigated by the target septal branch corresponded to the basal septal segment, where the maximum obstruction of the LVOT was generated, and not to another myocardial territory. Subsequently, 1 to 3 mL of alcohol was injected while continuously assessing the presence and degree of LVOT obstruction via hemodynamic monitoring and Doppler echocardiography. The procedure was considered effective if the LVOT pressure gradient fell by 50% or more.

In the first 10 patients this was done as described by Sigwart et al, with pressure monitored in the LVOT via a Brockenbrough catheter introduced transseptally.[7] In the following procedures, pressure monitoring at that level was done via a pigtail (5F) or multipurpose catheter (Cordis®; Johnson and Johnson. USA) via a retrograde arterial approach, thus reducing intervention time. In the patients who did not have a previously implanted dual-chamber pacemaker, the procedure was done via the introduction of a temporary pacemaker lead through the femoral vein that was kept in place for the first 48 hours. After ablation, the patients were admitted to the Coronary Unit in the first 48 hours and placed under electrocardiographic monitoring to detect possible rhythm disorders.

Clinical Follow-Up

All the patients were followed up by an interview in our center's outpatient clinic or by telephone (in 7 patients) to evaluate functional class according to the NYHA classification. Clinical follow-up was done by a clinical cardiologist different to the one who did the echocardiographic study. Both studies were performed within 30 days.

Echocardiogram

All the patients underwent an echocardiogram, prior to, during and after the procedure (within the first 24

hours) and at the end of follow-up. Different equipment available on the market was used (Sonos 5500, Philips, the Netherlands or Sequoia, Siemens, Germany) with 2.5-3.5 Mhz transducers. Following the recommendations of the American Society of Echocardiography,[9] left ventricular diameters in end-diastole and end-systole were measured, as well as thickness of the interventricular septum, left ventricular posterior wall, and the anteroposterior diameter of the left atrium. The gradient in the LVOT at rest and after the Valsalva maneuver was calculated using the modified Bernouilli equation, and the peak velocity in the LVOT was measured by continuous wave Doppler echocardiography.[10] Mitral regurgitation was assessed semiquantitatively through color-Doppler in four planes.[11]

Statistical Analysis

All the values are expressed as mean±SD for the quantitative variables. The Student *t* test was used for matched data to compare the echocardiographic dimensions before and after the procedure and at follow-up, using the Bonferroni correction for multiple comparisons. Discrete variables are presented as percentages and were compared with the χ^2 test. Functional class before and after the intervention was compared with the Wilcoxon sign test. A $P<.05$ was considered significant.

RESULTS

Thirty-five PSA were done in 34 patients with HOCM, out of the 38 selected for PSA. In four cases contrast echocardiography counterindicated the procedure due to the demonstrated passage of echo-contrast agent into unwanted territories (papillary muscle, anterior part of the interventricular septum, opacification of a large myocardial area, or the interior of the ventricular cavity), with the consequent risk of serious complications (extensive myocardial infarction, severe ischemic mitral regurgitation, etc.). In three patients, the initial target septal artery had to be changed as no significant fall in intraventricular gradient after balloon inflation was achieved. In two patients ablation was not effective: the obstruction could not be significantly reduced in one of them at any time, and this was later treated via surgical myectomy; in the other case, although there was an initial fall in pressure gradient, this reappeared at 6-month follow-up but was successfully treated by another septal ablation. Thus, the immediate efficacy rate regarding reducing the gradient by >50% compared to the previous level in those patients who could undergo PSA, was 93% immediately and 87% at follow-up. The applicability of the procedure was almost 90% depending on the anatomy of the septal branches.

One patient was lost to follow-up due to voluntary decision and there were two deaths, one during the procedure and another at 48 hours post-ablation (Figure 1). The average time of clinical and echocardiographic follow-up was 9 (3) months (range, 1 to 48 months).

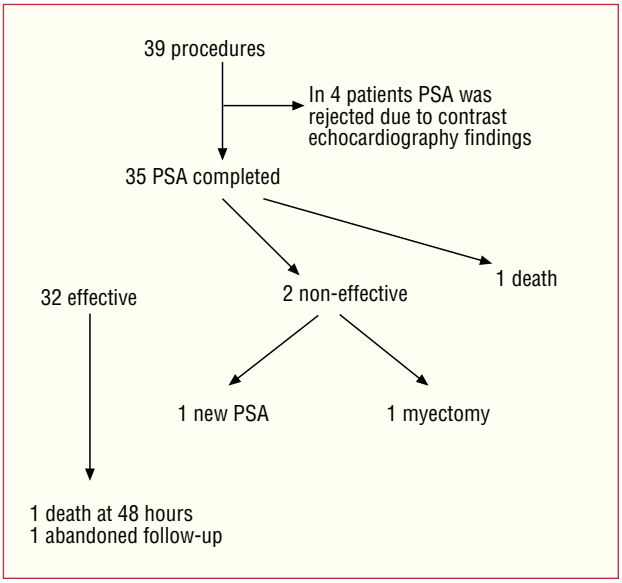

Figure 1. Flow chart of the patients included in the study. PSA: percutaneous septal ablation.

Clinical Characteristics

Follow-up finally included thirty patients diagnosed with HOCM and treated via PSA with alcohol which was initially effective. Some 70% (n=21) were women and the average age was 63 (12) years (range, 25-84), with a subgroup of 17 patients (56%) over 65 years old. Some 93% of the patients were in the NYHA functional class III-IV (24 patients in functional class III and four in functional class IV) despite optimized medical treatment. Some 70% (n=21) received betablocker therapy, 36% (n=11) calcium antagonists, and only two patients (6.6%) disopyramide therapy. The great majority of patients (87%) received only one type of drug, but three patients (9%) received a combination of three drugs. Some 66% (n=20) of the patients were fitted with a dual-chamber pacemaker before the PSA. On the other hand, only two patients presented atrial fibrillation (Table 1).

Echocardiographic Characteristics

Table 1 shows the baseline echocardiographic data of the 30 patients who completed follow-up. The average intraventricular wall thickness was 19±3 mm, and posterior wall thickness 14 (2) mm. The average left ventricular diastolic and systolic diameters were 47 (5) mm and 26 (4) mm, respectively. The baseline LVOT pressure gradient was 74 (25) mm Hg with a maximum provocable gradient of 96 (11) mm Hg. Some 53% of the patients (n=16) presented a degree of mitral regurgitation

TABLA 1. **Baseline Characteristics of the Population Analyzed.**

	n = 30
Age, mean (SD), y	63 (12)
Female	21(70%)
Beta blockers	21(70%)
Calcium antagonists	11(36.6%)
Disopyramide	2(6.6%)
Dual-chamber pacemaker	20(66%)
Interventricular septum (mm)	19 (3)
Posterior wall (mm)	14 (2)
Mitral regurgitation (grade ≥2)	16(53%)
Baseline PG LVOT (mm Hg)	74.2 (25.3)
Provocable PG LVOT (mm Hg)	96.4 (11.2)
Organic mitral valve disease	19(63%)
Atrial fibrillation	2(6.6%)

PG: pressure gradient; LVOT: left ventricle outflow tract.

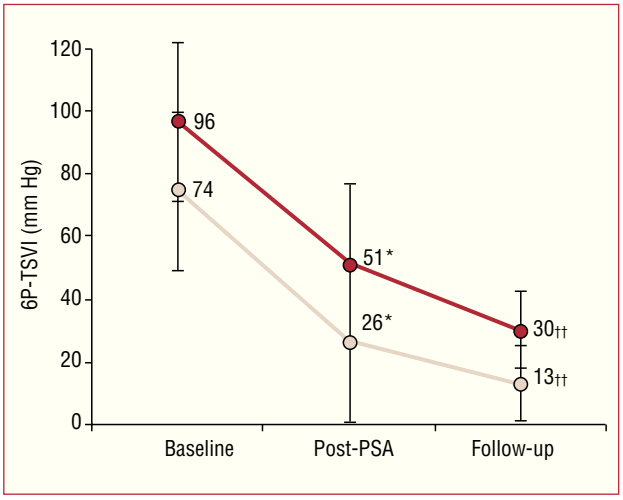

Figure 2. Global evolution of the pressure gradients in the left ventricular outflow tract at rest and provoked by Valsalva maneuvers. Post-PSA: post-percutaneous septal ablation. *P<.001; †P<.001. PG-LVOT: pressure gradient in the left ventricular outflow tract.

due to systolic anterior motion of the mitral valve equal to or higher than grade II. However, 19 patients with mitral regurgitation (63%) also presented organic abnormality of the valve, mainly in the form of mitral ring calcification.

Evolution of the Pressure Gradient in the Left Ventricular Outflow Tract

Immediately after septal ablation, there was a significant fall in LVOT pressure gradients, reaching 26 (25) mm Hg at rest and 51 (39) mm Hg after the Valsalva maneuver (Figure 2). This fall was kept throughout the follow-up period, finally reaching average baseline and provocable values of 13 (12) mm Hg and 30 (25) mm Hg, respectively. Percutaneous septal ablation was effective in 21 patients (70%), with complete disappearance of gradient immediately following the procedure in 10 of them. In addition, during follow-up, total disappearance of the obstruction in the LVOT was obtained in 16 more patients (53%), whereas in the rest (n=4) it fell to under 60% of the baseline value (Figure 3).

The thickness of the interventricular septum also decreased significantly at the end of follow-up from 19 (3) mm to 15 (2) mm, P<.0001. Furthermore, the ventricular diameters changed, with a significant increase in end-diastolic diameter (from 47 [5] to 52 [4] mm, P=.001) and end-systolic diameter (from 27 [4] to 34 [5] mm, P<.0001). Mitral regurgitation after the procedure also improved (P=.04) due to the disappearance of systolic anterior motion of the mitral valve, with just 6 patients (20%) preserving a degree of mitral regurgitation equal to or greater than grade II.

Echocardiographic improvement was accompanied by clinical improvement, with 86% (n=26) of the patients being in NYHA functional class I-II at the end of follow-up (Figure 4).

Septal Ablation in the Subgroup of Patients Over 65 Years Old

In this subgroup of patients (n=17, average age 72 [4] years, all female), the average thickness of the intraventricular septum and posterior wall were 18 (2) mm and 14 (1) mm, respectively, with prevailing concentric ventricular hypertrophy or basal septal hypertrophy. Percutaneous septal ablation also yielded an 87% fall in LVOT pressure gradient, changing from a baseline value of 66 (31) mm Hg to 14 (24) mm Hg and from 98 (13) mm Hg to 24 (27) mm Hg under provocation. Furthermore, there were no procedural complications in this subgroup of patients. Thirteen of them carried a pacemaker before the procedure and in the remaining four there were no alterations in atrioventricular conduction that subsequently required a permanent pacemaker. Table 2 compares the clinical characteristics of the two groups of patients (patients over 65 years old and patients under this age); there were no significant differences regarding parietal thickness, baseline and provocable intraventricular gradients, or treatment.

Complications Due to Percutaneous Septal Ablation

There were two deaths in our series. One occurred during the procedure as a consequence of a cardiac arrest secondary to a transseptal approach. The other case occurred 48 hours following ablation in the form of sudden death probably due to an arrhythmic episode; unfortunately, the episode occurred just after electrocardiographic monitoring was withdrawn and so this could not be documented.

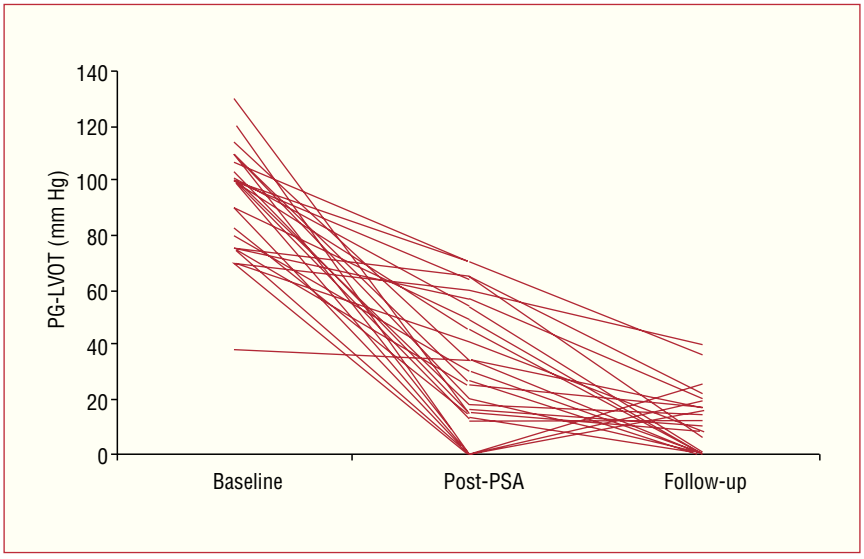

Figure 3. Individual evolution of pressure gradients in the left ventricular outflow tract. PSA: percutaneous septal ablation. PG-LVOT: pressure gradient in the left ventricular outflow tract.

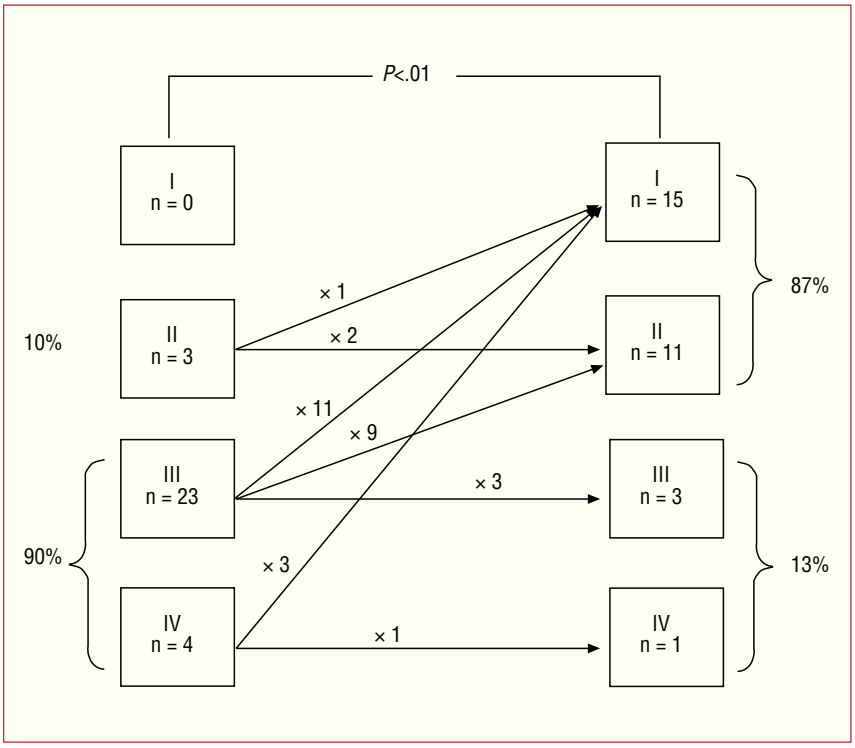

Figure 4. Evolution of functional class after percutaneous septal ablation with alcohol.

Non-fatal complications (n=8, 26%) included a transitory severe mitral regurgitation due to dysfunction of the anterior papillary muscle, endocarditis beginning on the temporary pacemaker lead and extending to the aortic valve, which required valve replacement and, finally, a non-complicated lower myocardial infarction. Among the alterations in atrioventricular conduction, permanent complete atrioventricular block was found in 6 patients (20%): five (16%) of them already carried permanent pacemakers and one did not.

DISCUSSION

Our experience indicates that percutaneous septal ablation with alcohol is an effective technique in the treatment of HOCM, yielding a sharp fall in LVOT pressure gradient in most patients treated with this technique. This fall in intraventricular gradient continues to progress throughout follow-up in most patients due to the gradual reduction in interventricular septal wall thickness secondary to the necrosis induced by the alcohol

TABLE 2. **Baseline Characteristics of the Two Population Subgroups: Over 65 Years Old and Under 65 Years Old.**

	Patients >65 Years (n=17)	Patients <65 Years (n=13)
Age, mean (SD), y	72 (4)	63 (12)
Female	17(100%)	11(84%)
Beta blockers	11(64.7%)	9(69.2%)
Calcium antagonists	4(35.3%)	4(30.7%)
Beta blockers + calcium antagonists	0	2(15%)
Dual-chamber pacemaker	13(76.4%)	6(46%)
Interventricular septum (mm)	18 (2)	20 (4)
Posterior wall (mm)	13 (1)	14 (2)
Mitral regurgitation (grade ≥2)	9(53%)	7(53%)
Baseline PG LVOT (mm Hg)	66 (31)	71 (18)
Provocable PG LVOT (mm Hg)	98 (13)	95 (11)
Organic mitral valve disease	13(76%)	3(23%)

PG: pressure gradient. LVOT: left ventricular outflow tract.

in the ablation area and to consequent ventricular remodeling. At the same time as the fall in gradient, a subjective clinical improvement in the patients' functional class is observed.

However, this is an interventional procedure and involves a significant rate of complications, some serious, which means that the indication for this therapeutic modality should be reserved for those patients with genuinely refractory symptoms, for those in whom it can be a valid alternative to surgery and, especially, patients with greater comorbidity or advanced age.

Efficacy of Percutaneous Septal Ablation With Alcohol

Percutaneous septal ablation with alcohol is a theoretically less aggressive procedure than surgical myectomy since it does not require surgery or cardiopulmonary bypass. Similar to our results, different series have demonstrated efficacy with regard to functional improvement and falls in LVOT pressure gradient.[4-7,12] In our experience, an 83% global reduction in pressure gradient was found during follow-up. Although functional class is determined in HOCM by multiple factors such as obstruction in the LVOT, mitral regurgitation, and diastolic dysfunction, at the same time as the fall in gradient, we found an improvement in functional class in 70% of the patients.

Dual-chamber stimulation has also been proposed as a treatment for obstruction in the LVOT for patients with HOCM. Although the initial results were encouraging, subsequently these have been strongly challenged.[13,14] On the other hand, different studies have demonstrated that surgical myectomy is an effective technique in eliminating obstruction in the LVOT, improving symptomatology with low preoperative mortality indexes (1-3% in the more recently published series).[4,6,12] In our context, Castedo et al. recently published a series of 26 patients with symptomatic HOCM refractory to medical treatment where extended septal myectomy and anterior mitral leaflet plicature was done, with good results regarding the fall in LVOT gradient.[15] However, surgical myectomy poses a corresponding surgical risk, involves cardiopulmonary bypass and, in addition, requires an experienced surgical team.

Although there are few studies that directly compare the results of surgical myectomy with those of septal ablation, and none of them are randomized, it is generally accepted that myectomy yields a slightly greater fall in LVOT pressure gradient than septal ablation.[1] Reasons for this difference might include the possibility of concomitantly repairing the mitral valve or when the part of the basal septum eliminated during surgery is greater than the necrosis induced by ablation with alcohol. On the other hand, and line with our results, the effects of septal ablation are obtained in the longer term, with a progressive fall in gradient during the first 6-12 months of follow-up, subsequently reaching the pressure gradient values obtained via myectomy. This progressive reduction is explained by the muscle regression and thinning phenomenon, ie, the remodeling that follows every myocardial infarction.

As septal ablation is a less invasive procedure, it has been suggested as the technique of choice in older patients with associated comorbidity and at high surgical risk.[1] In our series, the average age was 63±12 years, slightly higher than the average age of patients included in previous studies, with a subgroup of 17 patients (53%) over 65 years old, where hypertrophic cardiomyopathy associated with hypertension is more prevalent.

Complications of Percutaneous Septal Ablation With Alcohol

In our series, one patient died during the procedure as a consequence of a cardiac arrest secondary to a transseptal approach. Periprocedural deaths have been previously described in relation to dissection of the left anterior descending artery or free wall perforation of the right ventricle with the temporary pacemaker lead.[4,16] Another of our patients died at 48 hours following ablation due to sudden death. Several published series have described ventricular fibrillation, ventricular tachycardia, and complete atrial-ventricular block as potentially fatal arrhythmic events occurring after the first 48 hours of the procedure.[17,18] In view of the fact that there is no long-term follow-up of patients treated with septal ablation, it is difficult to attribute a proarrhythmogenic effect to the scarring produced by treatment with alcohol, especially in the context of an arrhythmogenic substrate such as HOCM itself. In addition, alterations in atrioventricular and intraventricular conduction are a frequent complication of septal ablation, mainly right branch block (60%-

100%).[17,19,20] It has been reported that atrioventricular block occurs transitorily in two-thirds of the patients and on an ongoing basis in 0%-25%. In our setting, complete atrioventricular block occurred in six patients (20%), five of whom were already carrying a permanent pacemaker. There were no atrioventricular conduction complications in the patients over 65 years old, although this could have escaped notice as most of them were already pacemaker carriers before PSA. However, at later follow-up, routine pacemaker check-up did not detect a greater frequency of complete atrioventricular block.

Finally, other complications detected during follow-up were a transitory mitral regurgitation, a lower myocardial infarction, and an endocarditis on the pacemaker lead and aortic valve that required valve replacement. The transitory dysfunction of the papillary muscle with consequent transitory severe mitral regurgitation, as well as the non-complicated lower myocardial infarction, can be explained as a consequence of the ablation of the well-developed septal branches that irrigate lower areas of the anterior septum and even reach the papillary muscle.[21] On the other hand, the appearance of electrocardiographic changes indicating ischemia during and after the procedure should lead to suspicion of complications, which are not especially infrequent, such as dissection of a epicardial coronary artery.[6,22]

Study Limitations

Clinical follow-up was done in the outpatient departments of our center or by telephone interview, meaning that we only have a subjective evaluation due to not carrying out routine explorations, such as the exercise stress test for oxygen consumption, that would provide objective data. This fact could indicate a possible placebo effect regarding the technique, although the fall in gradient of the intraventricular obstruction and the degree of mitral regurgitation are objective data that make it possible to expect objective clinical improvement.

On the other hand, variability in measuring the pressure gradient in a single patient is well-known.[23] However, having sequential controls in each patient and the uniform trend observed regarding the fall in pressure gradient underlines the reliability of the data.

CONCLUSIONS

Septal ablation is an effective therapy, although it carries a significant risk of complications in patients with symptomatic HOCM refractory to medical treatment, and especially in patients over 65 years old, inducing a progressive reduction in obstruction and significant functional improvement in most patients. Given that it is theoretically less aggressive and entails lower cost, this could be the technique of choice versus surgical myectomy in older patients or those with associated comorbidity.

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