ORIGINAL ARTICLE

Clinical and Functional Outcome of Percutaneous Alcohol Septal Ablation in Obstructive Hypertrophic Cardiomyopathy

Resultados clínicos y funcionales de la ablación septal percutánea con alcohol en la miocardiopatía hipertrófica obstructiva.

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ABSTRACT

Background: Percutaneous septal ablation is a therapeutic option for patients with obstructive hypertrophic cardiomyopathy refractory to optimal medical therapy. However, results of initial persistence and long-term safety are still controversial.
Objectives: The aim of this study was to report percutaneous alcohol septal ablation technique, clinical and functional outcome, cardiovascular events and its impact on long-term follow-up.
Methods: A total of 23 patients were included in the study. Functional class (FC), left ventricular outflow tract gradient before and after the procedure and long-term cardiovascular events were evaluated.
Results: Median follow-up was 52 months (IR 33-72). All patients were in FC III or IV prior to the procedure, under maximum tolerated medical therapy. The procedure was successful in 91% of cases, with 85% of patients currently in FC I and 15% in FC II. Baseline left ventricular outflow tract gradient decreased from 75 mmHg (95% CI 51-89) to 25 mmHg (95% CI 10-37) ($p < 0.003$) and with Valsalva maneuver from 118 mmHg (95% CI 88-152) to 38 mmHg (95% CI 16-69) ($p < 0.0002$), persisting in the long-term follow-up. During hospitalization, two patients presented with complete atrioventricular block requiring permanent pacemaker implantation. No cardiovascular deaths occurred during follow up.
Conclusions: Alcohol septal ablation is a promising option for the treatment of a selected population with hypertrophic obstructive cardiomyopathy, generating sustained clinical and functional improvement with low incidence of events in the long-term follow up.

Key words: Cardiomyopathy, Hypertrophic -Ablation Techniques

RESUMEN

Introducción: La ablación septal percutánea es una opción terapéutica para pacientes con miocardiopatía hipertrófica obstructiva refractarios al tratamiento médico óptimo. Sin embargo, la persistencia de los resultados iniciales y la seguridad en el seguimiento permanecen en controversia.
Objetivo: Comunicar la técnica de ablación septal percutánea con alcohol, la evolución clínica y funcional, los eventos cardiovasculares y su impacto en el seguimiento alejado.
Material y métodos: Se incluyeron 23 pacientes. Se evaluaron la clase funcional (CF), el gradiente en el tracto de salida del ventrículo izquierdo antes del procedimiento y después de él y los eventos cardiovasculares a largo plazo.
Resultados: La mediana de seguimiento fue de 52 meses (RI 33-72). Todos los pacientes se encontraban en CF III-IV previo al procedimiento, bajo máximo tratamiento médico tolerable. El procedimiento fue exitoso en el 91% de los casos; el 85% de los pacientes se encuentran en CF I y el 15% en CF II. Se observó una reducción del gradiente basal de 75 mmHg (IC 95% 51-89) a 25 mmHg (IC 95% 10-37) ($p < 0,003$) y con Valsalva, de 118 mmHg (IC 95% 88-152) a 38 mmHg (IC 95% 16-69) ($p < 0,0002$), que persistió en el seguimiento alejado. Durante la hospitalización, dos pacientes presentaron bloqueo auriculoventricular completo, que requirió el implante de un marcapasos definitivo. No se produjeron muertes de causa cardiovascular en el seguimiento.
Conclusiones: La ablación septal con alcohol representa una opción prometedora en el tratamiento de un grupo seleccionado de pacientes con miocardiopatía hipertrófica obstructiva, generando una mejoría clínica y funcional sostenida, con una incidencia baja de eventos en el seguimiento a largo plazo.

Palabras clave: Miocardiopatía hipertrófica - Técnicas de ablación

Abbreviations

ASA	Alcohol septal ablation	**ICD**	Implantable cardioverter defibrillator
CPK	Creatine phosphokinase	**LVOT**	Left ventricular outflow tract
FC	Functional class	**OHCM**	Obstructive hypertrophic cardiomyopathy

Rev Argent Cardiol 2015;83:217-222. http://dx.doi.org/10.7775/rac.v83.i3.5919

Received: 02/13/2015 - *Accepted:* 04/01/2015

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INTRODUCTION

Hypertrophic cardiomyopathy is a primary myocardial disease defined by the presence of left ventricular hypertrophy in the absence of any other underlying condition that might explain it. (1, 2)

Currently, various therapeutic options are available to mitigate the symptoms associated with this disease. Drugs, as beta-blockers or calcium channel blockers are still the first line therapy. (3-6) In case patients are refractory to pharmacological therapy, surgical myectomy or alcohol septal ablation (ASA) emerge as alternative treatments, whereas dual chamber pacing is applied in cases when the former options are not feasible. (7-11)

Alcohol septal ablation, introduced in 1983, is a treatment strategy that showed excellent initial results. However, contradictory reports have been published regarding the persistence of initial results and safety in the long-term follow-up. (12-18)

The aim of this study was to report the ASA technique, its clinical and functional outcome and the incidence of initial and long-term cardiovascular events following the procedure.

METHODS

All patients with symptomatic obstructive hypertrophic cardiomyopathy (OHCM) under maximum tolerated medical therapy were prospectively included in the study, and those with favorable anatomical conditions were selected to undergo ASA.

Between 2003 and 2010, the decision to incorporate patients was left to the criteria of the treating physicians after evaluation and discussion with the patient. Since 2010, the evaluation and management of all patients with diagnosis of hypertrophic cardiomyopathy was in charge of the Cardiomyopathy Center, composed of our institutional clinical and interventional cardiologists, electrophysiologists, surgeons, and experts in heart failure and imaging techniques. During the whole study period, patients were evaluated and referred both for septal ablation or myectomy according to their anatomical and clinical characteristics. Age, presence of comorbidities, septal thickness and access to branches, among other considerations, were taken into account to decide between myectomy or septal ablation.

Patients had to meet certain clinical, echocardiographic and angiographic criteria to undergo the procedure.

Clinical criterion:

Severe symptoms [functional class (FC) III-IV] of the New York Heart Association (NYHA) refractory to medical therapy, interpreted as lack of medical improvement with the use of drugs (beta-blockers and/or calcium channel blockers) up to maximum tolerated doses according to heart rate and blood pressure.

Echocardiographic criteria

Asymmetric septal hypertrophic cardiomyopathy was considered for interventricular septal thickness by echo-Doppler ≥15 mm and a ratio with respect to the inferolateral wall ≥1.5 mm.

Significant obstruction was defined as the presence of intraventricular gradient >30 mmHg at rest or >50 mmHg with maneuvers.

An echocardiogram was performed in all patients after the procedure during hospitalization and at the end of follow-up.

Echocardiographic studies were performed by a cardiologist specialized in echocardiography with IE33 Philips Medical Systems ultrasound system and 3-4 MHz transducer. Short-axis and long-axis paresternal views and apical 2-, 3-, 4- and 5-chamber views were acquired. Myocardial thicknesses were analyzed in M-mode and two-dimensional echocardiography, and atrial area and presence of systolic anterior motion of the mitral valve with two-dimensional echocardiography. The study of diastolic function was based on the analysis of diastolic mitral flow and the velocities of longitudinal cardiac fibers assessed by tissue Doppler imaging. Continuous-wave Doppler was used to evaluate the presence of dynamic gradients, both at rest and with Valsalva maneuver. Mitral regurgitation was estimated assessing the effective regurgitant orifice area and color jet area (Figure 1).

Angiographic criteria

Coronary angiography and left ventriculography were performed to identify the presence of septal branches in line with the distribution of septal hypertrophy, in the anterior descending artery or emerging from other coronary arteries, in the absence of atherosclerotic lesions (Figure 2). During this period, in one female patient it was impossible to angiographically identify the artery supplying the site of greatest hypertrophy. This patient did not undergo the procedure, was referred to programmed surgery and hence was not included in the study.

Angiographies were performed by an interventional cardiologist with Philips Allura or Clarity-Allura systems with rotational angiography and ventriculogram with simultaneous left coronary artery angiography in 30-degree RAO projection.

Alcohol septal ablation was considered to be successful when 50% reduction in baseline gradient or with maneuvers was obtained in the cath-lab.

Immediate post-ablation control

Serial electrocardiograms were performed in all patients, assessing cardiac rhythm, QRS and PR duration, presence of arrhythmias and atrioventricular and bundle-branch block. Total creatine phosphokinase (CPK) level was determined as manifestation of necrosis provoked by alcohol instillation. A CPK cut-off value of 195 U/L was defined. Functional class and presence of cardiovascular events were evaluated during hospitalization.

30-day and long-term clinical and echocardiographic follow-up

All patients were followed-up in the outpatient clinic of our center by a clinical cardiologist who evaluated FC, according to the New York Heart Association (NYHA) classification, and/or associated symptoms. A new Doppler echocardiogram was performed to evaluate the parameters described above and 24-hour electrocardiographic Holter monitoring was performed every 6 months during the first year and annually thereafter.

Statistical analysis

Continuous variables are expressed as mean±standard deviation and median±interquartile range according to their distribution, and categorical variables are expressed as per-

centages. Paired Student´s t test and Wilcoxon´s test for the analysis of continuous variables were used as appropriate. A p values <0.05 was considered as statistically significant.

The protocol was conducted according to the Helsinki Declaration and patient personal data were protected. The protocol was approved by the Institutional Ethics Committee.

SPSS Statistics for Windows, Version 21.0 software package was used for statistical analysis.

Percutaneous alcohol septal ablation

Technique

In the cath-lab, all patients receive conscious sedation (benzodiazepines and analgesics) delivered by an anesthesiologist. Following bilateral insertion of 6-7 Fr femoral or radial artery introducers, a 6 Fr pigtail cathether is introduced in the left ventricle through the aortic valve. A second pigtail catheter is placed in the aorta, 4 cm from the aortic valve to measure left ventricular outflow tract (LVOT) gradient, and the following pressures are compared: systemic, intraventricular, at baseline and after ventricular extrasystole. A temporary pacemaker is inserted due to the elevated risk of atrioventricular block. The identification of the branch supplying the basal septum to perform the ablation is performed by fixed and rotational projections. The latter provide additional information on subsidiary branches that do not necessarily arise from the anterior descending artery, but also from the circumflex or diagonal arteries. In addition, a simultaneous baseline angiography is performed.

Next, a 7 Fr guiding catheter is introduced in the main left coronary artery, a 0.014" guidewire is progressed to the established septal branch, and a 2.0 mm diameter by 8-12 mm long over-the-wire balloon is advanced.

The balloon is immediately inflated occluding the septal branch. After some minutes, the hemodynamic response is observed with transthoracic echocardiography and through baseline and post-extrasystolic gradients. This is followed by the injection of agitated 10% blood mixed with saline solution to contrast the septum and identify the site by echocardiography. Then, previously agitated diluted angiographic contrast material is administered through the balloon; branch size, its myocardial irrigation area and impact on the LVOT gradient are determined, and no contrast back flow to the anterior descending artery is verified (see Figure 2). It is a long intervention with a leading role of ultrasound guiding the whole procedure.

Depending on branch size, 1 to 3 ml of 96% alcohol is

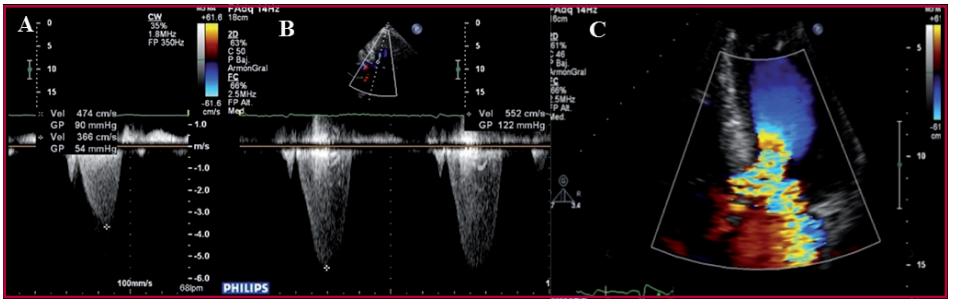

Fig. 1. Echocardiographic left ventricular outflow tract gradient measurement. **A.** Baseline left ventricular outflow tract gradient. **B.** Left ventricular outflow tract pressure gradient with Valsalva maneuver. **C.** Systolic anterior motion.

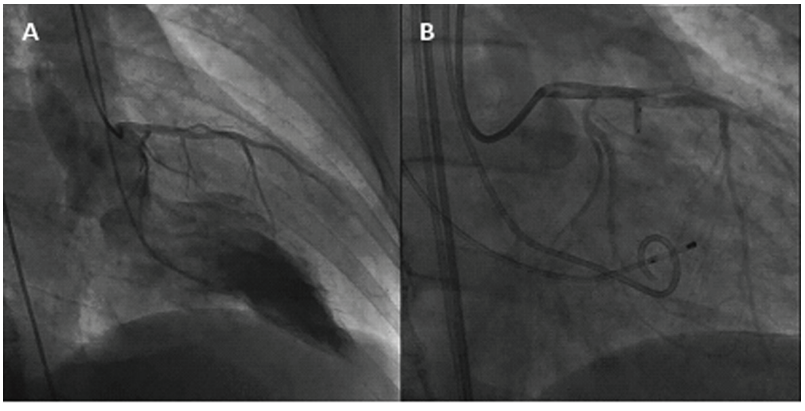

Fig. 2. Alcohol septal ablation techique. **A**. Coronary angiography with injection in the left main coronary artery and ventriculogram. **B**. Balloon inflation to identify left ventricular outflow tract gradient decrease.

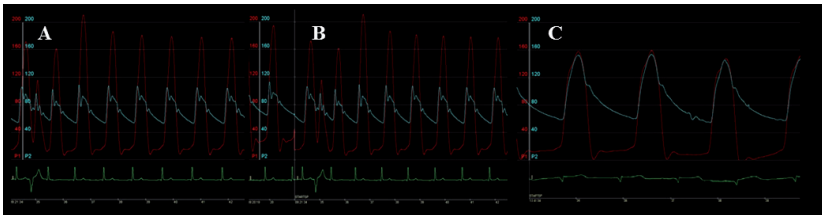

Fig. 3. Invasive measurement of intraventricular and systemic pressures. Baseline **(A)** and postextrasystolic **(B)** left ventricular outflow tract pressure gradient measurements prior to percutaneous septal ablation and the improvement after the procedure**(C).**

slowly injected with 1 ml syringe through the balloon while monitoring LVOT gradient changes (Figure 3) and electrocardiogram modifications. On rare occasions, it is necessary to occlude more than one septal branch, generally the second or third. The procedure is considered to be successful when it presents ≥50% reduction of baseline and postextrasystolic ventricular gradient (Brockenbrough-Braunwald-Morrow sign). By protocol, the balloon remains inflated for 15 minutes to avoid alcohol backflow into the coronary circulation. Subsequently, a control 12-lead electrocardiogram, coagulation tests and serial CPK are performed. The patient is transferred to the intensive care unit for 48 hours for monitoring and to control heart rhythm before removing the temporary pacemaker.

RESULTS

Population characteristics

Twenty-three consecutive patients were included between March 2013 and November 2014. Baseline population characteristics are detailed in Table 1. Mean age was 67±4 years and 45% of patients were men. Functional class III and IV was found in 55% and 45% of patients, respectively. Median LVOT gradient at rest and provoked was 75 mmHg (95% CI 51-89) and 118 mmHg (95% CI 89-152), respectively. Echocardiographic interventricular septal thickness was 21±2 mm.

Procedure data

In each patient, 2.2±0.5 ml of 96% alcohol was used in 1.3 septal branches. After ablation, resting gradient was reduced from 75 mmHg (95% CI 51-89) to 25 mmHg (95% CI 10-37) (p<0.003), whereas the provoked gradient was reduced from 118 mmHg (95% CI 88-152) to 38 mmHg (95% CI 16-69) (p<0.0002) (Figure 4), persisting in the long-term follow-up.

The degree of systolic anterior motion decreased in all cases, with concomitant reduction of the associated mitral regurgitation.

In-hospital outcome

During hospitalization, peak CPK was 909±243 U/L (666-1,151 U/L). The procedure was successful in 91% of patients. No deaths, stroke or acute myocardial infarction were recorded. One patient suffered severe pericardial effusion secondary to temporary pacemaker implantation, which was successfully treated with percutaneous drainage, with favorable in-hospital outcome.

No new cases of left bundle branch block or first and second degree atrioventricular block were found. Transient complete right bundle branch block was observed in three patients (13%); however, no significant changes were found in QRS and PR duration (p=0.3 and p=0.6, respectively). Two patients presented complete atrioventricular block requiring definitive pacemaker implantation, and two patients developed complex ventricular arrhythmias, receiving implantable cardioverter defibrillator implantation (ICD).

Table 1. Baseline patient characteristics (n=23)

Age, years	67 ± 4
Male gender, %	45
Hypertension, %	60
Dyslipidemia, %	55
Smoking, %	63
Diabetes mellitus, %	5
Prior CABG, %	9
Prior pacemaker, %	0
Atrial fibrillation, %	5
Betablockers, %	90
Calcium blockers, %	60
Interventricular septum, mm	21 ±2
Baseline peak LVOT gradient, mm Hg	75 (51-89)
Peak LVOT gradient with Valsalva, mm Hg	118 (89-152)
Preserved left ventricular function, %	95
SAM, %	100
Moderate-severe mitral regurgitation by SAM, %	60

LVOT: Left ventricular outflow tract. CABG: Coronary artery bypass graft surgery. SAM: Systolic anterior motion.

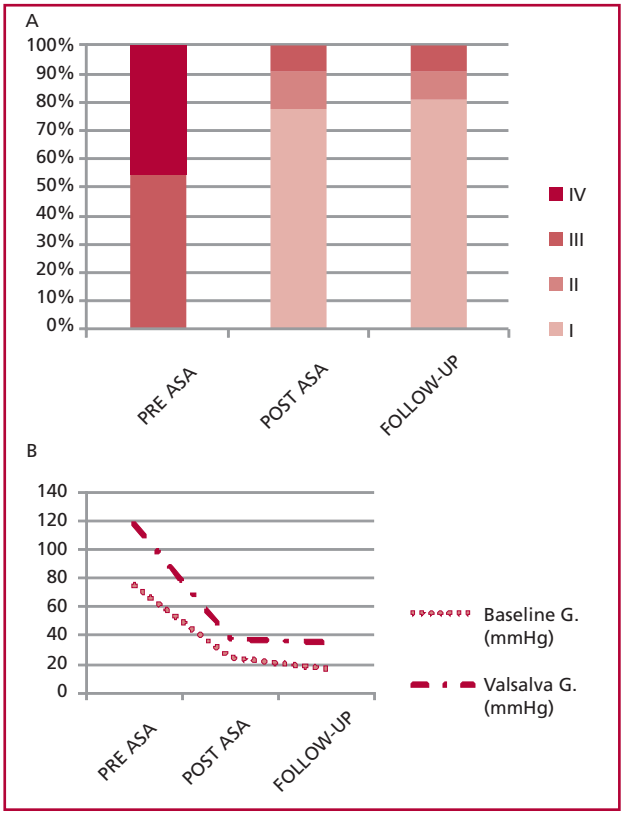

Fig. 4. Long-term clinical and echocardiographic outcome after alcohol septal ablation (ASA). Overall functional class **(A)** and resting and Valsalva left ventricular outflow tract pressure gradient **(B)** outcomes following percutaneous septal ablation.

30-day and long-term clinical outcome

Two patients showed no FC improvement after ASA; dual-chamber pacemaker implantation was decided in one patient and septal myectomy was performed in the other, both with clinical improvement.

At 30-day follow-up, 85% of patients successfully treated with ASA were in FC I and 15% in FC II (see Figure 4).

In the long-term follow-up [52 months (interquartile range 33-72)] all patients improved, remaining with good FC. No cardiovascular deaths or stroke were recorded in the long-term follow-up of patients submitted to ASA. Two additional patients (17%) presented complex ventricular arrhythmia detected by Holter, and ICD implantation was decided.

No shocks due to ventricular arrhythmias were recorded in the long-term follow-up of patients with ICD.

DISCUSSION

The present work shows that ASA is effective for the long-term reduction of OHCM-associated symptoms in a population of patients selected for their clinical presentation and angiographic and anatomical characteristics.

Moreover, it is a theoretically less aggressive procedure than surgical myectomy, and different series have demonstrated initial clinical efficacy and LVOT pressure gradient reduction, similarly to our results. (20-27) In our work, an elevated procedural success was achieved (91%), similar to that referred by high-volume centers worldwide, though it is highly dependent on the form of definition This resulted in median residual gradient of 25 mmHg, with short-term FC improvement, evidenced by 85% of patients in FC I.

Regarding the long-term outcome, there are few published studies exceeding 3-year follow-up, and with dissimilar results, which has generated doubts on the durability of the procedure effect. In this sense, the study by Sorajia et al. at the Mayo Clinic, including 177 patients with long-term follow-up of 5.7 years, reported that 67% of patients were free of symptoms and 78% were free of severe symptoms or death. (27) In our study, these results were 78% and 87%, respectively.

Therefore, ASA effects in dynamic obstruction are maintained in the long-term, with a progressive decrease of the gradient during the first months and persistence in the long-term follow-up, reaching the LVOT pressure gradients obtained with myectomy, according to the latest published series. (28-32)

Ventricular arrhythmia after ASA is still a matter of research. Histopathological studies of the myocardium following ASA, to assess its possible arrhythmogenic origin, demonstrated less connective tissue infiltration in the infarcted myocardium with lower myocardial mass than that observed due to atherosclerotic disease and a beneficial effect, since the risk of sudden death increases with the degree of hypertrophy.

In this sense, de Leonardi et al. and Cuoco et al. studies, among others, agree that the rate of all-cause mortality and sudden death are lower in ASA compared with surgical myectomy cohorts. They also found no significant differences in the rate of appropriate shocks in patients with ICD, either by primary prevention criteria or following ASA, suggesting that the generation of arrhythmias could be related with inherent factors of the disease rather than as a consequence of ASA. (18, 34-36) In the present study, two patients presented arrhythmias during follow-up, requiring ICD. However, no sudden deaths or arrhythmic events were observed.

In these patients, no ventricular arrhythmia or shocks were read or recorded in the ICD.

Management of this type of patient needs a clinical team specialized in their study and treatment to determine the best therapeutical option. The intervention represents a challenge both for the operator as for the imaging expert to identify the branch or sub-branch responsible of gradient or systolic anterior motion, requiring multiple hemodynamic evaluations through the generation of ischemia by balloon inflation. The use of echocardiography (generally transthoracic in patients with good acoustic window), with agitated serum or previously agitated diluted angiographic contrast material as guidance for the procedure, is essential to select the septal area responsible for the generation of LVOT obstruction. This would avoid the unnecessary infusion of alcohol in a non-responsible area, which might generate an extended infarction with the concomitant increased risk of complete atrioventricular block. (37) In our work, an 8% incidence of definitive pacemaker implantation due to complete atrioventricular block was lower than that reported by different series. (38, 39)

Ethical considerations

The protocol was approved by the institutional Ethics Committee.

Limitations

A limitation of this study was that the results analyzed in this prospective registry correspond to a small cohort of highly selected patients treated with ASA, with mid-term follow-up.

CONCLUSIONS

Alcohol septal ablation is an attractive therapeutic option for the treatment of patients with symptomatic OHCM refractory to optimal medical therapy, inducing a substantial sustained improvement of LVOT obstruction and FC, with low incidence of events in the long-term follow-up.

Conflicts of interest

None declared

(See author´s conflicts of interest forms in the web / Supplementary Material)

REFERENCES

1. Maron BJ. Hypertrophic cardiomyopathy: a systematic review. JAMA 2002;287:1308-20. http://doi.org/b6fwh8

2. Nishimura R, Holmes D. Hypertrophic obstructive cardiomyopathy. N Engl J Med 2004;350:1320-7. http://doi.org/drt6vx

3. Spirito P, Seidman CE, McKenna WJ, Maron BJ. The management of hypertrophic cardiomyopathy. N Engl J Med 1997;336:775-85. http://doi.org/bt3bn9

4. Fifer M, Vlahakes G. Management of symptoms in hypertrophic cardiomyopathy. Circulation 2008;117:429-39. http://doi.org/crg4cr

5. Consenso de Miocardiopatía Hipertrófica. Consenso Argentino SAC. Rev Argent Cardiol 2009;77:151-66.

6. 2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011;58;e212-e260. http://doi.org/bhr4td

7. Ommen S, Maron B, Olivotto I, Maron M, Cecchi F, Betocchi S, et al. Long-term effects of surgical septal myectomy on survival in patients with obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol 2005;46:470-6. http://doi.org/czx3gw

8. Arias A, Bagnati R, Pérez de Arenaza D, Oberti P, Falconi M, Pizarro R y cols. Perfil clínico de pacientes con miocardiopatía hipertrófica en un hospital universitario. Rev Argent Cardiol 2014;82:366-72. http://doi.org/3vs

9. Nishimura R, Hayes D, Ilstrup D, Holmes D, Tajik J. Effect of dual-chamber pacing on systolic and diastolic function in patients with hypertrophic cardiomyopathy. J Am Coll Cardiol 1996;27:734-9. http://doi.org/fkxw6q

10. Fananapazir L, Epstein N, Curiel R, Panza J, Tripodi D, McAreavey D. Long-term results of dual-chamber (DDD) pacing in obstructive hypertrophic cardiomyopathy. Circulation 1994;90:2731-42. http://doi.org/3vt

11. Maron B, Nishimura R, McKenna W, Rakowski H, Josephson M, Kieval R. Assessment of permanent dual-chamber pacing as a treatment for drug-refractory symptomatic patients with obstructive hypertrophic cardiomyopathy- A randomized, double-blind, crossover study (M-PATHY). Circulation 1999;99:2927-33. http://doi.org/3vv

12. Gabay J, Hita A. La embolización septal con alcohol está indicada en todos los pacientes sintomáticos con miocardiopatía hipertrófica y gradiente significativo. Rev Argent Cardiol 2007;75:124-31.

13. Delgado V, Sitges M, Andrea R, Rivera S, Masotti M, Francino A, et al. Seguimiento clínico y ecocardiográfico de pacientes con miocardiopatía hipertrófica obstructiva tratados con ablación septal percutánea. Rev Esp Cardiol 2006;59:1123-30. http://doi.org/cgg99j

14. Agarwal S, Murat Tuzcu E, Desai M, Smedira N, Lever H, Lytle B, et al. Updated meta-analysis of septal alcohol ablation versus myectomy for hypertrophic cardiomyopathy. J Am Coll Cardiol 2010;55:823-34. http://doi.org/ch67gh

15. Gimeno J, Tome MT, McKenna W. Alcohol septal ablation in hypertrophic cardiomyopathy: An opportunity to be taken. Rev Esp Cardiol 2012;65:314-8. http://doi.org/f2fmmz

16. Nagueh S, Ommen S, Lakkis N, Killip D, Zoghbi W, Schaff H, et al. Comparison of ethanol septal reduction therapy with surgical myectomy for the treatment of hypertrophic obstructive cardiomyopathy. J Am Coll Cardiol 2001;38:1701-6. http://doi.org/dgp8vq

17. Sorajja P, Valeti U, Nishimura R, Ommen S, Rihal C, Gersh B, et al. Outcome of alcohol septal ablation for obstructive hypertrophic cardiomyopathy. Circulation 2008;118:131-9. http://doi.org/fpmnhp

18. Gietzen F, Leuner G, Raute-Kreinsen U, Dellmann A, Hegselmann J, Strunk-Mueller C, et al. Acute and long-term results after transcoronary ablation of septal hypertrophy (TASH). Catheter interventional treatment for hypertrophic obstructive cardiomyopathy. Eur Heart J 1999;20:1342-54. http://doi.org/bsvxvx

19. Alam M, Dokainish H, Lakkis N. Alcohol septal ablation for hypertrophic obstructive cardiomyopathy: a systematic review of published studies. J Interv Cardiol 2006;19:319-27. http://doi.org/dfpzk5

20. Ben-Dor I, Maluenda G, Wang Z, Lindsay J, Satler L, Pichard A, et al. Alcohol septal ablation in hypertrophic obstructive cardiomyopathy. Cardiovasc Revasc Medicine 2012;13:72-4. http://doi.org/frnrm3

21. Ayala F, Maiers E, Pavón M, Ortúzar L. Ablación miocárdica septal percutánea con alcohol absoluto como tratamiento de la miocardiopatía hipertrófica obstructiva. Cardiología Clínica 2007;23:61-8.

22. Gietzen F, Leuner C, Obergassel L, Strunk-Mueller C, Kuhn H. Role of transcoronary ablation of septal hypertrophy in patients with hypertrophic cardiomyopathy, New York Heart Association Functional Class III or IV, and outflow obstruction only under provocable conditions. Circulation 2002;106:454-9. http://doi.org/b6g4wh

23. Jensen M, Almaas V, Jacobsson L, Hansen P, Havndrup O, Aakhus S, et al. Long-term outcome of percutaneous transluminal septal myocardial ablation in hypertrophic obstructive cardiomyopathy- A Scandinavian Multicenter Study. Circ Cardiovasc Interv 2011;4:256-65. http://doi.org/cf4jbv

24. Nagueh S, Groves B, Schwartz L, Smith K, Wang A, Bach R, et al. Alcohol septal ablation for the treatment of hypertrophic obstructive cardiomyopathy. J Am Coll Cardiol 2011;58:2322-8.

25. Spencer W, Roberts R. Alcohol septal ablation in hypertrophic obstructive cardiomyopathy. Circulation 2000;102:600-1. http://doi.org/3vw

26. Elliott P. The role of alcohol septal ablation in the treatment of left ventricular outflow tract obstruction in hypertrophic cardiomyopathy. J Am Coll Cardiol 2011;58;2329-31. http://doi.org/fjmggq

27. Sorajja P, Ommen SR, Holmes DR, Dearani JA, Rihal CS, Gersh BJ. Survival after alcohol septal ablation for obstructive hypertrophic cardiomyopathy. Circulation 2012;126:2374-80. http://doi.org/3vx

28. Maron BJ, Nishimura RA. Surgical septal myectomy versus alcohol septal ablation, assessing the status of the controversy in 2014. Circulation 2014;130:1617-24. http://doi.org/3vz

29. Qin J, Shiota T, Lever H, Kapadia S, Sitges M, Rubin D, et al. Outcome of patients with hypertrophic obstructive cardiomyopathy after percutaneous transluminal septal myocardial ablation and septal myectomy surgery. J Am Coll Cardiol 2001;38:1994-2000. http://doi.org/bkqvwf

30. Olivotto I, Ommen S, Maron M, Cecchi F, Maron B. Surgical myectomy versus alcohol septal ablation for obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol 2007;50:831-4. http://doi.org/cxgbk5

31. Nagueh S, Ommen S, Lakkis N, Killip D, Zoghbi W, Schaff H, et al. Comparison of ethanol septal reduction therapy with surgical myectomy for the treatment of hypertrophic obstructive cardiomyopathy. J Am Coll Cardiol 2001;38:1701-6. http://doi.org/dgp8vq

32. Talreja D, Nishimura R, Edwards W, Valeti U, Ommen S, Tajik J, et al. Alcohol septal ablation versus surgical septal myectomy. J Am Coll Cardiol 2004;44:2329-32. http://doi.org/d6m5gb

33. Leonardi RA, Kransdorf EP, Simel DL, Wang A, et al. Meta-analyses of septal reduction therapies for obstructive hypertrophic cardiomyopathy: comparative rates of overall mortality and sudden cardiac death after treatment. Circ Cardiovasc Interv 2010;3:97-104. http://doi.org/ftkczq

34. Cuoco F, Spencer W, Fernandes V, Nielsen C, Nagueh S, Sturdivant L, et al. Implantable cardioverter-defibrillator therapy for primary prevention of sudden death after alcohol septal ablation of hypertrophic cardiomyopathy. J Am Coll Cardiol 2008;52:1718-23. http://doi.org/d2m7hj

35. Nishimura R, Ommen R. Septal reduction therapy for obstructive hypertrophic cardiomyopathy and sudden death. Circ Cardiovasc Interv 2010;3:91-3. http://doi.org/bngnhx

36. Hori Y, Ueda M, Nakayama T, Saegusa N, Uehara M, Lee K, et al. Occurrence of de novo sustained monomorphic ventricular tachycardia induced after percutaneous transluminal alcohol septal myocardial ablation for hypertrophic obstructive cardiomyopathy. Int J Cardiol 2007;119:403-7. http://doi.org/cxjnfd

37. Faber L, Seggewiss H, Gleichmann U. Percutaneous transluminal septal myocardial ablation in hypertrophic obstructive cardiomyopathy results with respect to intraprocedural myocardial contrast echocardiography. Circulation 1998;98:2415-21. http://doi.org/3v2

38. Qin J, Shiota T, Lever H, Asher C, Popovic Z, Greenberg N, et al. Conduction system abnormalities in patients with obstructive hypertrophic cardiomyopathy following septal reduction interventions. Am J Cardiol 2004;93:171-5. http://doi.org/c2dkds

39. Faber L, Welge D, Fassbender D, Schmidt H, Horstkotte D, Seggewiss H. Percutaneous septal ablation for symptomatic hypertrophic obstructive cardiomyopathy: Managing the risk of procedure-related AV conduction disturbances. Int J Cardiol 2007;119:163-7. http://doi.org/djh534