EuroIntervention 2019;15:411-417 published online March 2019

Alcohol septal ablation for hypertrophic obstructive cardiomyopathy: a contemporary reappraisal

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This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-18-00959

KEYWORDS

- hypertrophic cardiomyopathy
- multidisciplinary Heart Team
- septal ablation

Abstract

Percutaneous alcohol septal ablation (ASA) is an effective and minimally invasive therapeutic strategy to resolve left ventricular outflow tract obstruction (LVOTO) in patients with hypertrophic cardiomyopathy who remain symptomatic on maximally tolerated medical therapy. First performed by Sigwart in 1994, the procedure consists in determining an iatrogenic infarction of the basal interventricular septum to reduce LVOTO and alleviate symptoms. Since its first description, numerous studies have demonstrated its efficacy and safety, proposing ASA as a valid and attractive alternative to surgical septal myectomy. The success rate of the intervention is profoundly affected by patient selection and centre experience. In this review, we sought to summarise current evidence on ASA, describing the procedure and proposing a cardiomyopathy team-based approach to resolve clinical disputes in clinical practice.

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SUBMITTED ON 30/09/2018 - REVISION RECEIVED ON 1st 29/01/2019 / 2nd 26/02/2019 - ACCEPTED ON 07/03/2019

DOI: 10.4244/EIJ-D-18-00959

Abbreviations

ASA	alcohol septal ablation
HCM	hypertrophic cardiomyopathy
HOCM	hypertrophic obstructive cardiomyopathy
LAD	left anterior descending
LVOT	left ventricular outflow tract
LVOTO	left ventricular outflow tract obstruction
OTW	over-the-wire
SAM	systolic anterior motion
SCD	sudden cardiac death

Introduction

Hypertrophic cardiomyopathy (HCM) is defined by an unexplained left ventricular hypertrophy, not solely explained by abnormal loading conditions[1]. Given the extreme heterogeneity, HCM has received over 70 different names by individual investigators since its original description. Between the 1950s and 1960s, a condition called asymmetrical septal hypertrophy with a high risk of sudden cardiac death (SCD) was described in the UK, while two gurus of modern cardiology, Braunwald and Morrow, first described and treated the dynamic left ventricular outflow tract obstruction (LVOTO) of a novel disease called idiopathic hypertrophic subaortic stenosis[2]. Detailed search methods used for this review are provided in **Supplementary Appendix 1**.

HCM is a common (prevalence 1:500), inherited disease in more than half of cases, with sarcomeric protein genes being the most frequent cause[2]. The diagnosis is based on echocardiography (or cardiac magnetic resonance) demonstrating the degree (left ventricular wall thickness >15 mm) and pattern (asymmetric, septal, concentric) of hypertrophy[1]. Differential diagnosis between HCM and athlete's heart is challenging, and a multiparametric approach (including pre-participation ECG and imaging tests for competitive sports) is usually necessary to distinguish between physiological versus pathological hypertrophy[3]. A dynamic LVOTO is encountered in 30% of patients at rest, and another 30% after Valsalva manoeuvre, physical or pharmacological stress[2]. HCM patients can remain asymptomatic during most of their life course, unless they develop arrhythmias, left ventricular obstruction, diastolic or systolic dysfunction, consequently experiencing heart failure symptoms[2]. Even in patients with documented resting/provocable obstruction, the degree of symptoms can be extremely variable, making a clear classification of clinical status challenging. Life-threatening ventricular arrhythmias may be the tragic onset of the disease, particularly in young patients and apparently healthy athletes[2,4]. Thus, the SCD risk should be routinely evaluated according to clinical features and individualised risk calculators (i.e., HCM Risk-SCD model)[4].

DIAGNOSTIC AND THERAPEUTIC WORKUP IN LVOTO

Left ventricular outflow tract (LVOT) gradient is dynamic and varies with loading conditions and contractility. The obstruction is caused by systolic anterior motion (SAM) of the mitral valve and mitral-septal contact[2]. Although initially considered pathognomonic of HCM, SAM is now recognised to characterise any conditions that alter mitral valve apparatus structure/function, mitro-aortic angle, and left ventricular structure/contractility **(Supplementary Figure 1)**. In HCM, SAM has generally been explained by the "Venturi effect", with a consequent decrease of the mitro-aortic angle[5]; however, primary abnormalities of the mitral apparatus (anterior-inward displacement of papillary muscles, leaflet elongation), and drag forces also play an important role. A unifying hypothesis suggests that, during ventricular systole, the Venturi effect may elevate the mitral valve, while drag forces facilitate an anterior displacement of the mitral valve. This synergistic mechanism pushes leaflets into the outflow tract, resulting in LVOTO and eccentric mitral regurgitation[6]. SAM is considered as severe if it accounts for more than 30% of systole.

LVOTO is defined by the presence of peak LVOT gradient >30 mmHg[1]. Echocardiography is the first-line technique in the diagnostic workup of hypertrophic obstructive cardiomyopathy (HOCM)[1,2]. M-mode echocardiography documents SAM, while continuous wave Doppler measures LVOT gradient showing a late-peaking systolic velocity **(Supplementary Figure 1)**. Cardiac catheterisation may be required if there is discordance between symptoms and echocardiographic findings[1], and peak-to-peak gradient at catheterisation most closely approximates instantaneous peak gradient by continuous wave Doppler echocardiography. European guidelines[1] recommend investigating the presence of a latent obstruction in symptomatic HCM patients routinely **(Supplementary Table 1)**. Although patients may generate large gradients under pharmacological provocation (dobutamine, nitrates), these manoeuvres do not reliably reflect the mechanism of obstruction; thus, exercise echocardiography represents the technique of choice for reproducing the presence of dynamic LVOTO[7]. The prognostic role of LVOTO remains debated as HCM-related death in patients with or without LVOTO is similar[8]. Accordingly, the obstruction should be regarded mainly as a determinant of clinical/haemodynamic status rather than a marker of ominous outcome[1]. Beta-blockers, non-dihydropyridine calcium channel antagonists, and disopyramide reduce LVOTO and alleviate symptoms by their negative inotropic/chronotropic effect. Dual-chamber pacing is also a feasible strategy for reducing LVOTO in selected cases with refractory symptoms and high-risk for surgical/interventional treatment[9].

Alcohol septal ablation: historical, clinical and anatomic considerations

The concept of non-surgical interventional therapy for HOCM has evolved since the 1980s. The suggestion to use alcohol for inducing infarction of an hypertrophic septum is derived from the electrophysiology studies by Brugada on the treatment of ventricular arrhythmias using intracoronary alcohol injection[10]. Those studies inspired the Berlin cardiologist G. Berghöfer who, in 1989, first described the concept of an alcohol septal ablation (ASA) technique for HOCM (Berghoefer, personal communication). From the early 1990s, Gietzen and Kuhn described several cases of outflow gradient reduction after temporary balloon occlusion of the first septal branch[10]. In 1995, Sigwart first published three cases

of percutaneous ASA in HOCM patients resistant to treatment, reporting the resolution of subaortic stenosis and improvement of symptoms from the day after the intervention[10]. To date, ASA is considered an effective, minimally invasive strategy in patients with LVOT gradient ≥50 mmHg and symptomatic HOCM despite maximally tolerated drug therapy[1]. It consists of an iatrogenic, localised infarction of the basal septum at the point of contact of the anterior mitral valve leaflet. Despite the absence of large-scale randomised studies, the growing volume of observational data has attracted clinical and interventional cardiologists, proposing ASA as an appealing alternative to surgical septal myectomy[1].

CLINICAL CONSIDERATIONS

The first step in the decisional algorithm should include history collection and physical examination to assess clinical status and exclude other conditions (i.e., respiratory disease, thyroid dysfunction, anaemia) that might lead to misdiagnosis **(Supplementary Figure 2)**. ASA is recommended in patients with moderate-to-severe symptoms (i.e., New York Heart Association Class III-IV, Canadian Cardiovascular Society grade III-IV angina pectoris), recurrent pre-syncope/syncope, or heart failure, which interfere substantially with lifestyle, despite optimal medical therapy[1]. The procedure might be of benefit in selected cases with mildly symptomatic and severe LVOTO, although further evidence in this setting is needed[11]. The preference for ASA according to clinical features (i.e., age, comorbidities, pacemaker presence, pre-existing right bundle branch block) depends on local expertise **(Supplementary Table 2)**. ASA remains controversial in children and adolescents because of the lack of long-term data.

ANATOMIC CONSIDERATIONS: VENTRICULAR OUTFLOW AND CORONARY CIRCULATION

The evaluation of outflow geometry, septum morphology, and valve apparatus anatomy is crucial in predicting ASA feasibility, and the existence of LVOT, mitral valve and/or papillary muscle anomalies must be excluded. A septal thickness of ≥17 mm is the currently proposed cut-off by the European Guidelines to perform a safe procedure and minimise the risk of iatrogenic ventricular septal defect[1]. Of note, this recommendation is based on expert opinions. Definitive data in patients with modest hypertrophy (15-16 mm) are currently lacking; in these cases, an isolated mitral valve repair/replacement has been proposed as an alternative to septal reduction[12]. ASA efficacy may be inadequate in patients with severe hypertrophy (i.e., basal septum ≥25 mm) or extensive septal scar, due to the intrinsic limitation of alcohol[10,13].

The coronary circulation anatomy and concomitant atherosclerosis should always be assessed preoperatively (and irrespective of angina) by invasive coronary angiography, to obtain information about the course and size of the coronary arteries and septal branches[13]. As an additional imaging technique, computed tomography coronary angiography can also provide further details with regard to coronary anatomy and septal vascular supply in preparation for ASA[14].

The correct identification of a septal perforator branch with compatible anatomy for ASA is the cornerstone for a successful procedure. The first septal perforator artery is often chosen as target, perfusing in most cases the basal septum which is responsible for the greatest part of the obstruction[13]. It generally arises from the left anterior descending (LAD) artery and courses close to the His bundle and right bundle branch; non-LAD septal perforator branches are reported in 15% of cases and should be systematically screened[15]. If multiple culprit septal branches (identified by preprocedural or intraprocedural imaging tests) are present, they should all be ablated with multiple alcohol injections at index and/or staged procedures (if reintervention is needed). Inability to identify a satisfactory culprit septal branch occurs in approximately 10% of ASA candidates[16]. In some patients, no “optimal” septal artery for ablation can be identified due to the presence of multiple submillimetre septal branches not accessible to the necessary armamentarium[15]. In other cases, target septal branches also supply the free wall of the left ventricle, the papillary muscles or the right ventricle structures, similarly preventing the use of ASA.

Alcohol septal ablation: description of the procedure

ASA consists of selective infusion of 95-96° absolute alcohol into the septal perforator branch supplying the LV side of the basal or mid-cavitary septum[13]. The rationale is to determine an alcohol-induced occlusion of the vessel, with a controlled infarct in the basal septum that progressively turns from viable hypertrophic myocardium to thin akinetic scar, reducing LVOTO. Radial and femoral access are both feasible, and the choice mainly depends on operator preference and patient anatomy. The two approaches showed similar short- and long-term success rates, although the radial approach has been associated with lower rates of vascular complications[17].

The main steps of the procedure are shown in **Figure 1**. After positioning an arterial sheath and temporary pacemaker, analgesic drugs (i.e., morphine) can be administered to control pain caused by alcohol injection and iatrogenic infarct.

Diagnostic catheterisation may initially be performed to evaluate the LVOT gradient[1,13]. Coronary angiography is then performed to select the septal branch for ethanol infusion and assess vessel anatomy, origin, angulation, and size. Septal vessel course can be appropriately visualised through right anterior oblique or postero-anterior cranial projections, while the left anterior oblique view allows differentiating whether septal branches course along the right or left side of the septum (i.e., selection of left-sided branches reduces the risk of atrioventricular block)[13].

After the engagement of the left main with a guide catheter providing extra support, a short over-the-wire (OTW) balloon (1.5-2.5 mm in diameter, 6-10 mm in length, with a balloon-artery ratio of approximately 1.3:1) is passed over a standard 180 cm 0.014-inch extra support wire and positioned into the target vessel. OTW balloons are recommended as they allow selective septal branch angiography during balloon inflation (1-2 ml of contrast slowly injected

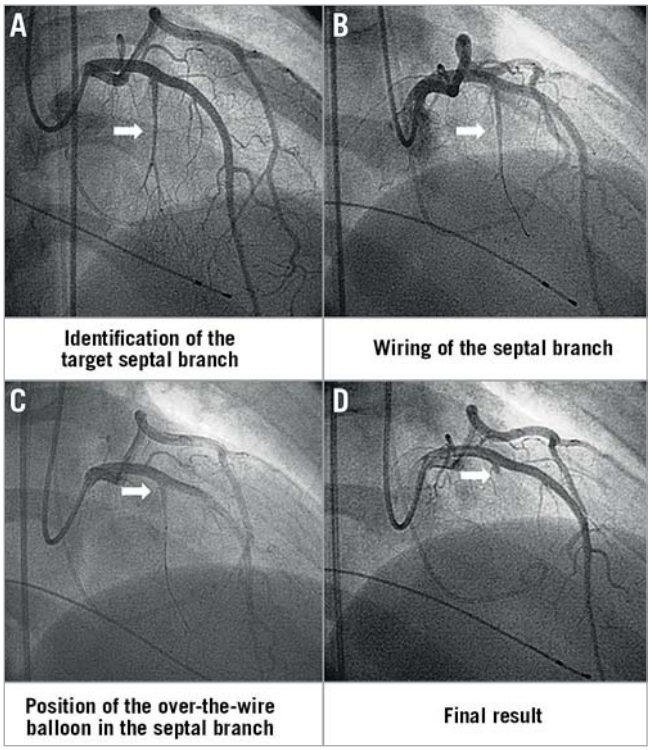

Figure 1. *Description of the procedure. A) Left coronary angiography allows identification of the target septal branch (arrow). B) The septal branch (arrow) is wired. C) An over-the-wire balloon is positioned in the proximal part of the septal branch (arrow) for injection of echo contrast and alcohol. D) Coronary angiography at the end of the procedure demonstrates the septal artery stump (arrow) after alcohol-induced occlusion.*

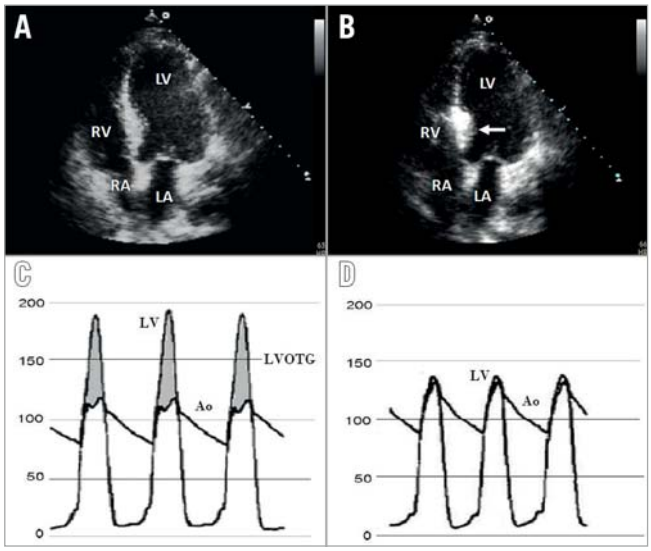

Figure 2. *Periprocedural monitoring. A) Transthoracic echocardiography before ASA showing asymmetric septal hypertrophy. B) Localisation of echo contrast (thick arrow) in the basal septum in apical four-chamber view. Cardiac catheterisation pressures showing the LVOTG between the LV and aorta before (C) and after ASA (D). Ao: aorta; LA: left atrium; LV: left ventricle; LVOTG: left ventricular outflow tract gradient; RA: right atrium; RV: right ventricle*

in the proximally occluded vessel) to test the correct positioning, complete septal occlusion, and absence of contrast reflux into the LAD. Due to high collateralisation between the left and right coronary, excluding the filling of any other coronary arteries through septal collaterals before alcohol injection is mandatory[18]. Then, the target vessel must be tested with myocardial contrast echocardiography **(Figure 2)**: 1-2 ml of echocardiographic contrast must be injected through the OTW balloon to visualise the target area and exclude contrast misplacement in other regions (i.e., inferior wall, papillary musculature, right ventricle), which represents an absolute contraindication to ethanol infusion[19]. Among echocardiographic contrast agents, first-generation Levovist® has been widely used, but is no longer available in many countries. Second-generation agents are rapidly washed out without formation of a good depot in the myocardium; Gelafundin®, a volume expander with good echocardiographic contrast, is also suitable for ASA. In more challenging cases, intracardiac echo or three-dimensional (3D) contrast echocardiography can be useful for intraprocedural guidance[20].

Thereafter, the operator can proceed with 1-3 ml ethanol injection over a one- to five-minute period in the target vessel[1]. The amount of alcohol is about 0.7-1 ml for every 10 mm of measured septal thickness[21]. During ethanol infusion, the inflated balloon must be firmly placed to occlude the vessel completely and avoid extensive myocardial damage[20]. Aggressive injection is discouraged as ethanol may traverse through collaterals and create inferior wall injury. Final coronary angiography excludes coronary injuries.

PROCEDURE EFFICACY: DEFINING A SUCCESSFUL ABLATION

The aim of ASA is to remove LVOTO and obtain a significant and sustained reduction in resting/provocable gradients (≥50% of baseline at six-month follow-up) **(Supplementary Figure 3)** and symptoms. Multinational studies have shown that after ASA approximately 90% of patients are in New York Heart Association Class I-II, the mean decrease of LVOTO is 76%[22,23], and need for reintervention about 7%[24]. Benefits may take up to 12 months to become clinically evident, particularly in younger patients[25]. Although a correlation between alcohol dose and the area of myocardial necrosis measured by cardiac biomarkers has also been reported (peak creatine kinase of 500-1,000 U/L per millilitre of ethanol injected)[26], cardiac enzyme levels have not been proved to predict procedural success or LVOT gradient reduction at follow-up[26]. The potential prognostic impact of ASA for reducing the risk of cardiovascular events is still a matter of debate[24,27], although residual LVOTO has been independently associated with an increased risk of arrhythmias and mortality[27].

PROCEDURAL SAFETY AND COMPLICATIONS

The most frequent complication related to ASA is transient or permanent complete atrioventricular block (approximately 30% and 10% of cases, respectively)[22,24], due to the anatomical proximity

of septal perforators with the conduction system. Complete atrioventricular block may also develop later (either as a delayed occurrence or a recurrence after recovery), especially in patients with advanced age or prolonged QRS. Thus, in selected cases, a temporary prophylactic pacemaker should be prolonged up to six days[28]. Pacemaker implantation is indicated if conduction disturbance persists for >24-72 hrs[13]. Since right bundle branch block occurs in more than 50% of cases, preprocedural pacemaker implantation might be considered in patients with pre-existing left bundle branch block[27]. In candidates for ASA, with a concomitant indication to receive an implantable cardiac defibrillator, device implantation should precede ASA in order to simplify post-procedural management. Of note, the HCM Risk-SCD model has been validated in patients undergoing ASA[29].

Other potential complications are the infarction of the anterior wall, papillary muscles, or right ventricle due to collateral septal flow to the right coronary artery or LAD[30]. As coronary occlusion during ASA may lead to immediate recruitment of collateral circulation, a single bolus injection of ethanol is suggested. If a second injection is needed, the presence of collaterals should be carefully re-checked before the additional injection[30]. The occurrence of procedure-related mortality is less than 1% (similar to surgical myectomy)[22,23]. Concerns have been raised about the association between higher alcohol dose (>2 ml) and worse prognosis[26]. Potential explanations could lie in the more extended infarct scar due to higher alcohol dose that can predispose to a higher risk of atrioventricular block and life-threatening arrhythmia. However, although some authors have reported a fivefold increase in the risk of ventricular arrhythmias with ASA compared with septal myectomy[31], this issue remains controversial. Proper patient selection and the use of low alcohol dose remain central to reduce the risk of complications.

Septal ablation for HOCM: personalised treatment

The choice of therapy should always be made on an individual basis with a multifactorial approach[10]. Shared decision making with patients should always be pursued, discussing the risks and benefits of each approach, then understanding the needs and preferences of the individual patient. In order to choose the best personalised treatment, it is crucial that the decision process is carried out with a multidisciplinary approach by a cardiomyopathy team working in dedicated cardiomyopathy centres of excellence.

CARDIOMYOPATHY TEAM

The concept of the "Heart Team" has been shown to improve decision making in coronary artery and valvular heart disease. Similarly, for HOCM, an experienced multidisciplinary "Cardiomyopathy Team" should analyse diagnostic evidence, put into context the clinical condition of patients, determine the need for interventions and the likelihood of safe and effective septal reduction with either ASA or myectomy. This team should ideally be composed of at least one clinical cardiologist, an interventional cardiologist, and a cardiac surgeon with recognised experience in the management of HOCM.

CARDIOMYOPATHY CENTRE

Results of both ASA and myectomy are largely dependent on the experience of the institutions to which patients are referred. When performed by experienced operators, ASA has been demonstrated to be safe and effective[1], although long-term data remain limited compared with surgical myectomy[24]. As regards myectomy, recent data suggest that the real-world mortality rate associated with myectomy is approximately 4-16%, as compared with <1% found in the best high-volume centres[23]. As regards ASA, a recent multicentre study has found that an institutional experience of >50 ASA procedures was associated with lower occurrence of complications, better cardiovascular survival, better haemodynamic and clinical effect, and less need for repeat interventions[32]. The American guidelines for HCM **(Supplementary Table 2)** recommend that septal reduction therapy - either septal myectomy or ASA - should be performed only by experienced operators in the context of a comprehensive HCM clinical programme, with the goal of a <1% operative risk for isolated septal myectomy and a major complication rate <3%[33]. To date, HCM centres with high-volume surgical programmes performing myectomy are not universally available. Moreover, procedural volumes are still low in most hospitals, and deviations from guidelines may result in critical issues[23]. Although specific data are lacking, a minimum of 10 ASA or 10 septal myectomies per operator per year seems to be a reasonable caseload to be required to maintain competence in septal ablation therapies[1].

Current limitations and future perspectives in LVOTO treatment

Although ASA represents a consolidated strategy, several limitations persist. The procedure-specific complication rate (particularly atrioventricular block) remains relevant. Long-term data supporting ASA are limited compared with surgical myectomy. Ultimately, operators with adequate experience are not widely available. To improve current practice in septal reduction, novel approaches have also been suggested. Percutaneous intramyocardial septal radiofrequency ablation is a safe and effective alternative to treat LVOTO, with a very low risk for conduction system injury[34]; however, further studies are needed to compare novel and standard techniques. More data are also required to clarify whether routine preprocedural computed tomography coronary angiography and intraprocedural guidance with additional imaging techniques (i.e., 3D or intracardiac echocardiography)[20] might improve practice in patients with challenging anatomy.

Conclusions

Two decades on from its introduction, ASA has proven to be effective and safe in patients with HOCM. Studies comparing ASA and myectomy have reported similarly low rates of complications, especially when performed in centres of excellence. As a weak point, the rates of reintervention and pacemaker implantation remain higher for ASA. In the near future, a multidisciplinary "Heart Team" approach, based on the consensus of clinicians, interventionalists, and surgeons

with recognised expertise in HOCM, has the potential to improve decisional strategy. Finally, the establishment of "cardiomyopathy centres" with high volume and dedicated skills should be considered to reduce procedural complications and improve outcomes in this special population. Further research is needed to assess the impact on daily clinical practice of these implementation strategies.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix 1. Search methods.

Supplementary Figure 1. Mechanisms of left ventricular outflow tract obstruction.

Supplementary Figure 2. Flow chart of the management of patients with left ventricular outflow tract obstruction.

Supplementary Figure 3. Long-term outcome.

Supplementary Table 1. Recommendations on septal reduction therapy from the 2014 European[1] and 2011 American[33] guidelines.

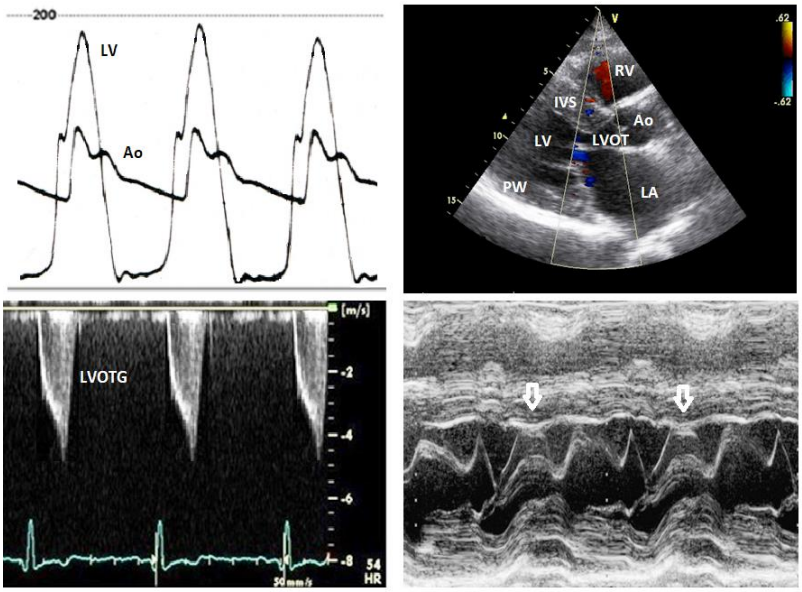
Supplementary Table 2. How to choose between alcohol septal ablation and surgical myectomy.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-18-00959

Supplementary data

Supplementary Appendix 1. Search methods

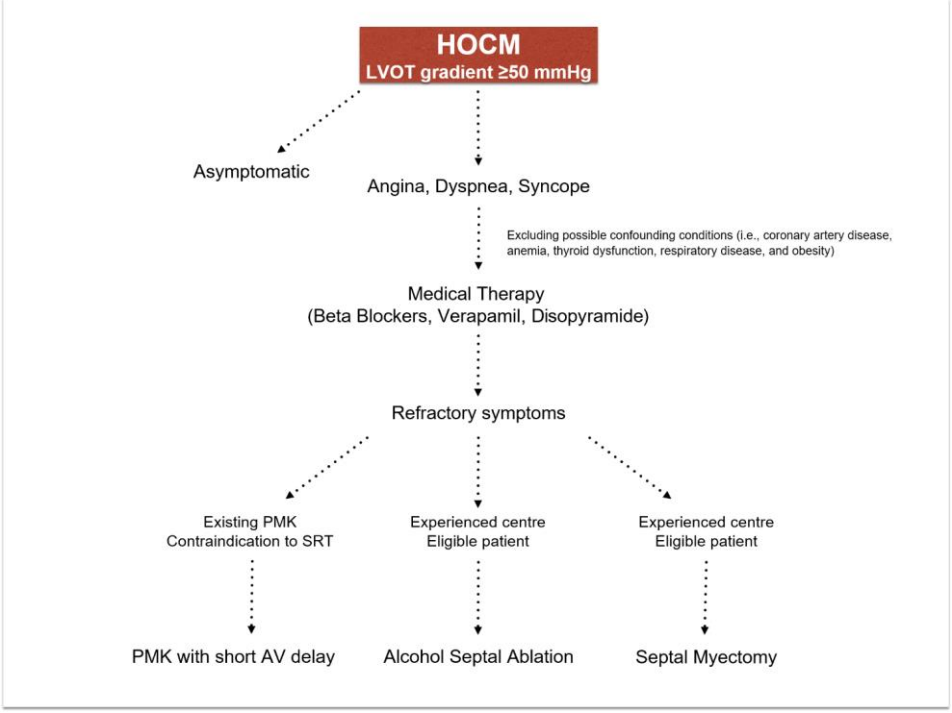
The methodology used for writing this review was based on the systematic search of available scientific information on ASA. Accordingly, the authors searched PubMed and Embase databases up to 31 August 2018 to identify relevant studies. Search keywords were the following: ‘alcohol septal ablation’, ‘hypertrophic cardiomyopathy’, ‘left ventricular outflow tract gradient’, ‘myectomy’, ‘myotomy’, ‘obstruction’, ‘outcome’, ‘prognosis’, ‘surgery’. Additional studies were searched in the Cochrane Library, Google Scholar, and Scopus. A thorough search through the bibliography of published trials, meta-analyses and reviews was also performed, also including studies presented or published in other languages. In addition, we searched the presentations at major cardiovascular scientific sessions including meetings of the American College of Cardiology, American Heart Association and European Society of Cardiology. No language restriction was enforced in order to minimise the risk of publication bias. The systematic review on ASA was conducted following current guidelines, including the Cochrane Collaboration and Meta-analysis Of Observational Studies in Epidemiology (MOOSE), and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) amendment to the Quality of Reporting of Meta-analyses (QUOROM) statement.



Supplementary Figure 1. Mechanisms of left ventricular outflow tract obstruction.

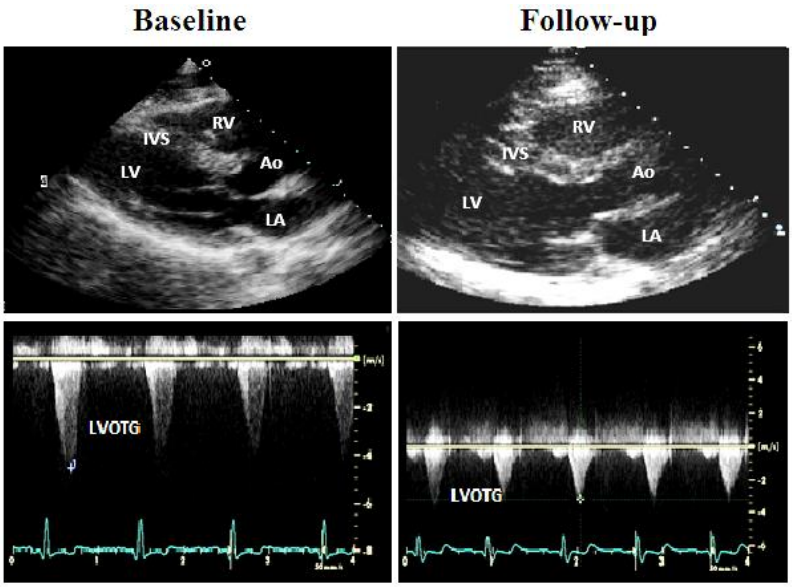
Cardiac catheterisation pressures (upper left) showing a dynamic LVOTG between the LV and aorta. Continuous wave Doppler echocardiogram across the LVOT (bottom left). Parasternal long-axis view demonstrating asymmetric septal hypertrophy with a SAM of the mitral valve leaflets (upper right). M-mode echocardiography shows the presence of SAM (thick arrows) documented by the contact of the anterior mitral valve leaflet with the septum (bottom right).

Ao: aorta; IVS: interventricular septum; LA: left atrium; LV: left ventricle; LVOT: left ventricular outflow tract; LVOTG: left ventricular outflow tract gradient; PW: posterior wall



Supplementary Figure 2. Flow chart of the management of patients with left ventricular outflow tract obstruction (modified from the 2014 ESC Guidelines).

AV: atrioventricular; HOCM: hypertrophic obstructive cardiomyopathy; LVOT: left ventricular outflow tract; PMK: pacemaker; SRT: septal reduction therapy



Supplementary Figure 3. Long-term outcome.

Long-axis views (upper panels) and continuous wave Doppler tracings (bottom panels) at baseline (left panels), and during follow-up (right panels). Following ASA, LV remodelling, septal thinning, and elimination of the LVOTG between the LV and aorta were observed.

Ao: aorta; IVS: interventricular septum; LA: left atrium; LV: left ventricle; LVOTG: left ventricular outflow tract gradient; RV: right ventricle

Supplementary Table 1. Recommendations on septal reduction therapy from the 2014 European [1] and 2011 American [33] guidelines.

Recommendation	Guidelines	Class of recommendation	Level of evidence
Septal reduction therapy should be performed only by experienced operators in the context of a comprehensive HCM clinical programme and only for the treatment of eligible patients with severe drug-refractory symptoms and LVOT obstruction.	ACCF/AHA 2011	I	C
When surgery is contraindicated, or the risk is considered unacceptable because of serious comorbidities or advanced age, alcohol septal ablation, when performed in experienced centres, can be beneficial in eligible adult patients with HCM with LVOT obstruction and severe drug-refractory symptoms (usually NYHA functional Class III-IV).	ACCF/AHA 2011	IIa	B
Alcohol septal ablation, when performed in experienced centres, may be considered as an alternative to surgical myectomy for eligible adult patients with HCM with severe drug-refractory symptoms and LVOT obstruction when, after a balanced and thorough discussion, the patient expresses a preference for septal ablation.	ACCF/AHA 2011	IIb	B
The effectiveness of alcohol septal ablation is uncertain in patients with HCM with marked (i.e., >30 mm) septal hypertrophy, and therefore the procedure is generally discouraged in such patients.	ACCF/AHA 2011	IIb	C
It is recommended that septal reduction therapies be performed by experienced operators, working as part of a multidisciplinary team expert in the management of HCM.	ESC 2014	I	C

Septal reduction therapy to improve symptoms is recommended in patients with a resting or maximum provoked LVOT gradient of 50 mmHg, who are in NYHA Class III-IV, despite maximum tolerated medical therapy.	ESC 2014	I	B
Septal reduction therapy should be considered in patients with recurrent exertional syncope caused by resting, or maximum provoked LVOTO gradient 50 mmHg despite optimal medical therapy.	ESC 2014	IIa	C
Septal myectomy, rather than ASA, is recommended in patients with an indication for septal reduction therapy and other lesions requiring surgical intervention (i.e., mitral valve repair/replacement, papillary muscle intervention).	ESC 2014	I	C

ACCF/AHA: American College of Cardiology Foundation/American Heart Association; ESC: European Society of Cardiology

Commented [RS1]: Does "ASA" need to be in bold?

Supplementary Table 2. How to choose between alcohol septal ablation and surgical myectomy.

Alcohol septal ablation	Surgical myectomy
Adults and elderlies	Children and adolescents
Septal bulge	Mitral valve intervention
Right bundle branch block	Left bundle branch block
Previous cardiac surgery	Low operative risk
Expert interventional team	Expert surgical team