Long-Term Outcome of Alcohol Septal Ablation in Patients with Obstructive Hypertrophic Cardiomyopathy: A Word of Caution

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Running head
Outcome After Alcohol Septal Ablation

Total word count:
5,782

Circulation Subject code
23-Catheter-based coronary and valvular interventions: other
Abstract

Background: The impact of alcohol septal ablation (ASA)-induced scar is not known. This study sought to examine the long-term outcome of ASA among patients with obstructive hypertrophic cardiomyopathy (HCM).

Methods and Results: Ninety-one consecutive patients (aged 54±15 years) with obstructive HCM underwent ASA. Primary study endpoint was a composite of cardiac death and aborted sudden cardiac death (SCD) including appropriate cardioverter-defibrillator (ICD) discharges for fast VT/VF. Secondary endpoints were non-cardiac death and other non-fatal complications. Outcomes of ASA patients were compared with 40 HCM patients who underwent septal myectomy. During 5.4±2.5 years primary and/or secondary endpoints were seen in 35 (38%) ASA patients, of whom 19 (21%) patients met the primary endpoint. The 1-, 5-, and 8-year survival-free from the primary endpoint was 96%, 86%, and 67%, respectively in ASA patients versus 100%, 96%, and 96%, respectively in myectomy patients during 6.6±2.7 years (log rank, \( P = 0.01 \)). ASA patients had a ~4 fold increase in the estimated annual primary endpoint rate (4.4% vs. 0.9%) compared with myectomy patients. In a multivariable model including a propensity score, ASA was an independent predictor of the primary endpoint unadjusted HR 5.2: 95% CI 1.2 to 22.1, \( P = 0.02 \); propensity score-adjusted HR 6.1: 95% CI 1.4 to 27.1, \( P = 0.02 \).

Conclusions: This study shows that ASA has potentially unwanted long-term effects. This poses special precaution given the fact that ASA is practiced worldwide at increasing rate. We recommend myectomy as the preferred intervention in patients with obstructive HCM.
Abbreviations and Acronyms

ASA  Alcohol septal ablation
HCM  Hypertrophic cardiomyopathy
ICD  Implantable cardioverter defibrillator
LV   Left ventricle or left ventricular
SCD  Sudden cardiac death
VF   Ventricular fibrillation
VT   Ventricular tachycardia

Keywords
Hypertrophic Cardiomyopathy; Ablation; Infarction; Mortality, Myectomy, Defibrillators
Introduction

Obstructive hypertrophic cardiomyopathy (HCM) is characterized by asymmetrical septal hypertrophy and dynamic left ventricular (LV) outflow tract obstruction. In symptomatic obstructive HCM patients surgical resection (myectomy) of the basal septum relieves LV outflow obstruction with improvement in long-term outcome. Alcohol septal ablation (ASA) is an alternative technique in which ethanol is injected into one or more septal perforator branches of the left anterior descending coronary artery. The efficacy of ASA has been proven with hemodynamic results mimicking those of myectomy. The septal morphologic appearance post-ASA is one of a myocardial infarction. It is not well-known whether this may produce an arrhythmic substrate and possibly trigger sudden cardiac death (SCD). Therefore, the present study sought to describe long-term post-ASA outcome.

Methods

Study Population

The study comprised 91 consecutive patients (aged 54±15 years) who underwent ASA between 1999 and 2007 at the Erasmus MC Rotterdam. Eligibility criteria for ASA were persistent New York Heart Association (NYHA) class III/IV dyspnoea and/or Canadian Cardiovascular Society class III/IV angina, despite standard medical therapy; LV outflow obstruction (gradient ≥50 mm Hg at rest or on Valsalva strain); ventricular septal thickness ≥15 mm and absence of need for surgical correction of mitral valve or coronary artery disease. Once indicated, patients were informed about ASA and myectomy as therapeutic options. The ASA cohort in the present study included all patients (n=31) from our center that were...
previously described in a multicenter center series. All patients gave written informed consent and the local institutional review board approved this study.

**Diagnostic Evaluation**

HCM was defined as a hypertrophied and non-dilated LV in the absence of other cardiac or systemic disease that could explain hypertrophy. All patients underwent a standard 2-dimensional echo-Doppler ultrasound examination, and clinical risk assessment including Holter monitoring and treadmill exercise testing.

**ASA procedure**

ASA was performed as previously described. In brief, using the standard Judkins technique, a 6F pacemaker lead was placed in the right ventricle, a 6F pigtail catheter was positioned into the LV, and a 7F Judkins guiding catheter in the ascending aorta. LV outflow tract peak systolic gradient was continuously monitored throughout the whole procedure. After initial coronary angiography for localizing the origin of the septal perforating arteries, a 1.5-2.5 x 10 mm balloon catheter was introduced over a 0.014-inch guide-wire into the target perforator artery and inflated. ASA was performed with the assistance of myocardial contrast (1 ml SonoVue, Bracco, Geneva, Switzerland) echocardiography to identify the septal region by the selected septal branch. If no contrast was seen outside the thickened basal septum, 0.5 mL alcohol was injected over 30 seconds followed by saline flush under continuous hemodynamic and ECG surveillance. A successful procedure was defined as absence of a residual invasive dynamic gradient >25 mm Hg. If the target reduction in pressure gradient was not achieved, alcohol injections were repeated after 5 minutes (maximum 2.5 mL) within the same
perforator branch. If not successful, the procedure was repeated in a second perforator branch. Once success was achieved, the balloon was deflated, and coronary angiography was repeated to confirm the occlusion of the septal branch and patency of the left anterior descending coronary artery. A temporary pacemaker lead was kept in place for at least 24 hours. A permanent pacemaker was used to treat a persistent high-grade AV block and a cardioverter defibrillator (ICD) implantation was considered at the discretion of the HCM cardiovascular specialist (FJTC).

**ICD**

ICD implantation for secondary prevention was considered for HCM patients who survived cardiac arrest and for primary prevention for HCM patients who had ≥2 conventional risk factors for HCM-related SCD. In addition, ICD was used as an alternative to conventional pacemaker in a few patients with post-ASA persistent high-grade AV-block. Device implantations were performed according to customary practice, with defibrillation thresholds routinely tested to document successful termination of lethal arrhythmias. For all patients, ICD programming was intended to avoid inappropriate therapy and tailored according to the clinical presentation. Mean ventricular tachyarrhythmia detection rate was 349±18 ms and the mean fibrillation detection rate was 283±15 ms.

Device interrogation was performed on a 3-month basis and otherwise following patients’ symptoms. Arrhythmias responsible for triggering defibrillator therapy were identified from the stored intracardiac electrograms. Defibrillator therapy was considered appropriate when triggered by VF or VT. Device therapy was considered inappropriate when triggered by “benign rhythms” with rates exceeding the programmed threshold, such as
supraventricular arrhythmias, sinus tachycardia, or device malfunction. Appropriate ICD discharge for lethal arrhythmia (fast sustained VT/VF) was considered equivalent to SCD.

**Study endpoints**

The primary study endpoint was a composite of cardiac death and aborted SCD including ICD appropriate shocks for fast VT (defined as sustained VT with a rate >260 bpm) or VF. Secondary endpoints included non-cardiac death, procedural failure, and other non-fatal complications. A failed ASA was defined as the need for re-intervention for persistent symptoms due to residual LV outflow tract gradient.14

**Myectomy patients**

Outcome of ASA patients were compared to outcome of 40 consecutive patients with obstructive HCM who underwent modified septal myectomy during the same period of enrollment of the ASA patients.5

**Follow-up**

Two investigators (FJTC, MM) examined all patients at 3, 6 and 12-months and then on yearly basis with complete follow-up to 9 years. Cause of death was documented from hospital records, general practitioners records and civil registries. SCD was defined as instantaneous and unexpected death within 1 hour after a witnessed collapse in patients who previously were in stable clinical condition, or nocturnal death with no antecedent history of worsening symptoms.
Statistical analyses

Qualitative variables were expressed as percentages and quantitative variables as mean (standard deviation). The normality distribution for continuous data was examined with the Shapiro–Wilk test. Comparison of numerical variables was performed using the two-sided Student’s t-test or Wilcoxon rank-sum test, and the chi-square or Fisher’s exact tests were used to compare qualitative variables. A continuous propensity score analysis was performed to adjust for the intergroup (ASA vs. myectomy) differences in baseline characteristics caused by the selection bias inherent to the nonrandomized nature of the study. A propensity score representing the likelihood of having ASA as opposed to myectomy was calculated for each patient by using a logistic regression analysis that identified variables independently associated with the type of procedure. All variables listed on Table 1 were included in a univariate regression analysis and variables exhibiting a P-value <0.20 were included in a multivariate model. Those variables (P<0.020) were: age, positive risk factors for HCM-related SCD, LV outflow tract peak gradient, of ventricular septum thickness, and LV end-systolic diameter. Kaplan-Meier curves were employed to delineate freedom from death or aborted SCD and compared with log-rank test. In addition, the incidence of post-procedural primary endpoint was further evaluated between groups as unadjusted, adjusted for propensity score in a multivariable regression analysis. The propensity score did not emerge as an independent predictor of the primary endpoint, suggesting that differences attributed to the type of intervention by the initial Cox regression analyses were not explained by bias in patient selection on the basis of their baseline characteristics. Results were expressed as hazard ratios (HRs) with 95% confidence intervals (CIs). A P value <0.05 was considered
significant. SPSS version 15.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results

Baseline characteristics

Table 1 lists baseline data of all patients. In 81 (89%) patients ASA was based solely on patient preference and 10 (11%) patients had a high surgical risk (Table 2).

Procedural data

Mean number of septal perforator arteries used for ASA was 1.1±0.3. Mean ethanol volume was 3.5±1.5 mL with a larger volume in the early (1st 25 patients) versus late (4.5±1.2mL vs. 2.4±1.0 mL) experience. LV outflow tract peak pressure gradient reduced from 92±25 at baseline to 8±17 mmHg (P<0.001) immediately post-ASA.

Primary endpoint

During 5.4±2.5 years, one or more events were seen in 35 (38%) patients post-ASA (Table 3), of whom 19 (21%) met the primary endpoint. Using Kaplan-Meier survival analysis, the estimated annual rate of the primary endpoint was 4.4% over 8-year (Figure 1). During follow-up 11 (12%) patients died due to cardiac causes in 9 and non-cardiac causes in 2.

-In hospital and 30-days primary endpoint

Procedure-related mortality was seen in 2 patients (2%) due to cardiac tamponade and intractable VF, respectively. This latter patient died during the ASA procedure after the first
0.5 mL ethanol injection. Autopsy did not reveal a specific cause. Four (4%) patients survived in-hospital cardiac arrest. One patient had VF on the day post-ASA; the patient refused to receive an ICD and died suddenly 2.3 years post-ASA. One patient had intra-procedural VF and follow-up went uneventful over 7.4 years. One patient survived 2 episodes of in-hospital VF (day 4) and sustained VT 5.6 years post-ASA. One patient survived in-hospital sustained VT with hemodynamic instability on the day post-ASA. In these latter 3 patients an ICD was implanted for secondary prevention.

-Long-term (>30 days) primary endpoint

During follow-up, 6 patients (7%) died due to SCD and one patient (1%) died 5.8 years post ASA due to end-stage heart failure. Eleven (12%) patients survived 1 or more episodes of ventricular tachyarrhythmia. In 4 patients the arrhythmia was successfully terminated by ICD discharge, for fast VT/VF 0.3, 0.6, 1.3, and 2.6 years after ICD implantation. Cycle length was 200, 230, 230, 330 ms, respectively (Figure 2). In the remaining 7 patients without ICD cardiopulmonary resuscitation was needed. Of those 7 patients, one later died during follow-up) and 3 patients who survived sustained VT with hemodynamic instability 3.2, 4.4 year and 5.6 years, respectively post-ASA, received an ICD.

Secondary endpoints

Twenty-eight patients (31%) had one or more secondary endpoints.

-In hospital and 30-days secondary endpoints (Table 3)

Eight (9%) patients had an ICD implantation. None of these patients had inappropriate discharge during the 30-days follow-up post-ASA. Two patients had non-fatal acute
myocardial infarction due to coronary artery dissection and ethanol spill into the left anterior descending coronary artery. These 2 patients were managed successfully and underwent myectomy at a later date. As mentioned before, ASA failure was seen in 3 patients due to technical causes. Four (4%) patients had a high-grade AV block and received a permanent pacemaker. One patient subsequently had extended hospitalization for pericardial effusion due to right ventricular perforation from temporary pacemaker placement. This patient underwent myectomy 2 months later due to unsuccessful reduction of LV outflow pressure gradient.

-Long-term (>30 days) secondary endpoints (Table 3)

Two patients (2%) died due to non-cardiac causes (suicide and cancer 2 years post-ASA). Eight (9%) patients had an ICD implantation, of whom 2 patients had inappropriate discharges due to atrial arrhythmias. At the most recent follow-up, 10 (11%) patients had failed ASA, of whom 7 (8%) patients had early successful reduction, but suffered progressive increase in LV outflow gradient associated with recurrence of symptoms. Five patients had repeat ASA and 5 patients underwent myectomy. One or more episodes of atrial fibrillation were reported in 10 (11%) patients.

Conventional risk factors for HCM-related SCD and the primary endpoint

Forty ASA patients (44%) had at least 1 conventional risk factor for HCM-related SCD, of whom 13 (14%) had 2 risk factors. No patient had a history of aborted SCD before ASA. In addition, there was no difference in the number of risk factors between patients with and without the primary endpoint (0.79±0.79 versus 0.54±0.72, P=0.21). Likewise, as seen in
Figure 3, incidence of primary or secondary end-points was not related to the number of conventional risk factors for HCM-related SCD.

**Outcome of myectomy versus ASA patients**

As seen in Table 1, patients who underwent myectomy had similar baseline characteristics as ASA patients. Also, comparable immediate reductions of LV outflow gradient were seen. There was 98% procedural success in myectomy patients and the in-hospital and 30 days post-operative clinical course went uneventful. During a mean follow-up of 6.6±2.7 years, 2 (5%) patients died and none had aborted SCD. The 1-, 5-, and 8-years survival free from the primary endpoint was 100%, 96%, and 96%, respectively, which was better than seen in the ASA patients (96%, 86%, and 67%, respectively; $\chi^2=5.9$, log-rank $P=0.01$: Figure 1). ASA patients had about 4.8-fold annual rate of the primary endpoint (4.4% versus 0.9%) compared to myectomy patients. A total of 5 (6%) patients had an ICD implantation in the myectomy group compared with a total of 16 (18%) in the ASA patients and 1 patient had permanent pacemaker for complete AV-block. ICD implantation was for primary prevention indication before (4 patients) and after (1 patient) myectomy. As abovementioned, ICD appropriate shocks were recorded in 4 (25%) of the ICD patients in the ASA group. None of the myectomy patients had an ICD shock during follow-up. Myectomy was repeated in 1 patient due to recurrent obstruction 8 days post-operative and in 1 patient due to dehiscence of the mitral valve patch 6 months post-operative. In both patients post-operative clinical course went uneventful with a follow-up of 8.6 and 3.8 years, respectively.

Cox proportional-hazards regression analysis among the total intervention group (n=131) including baseline variables that are listed on Table 1, type of intervention (ASA versus myectomy), ethanol volume and propensity score showed that only ASA was an
independent predictor of the primary endpoint with an unadjusted HR 5.2: 95% CI 1.2 to 22.1, P=0.02; propensity score-adjusted HR 6.1: 95% CI 1.4 to 27.1, P=0.02. Of note large (>2 mL) ethanol volumes were not associated with the primary endpoint (P=0.72) (Figure 4).

Importantly, only 1 of 10 (10%) ASA patients in whom myectomy was considered a high-risk procedure met the primary endpoint compared to 18 out of the remaining 81 (22%) low-to-moderate risk patients. The combined rate of post-procedural primary and secondary endpoints in myectomy patients was 15% compared with 38% among ASA patients, (χ²=5.8; adjusted P<0.02).

Discussion

The main finding of our study is that approximately 1 out of 3 HCM patients who underwent ASA had major cardiovascular complications during the procedure and follow-up, including cardiac death or resuscitated SCD in approximately 1 out of 5 patients. Compared with the myectomy patients, ASA patients had a 4.8-fold increase in the estimated annual primary endpoint, respectively.

Of note, the early (30-days) complication rate of ASA patients in our study was similar to the complication rate reported in a meta-analysis in ~3,000 ASA patients with respect to mortality (2.2% versus 1.5%), VF rate (3.3% versus 2.2%), permanent pacemaker dependency (11.0% versus 10.5%), pericardial effusion (1.1% versus 0.6%), and coronary artery dissection (1.1% versus 1.8%), whereas procedural failure occurred less often (3.3% versus 11.1%). Importantly, most serious adverse events were late and therefore, ASA carries a long-term risk. Of note, all ASA patients who died suddenly had no ICD, where there was no death among the patients who received an ICD. Since its introduction in 1994,
the number of ASA procedures has exceeded the number of surgical procedures by 10- to 35-fold during the same time period worldwide. The notion of our study is to provide a word of caution to the increased number of ASA procedures done.

**Arrhythmogenic ASA-induced scar**

The potential risk of arrhythmic events due to post-ASA healed myocardial infarction in patients prone to arrhythmias has been a matter of concern since early practice of ASA. Our group described post-ASA regional hyperenhancement on contrast-enhanced magnetic resonance imaging in the basal septum in all patients. Mean infarction size was 20±9 g, corresponding to 10±5% and 31±16% of LV and septal mass, respectively. Frequent episodes of non-sustained VT, and sustained VT and VF have been reported in several series early post-ASA. The high arrhythmogenic susceptibility of HCM patients could be attributed to myocardial fiber disarray.

In a large cohort of HCM patients, ICD interventions appropriately terminated VT/VF in 20% of patients with a 10.6% annual intervention rate for secondary prevention after aborted SCD and 3.6% per year for primary prevention of SCD. In a recent study, annual ICD intervention rate was 2.8% over a 3-years period in HCM patients who underwent ASA and ICD implantation for primary prevention of SCD.

The relation between the size of post-ASA infarction and arrhythmogenic risk is not clearly understood. In a recent paper, a lower ethanol volume was an independent predictor of improved long-term survival following ASA, a finding that we could not reproduce. Boekstegers et al. reported that electrophysiologic testing before and 4 to 6 months post-ASA did not suggest enhanced arrhythmogenesis. However, most of the arrhythmic complications
in our series occurred after 4 years post-ASA. Of note, the size of the septal infarction in our series\textsuperscript{19} was not different from other series.\textsuperscript{17}

ASA versus surgical treatment of obstructive HCM patients

Ideally, a randomized trial comparing myectomy and ASA should be performed to examine whether they are true equivalent therapeutic options. However, such a trial is unlikely to be undertaken.\textsuperscript{30} Alternatively, comparison of ASA and myectomy outcomes can be performed by analyzing data from single center registries. Maron et al. found in a small series of ASA patients a 4-fold increase in appropriate ICD intervention rate (10.3\% versus 2.6\% per year, respectively) compared with patients who had previously undergone surgical septal myectomy.\textsuperscript{26} In another report, myectomy patients with an ICD had over 10-fold fewer appropriate ICD discharges (0.2\% versus 4.3\% annually, respectively) compared to non-operated HCM patients with an ICD.\textsuperscript{31} In another report by Sorajja et al. surgical patients had significantly better symptom-free survival compared to ASA (89\% versus 71\%) over a 4-year follow-up.\textsuperscript{32} In our HCM cohort ASA induced relief of LV outflow obstruction with subsequent reduction in LV hypertrophy\textsuperscript{6, 11} and improvement in clinical status.\textsuperscript{6, 11} LV function,\textsuperscript{6, 11, 33} and microcirculation.\textsuperscript{6} However, the incidence of arrhythmic complications and cardiac death was approximately 4-fold as compared to myectomy patients.

In contrast to the findings described above, Kwon et al. did not suggest excess mortality on long-term follow-up in ASA versus myectomy patients when statistically corrected for the higher risk profile of ASA patients.\textsuperscript{34} However, their primary endpoint did not include arrhythmic complications, which occurred in ~half of patients with the primary endpoint in our series. In addition, “mortality” rate was 3-fold increased in the ASA patients
compared to myectomy patients (24% versus 8%). Most of the ASA mortality occurred in patients >65 years old.\textsuperscript{34} However, a log-rank test between the ASA and myectomy in 28 propensity matched patients was negative,\textsuperscript{34} obviously because ASA patients >65 years old were excluded in this analysis. In addition, 6 (11%) of the ASA patients underwent myectomy after failed ASA despite being high-risk candidates.\textsuperscript{34} It is not clear to what extent these crossed over patients to myectomy contributed to the mortality in that group. Fernandes et al. recently reported a 1.1% rate of SCD on long-term follow-up post-ASA\textsuperscript{35} However, contrary to our study 8% of patients were lost to follow-up.\textsuperscript{35} In addition, no data on arrhythmic complications were reported.

**Risk factors of HCM-related SCD and post-ASA outcome**

There is uncertainty as to precisely identify HCM patients at-greatest risk of SCD.\textsuperscript{36} In some studies, a single risk factor for SCD was sufficient to justify prophylactic ICD,\textsuperscript{26} whereas in other studies well known risk factors were not predictive of ICD therapy.\textsuperscript{27} In our study the number of risk factors for SCD in ASA patients was very low and was not different between patients with and without the primary endpoint. Moreover, the 9 patients who died due to cardiac cause without ICD had no major or minor risk factors for SCD except for 1 patient who had a family history of SCD and had recurrent episodes of non-sustained VT. A logical inference of our risk factor data is that ASA itself is a risk factor for SCD independent of the amount of ethanol, age and co-morbidities.

Of note, appropriate ICD discharges are not equivalent to SCD. In addition, the small sample size, might not rule out completely the possibility that large dosages of alcohol would
result in a larger myocardial infarction and thus more of a propensity to develop ventricular arrhythmias.

**Conclusions**

The therapeutic choice for ASA is limited by the lack of long-term safety data as compared to myectomy. Since a randomized study between ASA and myectomy is unlikely to be performed we can only rely on registries in single centers. Our data show that ASA is effective but has potentially adverse long-term effects. This poses special precaution given the fact that ASA is practiced worldwide at increasing rates. We recommend myectomy as the preferred treatment of choice in patients with symptomatic obstructive HCM.

**Acknowledgments**

The authors are grateful to Dr Eric Boersma, PhD (Department of Epidemiology and Statistics, Erasmus University, Rotterdam, The Netherlands), for the commenting on statistical analysis.

**Disclosure:**

None.
REFERENCES


5. van der Lee C, ten Cate FJ, Geleijnse ML, Kofflard MJ, Pedone C, van Herwerden LA, Biagini E, Vletter WB, Serruys PW. Percutaneous versus surgical treatment for


Figures Legends

**Figure 1.** Survival free from death and aborted SCD including ICD appropriate therapy of patients with obstructive hypertrophic cardiomyopathy (HCM): treated with alcohol septal ablation (ASA, n=91) and patients whom was treated with septal myectomy (n=40). Log-rank, \( P=0.01 \).

**Figure 2.** Appropriate ICD therapy for ventricular arrhythmia with atrio-ventricular dissociation. From top to bottom, bipolar atrial electrogram with marker annotations, and ventricular rate-sensing electrogram with marker annotations are shown. The rhythm before the marker annotation "Shock 1" displays a ventricular tachyarrhythmia (mean ventricular cycle length ~200 ms) detected in the ventricular fibrillation detection zone. The arrhythmia is terminated by shock therapy (marker annotation “Shock”), which restores sinus rhythm with atrio-ventricular sequential pacing.

**Figure 3.** Graphic display of the percentage of patients with the study endpoints who had 0, 1, or ≥2 risk factors for HCM-related SCD.

**Figure 4.** Survival free from death and aborted SCD including ICD appropriate therapy after alcohol septal ablation (ASA) of patients treated with ≤2mL (in continuous line) and >2mL ethanol (in dotted line).
Table 1. Baseline Characteristics of the HCM Patients

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<th>ASA</th>
<th>Myectomy</th>
<th>P Value</th>
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<td>(n=40)</td>
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<tr>
<td><strong>Demographics</strong></td>
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<td>54±15</td>
<td>49±15</td>
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<td>50(55%)</td>
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<tr>
<td>Coronary artery disease</td>
<td>4(4%)</td>
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<td><strong>Risk factors for HCM-related SCD</strong></td>
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<td>History of SCD</td>
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<td>Spontaneous sustained VT</td>
<td>15(16%)</td>
<td>5(13%)</td>
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<td>Family history of SCD</td>
<td>10(11%)</td>
<td>5(13%)</td>
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<td>Non-sustained VT</td>
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<td>Abnormal blood pressure response to exercise</td>
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<td>Ventricular septum &gt;30 mm</td>
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<td>2(5%)</td>
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<td>Diabetes mellitus</td>
<td>1(1%)</td>
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<td>7(8%)</td>
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<td>Atrial fibrillation</td>
<td>5(5%)</td>
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<td>39±4</td>
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<td>23±5</td>
<td>21±6</td>
<td>0.05</td>
</tr>
<tr>
<td>Mitral regurgitation– grade</td>
<td>1.5±0.9</td>
<td>1.7±0.8</td>
<td>0.23</td>
</tr>
<tr>
<td>Systolic anterior motion of the mitral valve– grade</td>
<td>2.3±0.9</td>
<td>2.4±0.9</td>
<td>0.56</td>
</tr>
<tr>
<td>LV ejection fraction– %</td>
<td>69±6</td>
<td>68±6</td>
<td>0.38</td>
</tr>
<tr>
<td>Left atrial diameter– mm</td>
<td>49±9</td>
<td>50±11</td>
<td>0.59</td>
</tr>
</tbody>
</table>

Values are mean±SD or n(%) and otherwise stated; CCS = Canadian Cardiovascular Society; HCM = Hypertrophic cardiomyopathy; ICD = Implantable cardioverter defibrillator; LV = Left ventricular; NYHA = New York Heart Association functional class; VF = VT ventricular fibrillation; VT = Ventricular tachycardia
### Table 2. Cited Reasons for Selection of ASA or Myectomy

**ASA patients (n=91)**
- Patient preference: 81 (89%)
- Co-morbidities: 10 (11%)
- Prior failed myectomy: 0

**Myectomy patients (n=40)**
- Patient preference: 2 (5%)
- Failed ASA: 5 (13%)
- Mitral valve abnormalities: 31 (78%)
- Three-vessel disease: 1 (3%)
- Coronary anatomy not suitable for ASA: 1 (3%)

Abbreviations see Table 1.
ASA = Alcohol septal ablation
Table 3. Study Endpoints Among ASA Patients (n=91)

<table>
<thead>
<tr>
<th>Primary Endpoint (n=19)</th>
<th>Early &lt;30 days</th>
<th>Late ≥30 days</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no of patients (percentage)</td>
<td>6(6%)</td>
<td>13(14%)#</td>
<td>19(21%)#</td>
</tr>
<tr>
<td>Cardiac mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Total</td>
<td>2(2%)</td>
<td>7(8%)</td>
<td>9(10%)</td>
</tr>
<tr>
<td>-SCD</td>
<td>1(1%)</td>
<td>6(7%)</td>
<td>7(8%)</td>
</tr>
<tr>
<td>-Other cardiac death</td>
<td>1(1%)</td>
<td>1(1%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>Arrhythmogenic complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Total</td>
<td>4(4%)</td>
<td>7(8%)</td>
<td>11(12%)</td>
</tr>
<tr>
<td>-Resuscitated SCD</td>
<td>4(4%)</td>
<td>3(3%)</td>
<td>7(8%)</td>
</tr>
<tr>
<td>-Appropriate ICD shocks</td>
<td>0</td>
<td>4(4%)</td>
<td>4(4%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary Endpoints (n=28)#</th>
<th>Early &lt;30 days</th>
<th>Late ≥30 days</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-cardiac death</td>
<td>0</td>
<td>2(2%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>ICD implantation</td>
<td>8(9%)</td>
<td>8(9%)</td>
<td>16(18%)</td>
</tr>
<tr>
<td>Inappropriate ICD therapy</td>
<td>0</td>
<td>2(2%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>2(2%)</td>
<td>0</td>
<td>2(2%)</td>
</tr>
<tr>
<td>ASA failure</td>
<td>3(3%)</td>
<td>7(8%)</td>
<td>10(11%)</td>
</tr>
<tr>
<td>Permanent pacemaker dependency</td>
<td>4(4%)</td>
<td>0</td>
<td>4(4%)</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>1(1%)</td>
<td>0</td>
<td>1(1%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1(1%)</td>
<td>10(11%)</td>
<td>11(12%)</td>
</tr>
</tbody>
</table>

# Some patients had more than 1 endpoint.
Abbreviations see Table 1.
Survival Free From Death and Aborted Sudden Cardiac Death Including Appropriate Defibrillator Shocks (%)

Log-rank test P = 0.72

<table>
<thead>
<tr>
<th>Follow-Up Time (yrs)</th>
<th>No at risk</th>
<th>Ethanol $\leq 2\text{ mL}$</th>
<th>Ethanol $&gt;2\text{ mL}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>20</td>
<td>60</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>16</td>
<td>46</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ethanol $\leq 2\text{ mL}$
Long-Term Outcome of Alcohol Septal Ablation in Patients with Obstructive Hypertrophic Cardiomyopathy: A Word of Caution
Folkert J. ten Cate, Osama I.I. Soliman, Michelle Michels, Dominic A.M.J. Theuns, Peter L. de Jong, Marcel L. Geleijnse and Patrick W. Serruys

Circ Heart Fail. published online March 23, 2010;
Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3289. Online ISSN: 1941-3297

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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