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Implantable Cardioverter-Defibrillator Therapy for Primary Prevention of Sudden Death After Alcohol Septal Ablation of Hypertrophic Cardiomyopathy

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Objectives The purpose of this study was to examine the effects of alcohol septal ablation (ASA) on ventricular arrhythmias among patients with obstructive hypertrophic cardiomyopathy (HCM), as measured by appropriate implantable cardioverter-defibrillator (ICD) discharges.

Background Alcohol septal ablation is an effective therapy for patients with symptomatic HCM. However, concern has been raised that ASA may be proarrhythmic secondary to the iatrogenic scar created during the procedure. The impact of ASA on ventricular arrhythmias has not been well described.

Methods This prospective study included 123 consecutive patients with obstructive HCM who underwent ASA and had an ICD implanted for primary prevention of sudden cardiac death (SCD). The ICDs were implanted based on commonly accepted risk factors for SCD in the HCM population. Data from ICD interrogations during routine follow-up were collected.

Results Nine appropriate ICD shocks were recorded over a mean follow-up of 2.9 years in the cohort, which had a mean of 1.5 ± 0.9 risk factors for SCD. Using Kaplan-Meier survival analysis, the estimated annual event rate was 2.8% over 3-year follow-up. There were no significant differences in the incidence of risk factors between patients who did and did not receive appropriate shocks.

Conclusions The annual rate of appropriate ICD discharges after ASA is low and less than that reported previously for primary prevention of SCD in HCM. This suggests that ASA is not proarrhythmic. Traditional SCD risk factors did not predict ICD shocks in this cohort. (J Am Coll Cardiol 2008;52:1718–23) © 2008 by the American College of Cardiology Foundation

Hypertrophic cardiomyopathy (HCM) is associated with significant morbidity, and it is one of the leading causes of sudden death under the age of 35 years (1–6). Traditionally, surgical myectomy is used to relieve outflow tract obstruction and improve symptoms in this population (7–12). More recently, alcohol septal ablation (ASA) has become an increasingly common nonsurgical treatment for obstructive HCM. This procedure results in an iatrogenic myocardial infarction, which in turn decreases septal thickness and systolic anterior motion (SAM) of the mitral valve, reducing resting and provocable left ventricular outflow tract (LVOT) gradients (13–18). It is an effective treatment for the symptoms of obstruction, resulting in decreased angina, reduced heart failure symptoms, and improved exercise tolerance (18).

Despite the clear benefit of ASA on the symptoms associated with HCM, the effects of this procedure on the arrhythmia substrate for sudden death remain controversial. On one hand, the septal myocardial infarction could be a substrate for ventricular tachyarrhythmias and increase the incidence of sudden death (19). On the other hand, the remodeling that occurs after ASA with reductions of outflow tract gradient and septal thickness could reduce the risk of sudden death (20). Despite this controversy, there are no large studies evaluating the risk of life-threatening arrhythmias or sudden death in HCM after ASA. Accordingly, the present study was a prospective long-term evaluation of implantable cardioverter-defibrillator (ICD) therapy after ASA.

Methods

Patient eligibility. This study included 123 consecutive patients undergoing ASA for symptomatic HCM who had

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an ICD for primary prevention of sudden cardiac death (SCD) at either the Medical University of South Carolina or Baylor College of Medicine. The criteria for selection of patients for ASA were reported previously (16). All patients signed a written informed consent form, and this study was approved by the local institutional review boards.

The ICDs were implanted for the primary prevention of SCD based on commonly accepted risk factors. These risk factors included: 1) a family history of SCD in a first-degree relative; 2) a history of syncope or near-syncope not explained by other mechanisms; 3) an abnormal blood pressure response during exercise treadmill test (a failure to increase systolic blood pressure by >20 mm Hg during peak exercise using a Bruce protocol); and 4) marked septal hypertrophy (septal thickness ≥3 cm). The decision for ICD implantation was left to the clinical discretion of the primary physician. Patients were excluded from the study if they had a history of SCD, sustained ventricular arrhythmias (before study enrollment), or appropriate ICD therapy before their ASA. To minimize the risk of selection bias, only those patients with an ICD implanted before ASA or during the procedural hospitalization were included.

ASA procedure. The details of the ablation procedure have been described in previous reports. Briefly, the septal arterial branches supplying the septal bulge were identified with the assistance of contrast echocardiography. Between 1 and 3 ml ethanol was used in each septal branch. Gradients across the LVOT were measured before and after ethanol injection, and initial success was defined as a decrease in LVOT gradient at rest by >50% as measured by Doppler echocardiography or catheter immediately after the procedure. Additional septal branches were targeted if initial success was not achieved. A temporary pacemaker in the right ventricular apex was used in all patients who did not have a permanent pacemaker or ICD, and was removed if there was no evidence of high-grade atrioventricular (AV) block after ASA. If high-grade AV block did occur, the temporary pacemaker remained in place until baseline conduction returned or a permanent pacemaker was implanted. Of note, ICD implantation was only performed if patients were at risk for sudden death by clinical criteria as described above, not for the treatment of heart block. The ICD programming was left to the discretion of the implanting physician, but in general only shock therapy was used to treat ventricular tachyarrhythmias and not antitachycardia pacing.

ICD follow-up. The patient follow-up period began immediately after ASA and ICD implantation. The ICD data were collected during routine follow-up visits (every 3 to 6 months). The ICD shocks were verified by 2 investigators, and deemed appropriate if they treated an episode of ventricular tachycardia (VT) or ventricular fibrillation (VF). Dual-chamber stored electrograms were available in all patients to facilitate the interpretation of events. For survival analysis, follow-up was censured at the time of first appropriate ICD therapy. Inappropriate therapies (attributable to rapidly conducted atrial fibrillation, sinus tachycardia, or other causes) were noted, but were not an end point in this study.

Statistical methods. Data are expressed as a mean ± SD. Continuous variables were compared using the Student *t* test, whereas categorical variables were analyzed using the Fisher exact test. Survival analysis for shock-free survival was performed using the Kaplan-Meier method. A p value ≤0.05 was considered statistically significant. Survival analysis and statistical calculations were performed using the GraphPad Prism software package (GraphPad Software, Inc., San Diego, California).

Abbreviations and Acronyms

- **ASA** = alcohol septal ablation
- **AV** = atrioventricular
- **HCM** = hypertrophic cardiomyopathy
- **ICD** = implantable cardioverter-defibrillator
- **LVH** = left ventricular hypertrophy
- **LVOT** = left ventricular outflow tract
- **NSVT** = nonsustained ventricular tachycardia
- **SAM** = systolic anterior motion
- **SCD** = sudden cardiac death
- **VF** = ventricular fibrillation
- **VT** = ventricular tachycardia

Results

Data from all 123 consecutive subjects with HCM undergoing ASA were collected and available for analysis. Ten patients (8.1%) had at least 1 repeat ASA, and 1 had a total of 3 septal ablation procedures. The ICD implantation was performed after the ASA procedure in 87 patients (70.7%), whereas the remaining 36 patients underwent implantation before the initial procedure (802 ± 853 days). All patients received dual-chamber devices (right atrium, right ventricular apex) to allow for atrial based pacing, if needed.

Baseline characteristics. Table 1 compares the baseline characteristics of the patients in this study who underwent ASA and had an ICD implanted for primary prevention with a similar cohort of consecutive patients who underwent ASA at the Medical University of South Carolina but did not receive ICDs. The baseline characteristics and data from the ASA procedures for the study population are summarized in Table 2. The mean age of the ICD cohort was 48 ± 15 years, and 81 patients (66%) were male. The subjects had

Table 1 Comparison of Baseline Characteristics in Patients Who Underwent ASA and Received an ICD for Primary Prevention With a Non-ICD Cohort

	Non-ICD Cohort (n = 284)	ICD Cohort (n = 123)	p Value
Age (yrs)	53 ± 16	48 ± 15	0.003
Gender (male/female)	146/138	81/42	0.009
Resting gradient before ASA (mm Hg)	66 ± 37	61 ± 36	0.237
Resting gradient after ASA (mm Hg)	7 ± 12	14 ± 11	<0.001
Septal thickness (cm)	2.1 ± 0.5	2.2 ± 0.5	0.079
Risk factors for SCD	1.1 ± 0.9	1.5 ± 0.9	<0.001

Values are mean ± SD.
ASA = alcohol septal ablation; ICD = implantable cardioverter-defibrillator; SCD = sudden cardiac death.