Clinical Characteristics and Outcome of Alcohol Septal Ablation With Confirmation by Nitroglycerin Test for Drug-Refractory Hypertrophic Obstructive Cardiomyopathy With Labile Left Ventricular Outflow Obstruction

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Careful evaluation, including provocation tests, is needed to specify an indication for septal reduction therapy in patients with drug-refractory hypertrophic obstructive cardiomyopathy. This study aimed to evaluate the outcome of alcohol septal ablation (ASA) using an intravenous nitroglycerin test (IV-NTG). Of consecutive 156 patients, after excluding cases of severe valvular disease and repeat septal reduction therapy, we investigated the clinical characteristics of patients with labile obstruction (n = 32) and the outcomes after ASA using the IV-NTG test; comparisons were made with those exhibiting basal obstruction (a resting gradient of ≥30 mm Hg). The patients with labile obstruction had less left ventricular mass (141 ± 47 vs 182 ± 59 g, p = 0.003) and less brain natriuretic peptide values (414 ± 576 vs 744 ± 625 pg/ml, p <0.001) than those with basal obstruction. Immediately after ASA, the gradients improved from 15 ± 7 to 5 ± 5 mm Hg and the IV-NTG-provoked gradients improved from 74 ± 25 to 13 ± 9 mm Hg, respectively. At 1-year follow-up, the New York Heart Association functional class had improved from 2.7 ± 0.5 to 1.3 ± 0.5. There was no sudden cardiac death during the follow-up period (5.1 ± 3.0 years), and 8-year survival free from cardiovascular death was 94%. In conclusion, patients with labile obstruction had less-severe left ventricular hypertrophy but exhibited symptoms comparable to those with basal obstruction. The IV-NTG test is a useful method for rapidly confirming acute reduction of the latent gradient after the ASA procedure, and the outcome of ASA for labile obstruction was favorable. **(Am J Cardiol 2015;116:945−951)**

Alcohol septal ablation (ASA) has been performed for hypertrophic obstructive cardiomyopathy (HOCM) when symptoms cannot be treated effectively even after optimization of medical treatment.[1−8] To achieve optimal results with ASA in patients with refractory symptoms related to labile obstruction, the nature of the obstruction of the left ventricle (LV) should be accurately described. Previous studies focused on ASA for provocable obstruction have been reported.[9,10] Both studies demonstrated that provocable obstruction could cause drug-refractory symptoms and ASA was effective for patients without a baseline gradient. In contemporary clinical practice, Valsalva maneuver and postextrasystolic potentiation have been used as nonpharmacologic methods to elucidate immediate improvement of the latent gradient[11]; however, it is unclear which provocation method was most appropriate during the ASA procedure. The use of nitrates, which mainly decrease the LV afterload, has been described as a conveniently administered method for immediate detection of the gradient.[12] Nevertheless, there have been no reports that address the usefulness of nitrates during the ASA procedure. Therefore, the purposes of this study were (1) to demonstrate the clinical characteristics of labile obstruction, (2) to determine the usefulness of the intravenous nitroglycerin (IV-NTG) test, and (3) to conduct a follow-up study after ASA for labile obstruction.

Methods

We reviewed the institutional registry data of patients with drug-refractory HOCM who underwent ASA. Of consecutive 156 patients, after excluding cases of severe valvular disease and repeat septal reduction therapy, we investigated the clinical characteristics of patients with labile obstruction (n = 32) and the outcomes after ASA using the IV-NTG test, comparisons were made with those exhibiting basal obstruction (a resting gradient of ≥30 mm Hg, n = 120). In this study, IV-NTG bolus tests were administered during ASA to confirm their acute effects in patients with a resting gradient <30 mm Hg at baseline. At the initial presentation, we had reviewed and optimized the prescribed patient medications. Basically, symptomatic patients with HOCM were

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See page 950 for disclosure information.

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http://dx.doi.org/10.1016/j.amjcard.2015.06.023

Table 1
Baseline characteristics of the study population in comparison with basal obstruction

Variable	Labile Obstruction (n = 32)	Basal Obstruction (n = 120)	p value
Age (years)	65 ± 12	61 ± 15	0.282
Female	25 (78%)	85 (71%)	0.508
Height (m)	1.55 ± 0.12	1.55 ± 0.10	0.826
Body weight (kg)	59 ± 13	57 ± 12	0.405
Body mass index (kg/m^2)	24.3 ± 3.3	23.6 ± 3.9	0.215
Brain natriuretic peptide (pg/mL, normal <18.4pg/mL)	414 ± 576	744 ± 625	<0.001
Atrial natriuretic peptide (pg/mL, normal <43.0pg/mL)	162 ± 188	162 ± 127	0.691
Family history of sudden cardiac death	5 (16%)	15 (13%)	0.769
Septal thickness ≥ 30 mm	1 (3%)	6 (5%)	1.000
Ventricular Tachycardia/Fibrillation	5 (17%)	19 (16%)	0.502
Unexplained syncope	9 (28%)	30 (25%)	0.795
Abnormal blood pressure response	7/15 (47%)	9/59 (15%)	0.014
Implantable cardioverter-defibrillator implantation	4 (13%)	6 (5%)	0.219
Dual chamber pacemaker implantation	2 (7%)	0 (0%)	0.043
History of congestive heart failure	7 (22%)	25 (21%)	1.000
Coronary artery disease	4 (13%)	2 (2%)	0.018
Atrial fibrillation	5 (16%)	30 (25%)	0.054
Hypertension	17 (53%)	50 (42%)	0.317
Dyslipidemia	18 (56%)	54 (45%)	0.320
Diabetes mellitus	6 (19%)	8 (7%)	0.077
Smoker	9 (28%)	37 (31%)	0.162
Obstruction Type			0.814
Left ventricular outflow tract type	20 (63%)	81 (68%)	
Mid-ventricular obstruction	3 (9%)	14 (12%)	
Combined obstruction	9 (28%)	25 (21%)	
New York Heart Association functional class	2.7 (0.5)	2.7 (0.5)	0.692
Anginal symptoms	18 (56%)	60 (50%)	0.691
Faintness ~ Syncope	16 (50%)	54 (45%)	0.694
Aborted cardiac arrest	1 (3%)	4 (3%)	1.000
Measurements of the left-sided heart			
Interventricular septum thickness (mm)	16.9 ± 3.8	18.6 ± 4.1	0.014
Posterior wall thickness (mm)	11.7 ± 2.4	12.8 ± 3.1	0.120
Left ventricular end-diastolic diameter (mm)	42.2 ± 5.6	42.2 ± 6.1	0.980
Left ventricular end-systolic diameter (mm)	22.9 ± 4.3	23.9 ± 4.8	0.320
Left atrial diameter (mm)	42.0 ± 6.5	44.9 ± 7.8	0.057
Mitral regurgitation area (cm^2)	5.4 ± 5.2	7.1 ± 5.3	0.101
Left ventricular mass (g)	141 ± 47	182 ± 59	0.003
Number of hypertrophic segments	2.4 ± 1.6	4.2 ± 2.9	0.009
Medications at alcohol septal ablation procedure			
Beta blockers	30 (94%)	110 (92)	1.000
Class Ia agents	27 (84%)	77 (64%)	0.033
Class III agents	0 (0%)	4 (3%)	0.580
Calcium-channel blockers	6 (19%)	34 (28%)	0.367
Angiotensin-converting enzyme inhibitors/Angiotensin receptor blockers	4 (13%)	18 (15%)	1.000
Diuretics	6 (19%)	30 (25%)	0.640
Nitrates	1 (3%)	0 (0%)	0.211

given β blocker if titrated. Then, class Ia was added in patients with residual symptoms to improve gradient. Patients were considered as ASA candidates if symptoms were life limiting (New York Heart Association [NYHA] functional class IIm to IV) after optimization of medication and a provoked gradient >50 mm Hg was confirmed by at least 1 method during simultaneous pressure recordings as described in the following. We carefully excluded patients with subaortic stenosis, abnormal insertion of papillary muscle, extreme elongation of anterior mitral leaflet and large apical aneurysm. All patients who underwent ASA had been consecutively assigned to the institutional registry database at the Nippon Medical School Hospital. The institutional review committee approved the study. All patients gave written informed consent.

Diagnosis of hypertrophic cardiomyopathy (HCM) has been established by transthoracic echocardiography (TTE). The definition of HCM in echocardiography was based on the presence of a maximal LV wall thickness ≥15 mm[7] and the absence of other conditions that might explain left ventricular hypertrophy (LVH) during the clinical course. LV cavity size, LV wall thickness, and left atrial diameter