Non-Surgical Septal Reduction in Hypertrophic Obstructive Cardiomyopathy

Thesis
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Abstract

Key Words: hypertrophic-cardiomyopathy- alcohol-septal ablation-echocardiography

Background— Alcohol septal ablation (ASA) has been introduced as alternative therapy for hypertrophic obstructive cardiomyopathy that's refractory to medical treatment.

Methods and Results—In this study we report the acute and short term of results of ASA in 21 symptomatic patients(44.45 ±12.48 years) with hypertrophic cardiomyopathy. They had resting or provoked left ventricular outflow tract (LVOT) pressure gradient ≥ 30 mmHg. Peak invasive LVOT gradient at rest was 75.8 ± 42.6 mmHg and dropped to 18 ± 23 mmHg with a p-value < 0.001, in the cath lab after ASA. One month later, the peak Doppler LVOT gradient decreased to 20 ± 13 mmHg (p-value < 0.001) compared to Doppler baseline. One patient developed CHB and a permanent pace maker was implanted. After one month symptoms improved as NYHA functional class decreased from 2.63 ± 0.91 to 1.02 ± 0.51 with p-value of < 0.001. Those with angina pectoris class 2.141 **±** 1.08, decreased to 0.71 ± 0.56 with p-value of < 0.001.

Conclusion— Alcohol septal ablation is an effective and safe procedure for the management of patients with HCM refractory to medical therapy.

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LIST OF ABBREVIATIONS

2-D	Two-dimensional
A	Mitral flow A-wave
A 1	Mitral flow A-wave baseline
A 2	Mitral flow A-wave 24h post ASA
A 3	Mitral flow A-wave month after ASA
AAI	Single chamber pace maker (atrial)
ACC	American collage of cardiology
ACE	Angiotensin converting enzyme
AF	Atrial fibrillation
AHA	American heart association
AICD	Automatic implantable cardioverter defibrillator
AMP	Adenosine monophosphate
ASA	Alcohol septal ablation.
ATP	Adenosine triphosphate
AV	Atrioventricular
CABG	Coronary artery bypass graft.
CCS	Canadian cardiology society
CCU	Cardiac care unit
CHB	Complete heart block
CHB 1	Complete heart block before ASA
CHB 2	Complete heart block after ASA
CK	Creatine kinase
cTnI	Cardiac troponin I
DDD	dual-chamber pace maker
ECG	Electrocardiogram
E	Mitral flow E-wave
E 1	Mitral flow E-wave baseline
E 2	Mitral flow E-wave 24h post ASA
E 3	Mitral flow E-wave month after ASA
EF	Ejection fraction
EF 1	Ejection fraction 24h post ASA
EF 2	Ejection fraction 24h post ASA
EF 3	Ejection fraction month after ASA

HCM	Hypertrophic cardiomyopathy
HF	Heart failure
HOCM	hypertrophic obstruction cardiomyopathy
LA	Left atrium
LA 1	Left atrium baseline
LA 2	Left atrium after 24h of ASA
LA 3	Left atrium 1 month after ASA
LAD	left anterior descending artery
LAMP2	Lysosome-associated membrane protein 2
LBBB	Left bundle branch block
LBBB 1	Left bundle branch block before ASA
LBBB 2	Left bundle branch block after ASA
LV	Left ventricle
LVEF	Left ventricular ejection fraction
LVEF 1	Left ventricular ejection fraction before ASA
LVEF 2	Left ventricular ejection fraction after 24h of ASA
LVEF 3	Left ventricular ejection fraction 1 month after ASA
LVH	Left ventricular hypertrophy
LVIDD	Left ventricle internal dimensions in diastole
LVIDD 1	LVIDD baseline
LVIDD 2	LVIDD after 24h of ASA
LVIDD 3	LVIDD 1 month after ASA
LVIDS	Left ventricle internal dimensions in systole
LVIDS 1	LVIDS baseline
LVIDS 2	LVIDS after 24h of ASA
LVIDS 3	LVIDS 1 month after ASA
LVOT	left ventricular outflow obstruction
MAZE	Surgical procedure to abolish atrial fibrillation;
MCE	Myocardial contrast echocardiography
MLP	muscle LIM protein
MPI	Myocardial perfusion imaging
MR	Mitral regurgitation
MR 1	Mitral regurgitation baseline
MR 2	Mitral regurgitation 24h of ASA
MR 3	Mitral regurgitation 1 month after ASA
MRI	Magnetic resonance imaging

MVG	Velocity gradient
MVR	Mitral valve replacement
NSRT	Non-surgical septal reduction therapy
NSVT	Non-sustained ventricular tachycardia
NYHA	New York heart association
PAPSP	Pulmonary artery predicted systolic pressure
PAPSP 1	PAPSP baseline
PAPSP 2	PAPSP after 24h of ASA
PAPSP 3	PAPSP 1 month after ASA
Pg	Pressure gradient
Pg1	Baseline doppler pressure gradient
Pg2	In cath. acheived doppler pressure gradient
Pg3	Doppler pressure gradient after 24h
Pg4	Doppler pressure gradient after month
Pgi1	Invasive pressure gradient baseline
Pgi2	Invasive pressure gradient after ASA
PRKAG2	gamma-2 regulatory subunit of adenosine monophosphate-activated protein kinase (PRKAG2
PV	Pulmonary vein
PWT	Posterior wall thickness
PWT 1	Posterior wall thickness before ASA
PWT 2	Posterior wall thickness after 24h
PWT 3	Posterior wall thickness
RAAS	Rrenin-angiotensin-aldosterone system
RBBB	Right bundle block
RBBB 1	Right bundle block before ASA
RBBB 2	Right bundle block after ASA
SAM	systolic anterior motion
SAM 1	systolic anterior motion baseline
SAM 2	systolic anterior motion 24h after ASA
SAM 3	systolic anterior motion after 1 month
SCD	Sudden cardiac death
SD	Sudden death
SWT1	Septal wall thickness baseline
SWT2	Septal wall thickness 24h after ASA
SWT3	Septal wall thickness after 1 month
TASH	Transcoronary ablation of septal hypertrophy

TDE	Tissue Doppler echocardiography
VF	Ventricular fibrillation
VPBs	Ventricular premature beats
VT	Ventricular tachycardia
VTI	Velocity time integral
VTI 1	Velocity time integral baseline
VTI 2	Velocity time integral 24h after ASA
VTI 3	Velocity time integral after 1 month
VVI	Single chamber pace maker (ventricular)
WPW	Wolff-Parkinson-White

Introduction and aim of work

Hypertrophic cardiomyopathy (HCM) is a unique disease entity that has fascinated cardiologists for decades. The original description of a patient with hypertrophic cardiomyopathy was by Sir Russell Brock in 1958 when he found a normal aortic valve at the time of operation for “severe” aortic stenosis. One year later Dr. Donald Teare reported on several patients who died suddenly and were thought to have a hamartoma in the heart (1). In early 1960s, Eugene Braunwald described the unique hemodynamic of the disease entity known at that time as *idiopathic hypertrophic subaortic stenosi*s. Originally defined as a cardiomyopathy in which there is severe hypertrophy in the absence of a known etiology (2).

The prevalence of HCM appears to be about 0.2 percent in the general population. It is possible; however, that many individuals with HCM go undetected in the community because they manifest mild symptoms and are not referred for echocardiographic studies presentation is sudden death. HCM patients at high risk for sudden death are young, with no or only mild symptoms and preserved systolic function (3).

Relief of left ventricular outflow obstruction (LVOT) obstruction in hypertrophic obstruction cardiomyopathy (HOCM) leads to positive clinical and hemodynamic effects. Obstruction can be relieved by medications, surgery or dual-chamber pacing. Medications are tolerated by some patients and their positive clinical and hemodynamic effects may be maintained. Surgical myotomy-myomectomy is effective in relieving the LVOT gradient, but it requires open heart surgery and surgical studies have reported a small incidence of postoperative atrial fibrillation, aortic insufficiency, complete heart block, remyectomy, ventricular septal defect and death. Dual-chamber pacing studies have demonstrated a modest gradient reduction associated with subjective symptomatic improvement. The mechanism of benefit is unclear, but may be related to both an acute decrease in the LVOT gradient and induced by

alteration in septal activation and a long-term effect due to ventricular remodeling. Non-surgical septal reduction (alcohol septal ablation) has been introduced as an alternative modality to treat patients with incapacitating symptoms due to HOCM. All the reported studies so far have documented a significant improvement in symptoms along with a significant reduction in LVOT gradient immediately after the procedure and up to one year afterwards (4).

So the aim of work is to assess:

1- Subjective and objective short term results of the procedure.

2- Evaluate alcohol septal ablation (ASA) procedure.

Etiology and Genetics of Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is a primary disorder of the myocardium. Although unexplained left ventricular hypertrophy (LVH) is an important pathologic hallmark of disease, altered cardiac morphology is usually age-dependent and is often lacking in children (5, 6).

The prevalence of HCM in the general population, as determined from echocardiographic studies in the United States, Japan, and China, has ranged from 0.16 to 0.30 percent. (3,5-8)Men and blacks appear to be affected more than twice as often as women and whites, respectively (3). It is not known if this number reflects an accurate incidence of familial disease.

Histopathology:

Reveals signs of disorganized myocyte architecture, including disarray of myocyte fibers, intertwined hypertrophied myocytes with bizarre-shaped nuclei, and focal or widespread interstitial fibrosis. In addition to myocyte hypertrophy, the collagen matrix is disorganized and thickened, suggesting that HCM involves changes in connective tissue elements as well as sarcomere proteins (3). Myocyte disarray appears to be a direct response to functional and structural abnormalities of the mutated sarcomeric protein, while fibrosis and small vessel disease are secondary phenomena unrelated to the disarray, but modified by other factors such as left ventricular mass and perhaps local autocrine factors (8).