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RESEARCH ARTICLE

PERCUTANEOUS TRANSLUMINAL SEPTAL MYOCARDIAL ABLATION IN HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY: ACUTE AND INTERMEDIATE RESULTS IN TEN PATIENTS

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ABSTRACT

Background: In the treatment of Hypertrophic Obstructive Cardiomyopathy, surgical myectomy is considered as standard procedural extension to drug therapy with negatively inotropic agents. Percutaneous Transluminal Septal Myocardial Ablation has been introduced as an alternative to the surgical myectomy for reducing left ventricular outflow tract gradient. We report the acute and intermediate results after percutaneous transluminal septal myocardial ablation in symptomatic patients with hypertrophic obstructive cardiomyopathy. **Methods and Results:** Ten patients with a mean age of 46.5 ± 6, in NYHA class 2.9 ± 0.31symptoms, resistant to maximal medical management and a coronary artery anatomy suitable for intervention were selected. Percutaneous transluminal septal myocardial ablation was performed by injection of 1± 0.5 mlof 96% alcohol into 1.2 ± 0.42 septal arteries. Mean post-interventional creatine kinase rise was 867.8 ± 301. During the procedure 3 patients developed transient complete heart block, which was present for a mean duration of 11.8 ± 9.7 hours. No patient required permanent pace maker implantation. The left ventricular outflow tract gradient decreased from 98.4 ± 26.8 (64 -160) to 7.6 ±3.5 (0-12) mm of Hg at rest and after an ectopic from 128 ± 24.7 (98-190) to 17.5 ±5.5 (11-30) mm of Hg. They were discharged at 5± 0.81 days after an uncomplicated hospital course. Clinical and echocardiographic follow up was achieved at the end of 6 months, which showed a further reduction in the gradient from 87.3 ± 11 to 13.4 ± 5.37mm of Hg with NYHA class reduction from 2.9±0.31 to 1. 1±0.31. **Conclusion:** Percutaneous transluminal septal myocardial ablation is an effective non-surgical technique for reduction of symptoms and left ventricular outflowtract gradient in HOCM.

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INTRODUCTION

Hypertrophic obstructive cardiomyopathy (HOCM) is primarily a familial and genetically determined myocardial hypertrophy with a dynamic left ventricular out flow tract obstruction (LVOT) and occasionally, the right ventricle.[1,2] HOCM is a frequent cause of stress inducedsyncope or sudden cardiac death.[3]Therapeutic approaches aim at reducing the extent of outflowtract obstruction, thus improving the clinical symptoms. Negatively inotropic agents[4-6],theimplantation of Dual chamber pace maker8-10, as well as surgical myectomy have all been usedsuccessfully.[11-19]Through transitory balloon occlusion of a septal branch, a reduction in the LVOTgradient could be established in individual cases.[20]In 1995, as a result of these positive experiences, SIGWART was the first to describe the successful non-surgical ablation of hypertrophied septal myocardium in three patients with a consecutive decrease in obstruction.[21]We report the acute and intermediate (six months) follow up of the haemodynamic results in tenpatients treated with this procedure. The aim of the study was to assess the efficiency of percutaneous transluminal septal myocardial ablation (PTSMA) in patients with hypertrophicobstructive cardiomyopathy.

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METHODS

Between February 2018 to June 2019 we treated 10 patients, (7 males and 3 females)of mean age 46.5± 6.1 (range 40 - 55 years) with a mean disease duration of 2.5 ±1.2 years. All ten patients were symptomatic despite maximum tolerable medical treatment and were in New York Heart Association (NYHA) functional class 2.9 ±_0.31. No patient had undergone surgical myectomy or Dual Chamber pacemaker (DDD) implantation.

The viability and novelty of this therapeutic procedure was explained to the patients. The possible requirement of permanent pacemaker implantation was explained, and written consent was also taken. In all the patients the diagnosis of HOCM was confirmed by clinical and non-invasive methods. Before and as well as after the intervention the LVOT gradient was determined by Doppler echocardiography. The Left Ventricular (LV) internal dimensions including interventricular septal thickness was measured. The occurrence of systolic anterior movement of mitral valve (SAM) and mitral regurgitation werealso recorded.These measurements were taken before, 4-6 days and 6 months after the procedure.

PROCEDURE: After both non-invasive and invasive pre intervention diagnosis that excluded aortic valve gradient, the intervention was carried out. RHC and LHC were done through right femoral approach. Temporary pacing wire was placed in RV apex. Left femoral artery was punctured and 7F end hole catheter was positioned at LV apex which served to record aortic pressure and thus LV- Aorta gradient was monitored throughout the procedure. The LVOT gradient was measured at rest and after an ectopic. After adequate heparinization (70 IU/Kg) left coronary angiography was done to delineate the septal branches of LAD. After the LCA cannulation, over the wire balloon (2.5 mm x 10 mm Concerto) waspositioned across the septal artery and a probatory balloon occlusion for five minutes was performed. If a significant reduction in LVOT gradient was achieved after balloon inflation, this vessel was identified as the culprit septal artery. Then the guide wire was pulled out and the balloon position was reconfirmed by injection of contrast into the septal artery. This was done to ensure that there was no reflux of contrast medium and subsequent alcohol into LAD. Initially 0.5 ml of absolute alcohol was injected over 5 minutes while simultaneously measuring LVOT gradient. If sufficient reduction in LVOT gradient was not achieved, and then additional amount of alcohol was injected up to a maximum of 1.5ml. Subsequently other septal branches were also ablated if the gradient reduction was not achieved with single septal branch occlusion. After renewed determination of the LVOT gradient, the investigation was brought to an end. Post interventional monitoring of the patients was carried outin the intensive care unit. Intensive care included both Electrocardiographic monitoring anddetermination of creatine kinase (CK) and creatine kinase MB (CPKMB) fraction values. Postprocedure follow up was by daily ECG recording till discharge. After 6 months all patients underwent clinical and noninvasive follow up examination.

STATISTICAL ANALYSIS: Continuous variables are expressed as mean value ± SD.

RESULTS

Acute Result: During the intervention, a mean of 1.2 ±0.42 septal branches were occluded by injection of 1± 0.5 ml of alcohol after probatory balloon occlusion. The mean procedural time was 52.3 ± 14. 7(range 40-92 mins) with a mean fluoroscopy time of 18.7 ± 4.02 mins (range 14-28 mins). Chestpain during the procedure was alleviated with Injection Morphine. In two of the patients, gradientreduction could not be achieved with occlusion of a single septal artery, and in these patients the haemodynamic results improved with ablation of second septal artery. In one patient aged 55 years, who had hypertrophic obstructive cardiomyopathy along with ischemic heart disease, septalablation procedure was combined with angioplasty to LAD. Reduction of LVOT gradient was achieved in all ten patients. The mean LVOT gradient decreased from a mean of 98.4 ± 26.8 (64-115) to 7.6 ± 3.5 (0-11) after septal ablation by alcohol. The post ectopic gradient reduced from 128 ± 24.7 (98-190) to 17.5 ± 5.5 (11-30).LVOT gradient by echocardiography reduced from a mean of 87.3 ±11 (70-102) to 13.5 ± 5.03(5-20). After six months follow up, LVOT gradient remained at 13.4 ± 5.37 (4-22).Echocardiography revealed new wall motion abnormality in basal septum in all patients. Three patients had complete heart block, which was present for a mean period of 11.85 ± 9.7hours, requiring temporary pacing. However permanent pacemaker implantation was not required for any of the patients. RBBB was persistent in eight patients at discharge. During alcohol injection, all patients complained of marked chest pain requiring IV administration of 4 mg of Morphine. Peak CPK was 867.8 ± 301.7 U/Litre (624-1438) and peak CPK-MB fraction was 108.8 ±41.6 (68-196). The patients were monitored in ICCU for a mean duration of 2.85 ±0.69 days and were discharged after a mean duration or 5 ± 0.81 days. All the patients had significant clinical improvement with a NYHA class reduction from 2.9 ± 0.31 to 1.3 ± 0.48-postprocedure. In the patient who underwent PTCA to LAD along with septal ablation both the procedures were successful. Drug treatment was continued with low dose beta-blocker in all the patients at the time of discharge.

Six month follow up: After six months, a clinical and Echocardiographic assessment was carried out in all ten patients. At this time, there was significant clinical improvement in all patients with a mean reduction from baseline NYHA class 2.9 ± 0.31 to 1.1 ± 0.31. Echocardiography was done in all ten patients witha LVOT gradient of 13.4 ± 5.37 (baseline: 87.3 ± 11). Interventricular septal thickness decreased from 2.39 ± 0.31 to 1.37 ± 0.14 *(Table 1)*. All ten patients had regional wall motion abnormality limited to the basal septum region. However, LV global function was normal in all the patients.

	Pre	Post	6 Months
NYHA	2.9±0.31	1.3±0.48	1.1±0.31
IVS	2.39±0.31	1.38±0.13	1.37±0.14
LVOTG	87.3±11	13.5±5.03	13.4±5.37
LVIDd	4.6±0.08	4.7±0.09	4.8±0.09

DISCUSSION

Symptoms and disease manifestations of patients with HOCM include dyspnoea, angina, palpitations, syncope, heart failure and sudden cardiac death with obstruction to left ventricular outflow tract, diastolic dysfunction and rhythm disturbances being the underlying causes. [23,24] Symptomatic patients not only suffer from impaired quality of life but also seem to have anadverse prognosis.[25]Treatment of symptomatic patients with HOCM aims at reducing thesymptoms, outflow tract gradient, and reduction of sudden cardiac death. In most patients thesymptoms are directly related to LVOT gradient. This reduction of LVOT obstruction could beachieved by drug therapy through the administration of negatively inotropic substances, especially,the beta blocker [4-6] and calcium antagonists like verapamil.[7] The implantation of a DDD pacemaker system was able to reduce the outflow gradient by greater than 30%, also leading to symptomatic improvement without altering the septal thickness.[8-10]However, recently two

randomized trials showed limited haemodynamic and clinical improvements in patients of HOCM treated with DDD pacemaker implantation [26,27]. As the success of pacemaker implantation cannot be predicted in individual cases, it cannot be recommended for routine application.[27]

Surgical myectomy gained increased significance after its introduction by Cleveland in1958 [11-19]. The operative procedure is complicated by high mortality rate of 1.6 – 10% and there is apossibility of per operative complications such as the occurrence of VSD, complete heart block, and cerebral embolism, particularly in connection with an intraoperative myectomy 34 The localized "therapeutic infarction"[28]induced by PTSMA as a result of alcohol injection into aseptal perforator artery leads to thinning of involved septal area and expands the left ventricular out flow tract. This eliminates or reduces systolic anterior movement of the mitral valve andoutflow obstruction.[21]After a local remodelling process, the morphologic as well ashaemodynamic result resembles that of surgical myectomy with a channel like scar in place ofseptal bulge.[29,30]A significant LVOT gradient reduction is associated with an improvement in NYHA class and clinical symptoms.[29] The first preliminary studies leading to this catheter based imitations of surgical myectomydate back to the 1980's.[31] In '1994, probatory balloon occlusion of septal branches of LCA leadingto transient ischemia induced LVOT gradient reduction was reported.[32]In 1995 Sigwart published the first report on definitive alcohol induced septal reduction in three severely symptomaticpatients.[21]Further, Faber et al reported PTSMA-for HOCM - long term follow up of first series of25 patients with significant improvement in clinical and echocardiographic profile.

In our study we had ten patients who were drug refractory and symptomatic and in all the patients there was significant symptomatic improvement. IVS thickness reduced from 2.39 ± 0.31to 1.37 ± 0.14 cms at the end of six months follow up. LVOT gradient reduction could be achieved in all the ten patients from 87.3 ± 11 to 13.5 ± 5.03 after the procedure, which was also demonstrable at the end of six months (13.4 ± 5.37). Three patients had transient complete heart block requiring temporary pacemaker support for a maximum of 24 hours. However, no patient required permanent pacemaker implantation. We also have shown that the angioplasty of an occluded arterycan be combined with septal ablation procedure successfully. Segewiss et al showed acute results and three months follow up in 25 patients in which he showed LVOT gradient reduction from 61.8 ± 29.8 mm of Hg to 19.4 ± 20.8 mm Hg at rest ($p < 0.0001$) and from 141.4 ± 45.3 mm to 61.1 ± 40.1 mm. Post ectopic clinical and echocardiographic follow up was achieved in 24 patients with a significant clinical improvement with a NYHA class of 1.4 ± 1.1 from 2.8 ± 0.6 with a further LVOT gradient reduction in 14 patients (58%).[29]

Faber et al determined long term follow-up of first series of 25 patients with a follow up of30 months (24 - 36 months) where he showed LVOT gradient regression comparable to short termfollow up. All patients had greater than 50% LVOTG reduction and seventeen patients (71 %) hadcomplete LVOTG eliminations.[35] The crux of the problem is the appropriate selection of target branch supplying exactly the septalmyocardium involved in LVOT obstruction and gradient. Originally, probatory balloon occlusion of presumed target vessel was performed which we did in our cases and the effect of transient ischemia on LVOT obstruction was analysed before injecting the alcohol into the vessel.[21,33]However the role of PBO in prediction of LVOT gradient was not very high.[29]To overcome this limitation, intraprocedural myocardial contrast echocardiography (MCE) has emerged as an additional tool for selection of the target branch. Using 'myocardial contrast echocardiography the necessity of DDD implantation after PTSMA reduced from 20% to 9%.[34] Echocardiographic guidance with echo-contrast-mediated identification of the target septal branch was clearly the most significant improvement of the original technique and has become indispensable to the procedure.[34] Before any alcohol injection, an echocardiographic contrast agent is administered through the central lumen of the balloon catheter under real-time transthoracic 2-dimensional echocardiographic and colour Doppler monitoring. Injection into the optimal septal branch will cause an obvious opacification of the septal area next to maximal flow acceleration that involves the point of contact between the mitral valve and the septum during systole. It is evident that myocardial contrast echocardiography can change the interventional strategy by dictating the need to change the target branch or even abandon the procedure if the proper septal branch can not be identified. Alcohol is injected only when the correct target has been proven and its amount depends mainly on the echocardiographically estimated size of the contrasted septal area.[36] We intend to do a larger study using myocardial contrast echocardiography to identify the culprit septal artery.

Conclusion

Percutaneous transluminal septal myocardial ablation (PTSMA) is a promising interventional modality for patients with hypertrophic obstructive cardiomyopathy (HOCM) who do not show satisfactory response to drug treatment.

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