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Original Article

# Alcohol septal ablation for hypertrophic obstructive cardiomyopathy – 8 years follow up

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ABSTRACT

*Background:* Alcohol septal ablation is emerging as an alternative to surgical myectomy in the management of symptomatic cases of Hypertrophic obstructive cardiomyopathy (HOCM). This involves injection of absolute alcohol into 1st septal perforator thereby producing myocardial necrosis with resultant septal remodelling within 3–6 months. This results in reduction of septal thickness and LV outflow gradients with improvement in symptoms.

*Methods:* Fifty three patients had undergone alcohol septal ablation, there were 2 early and 2 late deaths and 4 patients lost to follow up. Forty-five (85%) of them were followed up to a mean period of 96 ± 9.2 months. Clinical, ECG, and Echocardiographic parameters were evaluated during follow up.

*Results:* Only 4 out of 51 patients remained in NYHA class III or IV at the end of 6 months. Significant reduction of LV outflow gradients (79 ± 35 to 34 ± 23 mmHg) and septal thickness (23 ± 4.7 mm to 19 ± 3 mm) were observed during 6 months follow up. Beyond 6 months there was no further decrease in either septal thickness or LVOT gradients noted. Ten percent of patients needed pacemaker implantation. There was 92% survival at the end of 8 years.

*Conclusion:* Alcohol septal ablation is a safe and effective nonsurgical procedure for the treatment of HOCM. By minimizing the amount of alcohol to ≤2 ml, one can reduce complications and mortality. The long-term survival is gratifying.



## 1. Introduction

In the management of symptomatic patients of hypertrophic obstructive cardiomyopathy (HOCM) dual chamber pacemaker implantation or surgical myectomy were the therapeutic options in the past. In 1995 Ulrich Sigwart[1] introduced transcoronary alcohol ablation of septal hypertrophy (TASH) and in the same year Kuhn et al[2] from Germany also reported TASH procedure for the management of HOCM. From India cases of successful TASH were reported by Bahl et al[3] and also Bhargava et al.[4] TASH procedure involves

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**Table 1 – Symptoms ($n=53$).**

| | |
|---|---|
| F0D8 | Dyspnea: 40 (75.5%) |
| F0D8 | Angina: 25 (47.2%) |
| F0D8 | Palpitations: 14 (26.4%) |
| F0D8 | Syncope: 11 (20.7%) |
| F0D8 | Pulmonary edema: 5 (9.4%) |

injection of absolute alcohol into the first septal artery supplying the basal part of the interventricular septum, resulting in chemical necrosis there by producing controlled septal infarction. This results in gradual septal remodelling due to thinning of the septum thereby reducing the LV outflow gradient resulting in relief of symptoms.

We are reporting single center retrospective analysis in TASH procedure, the largest series from India, in meticulously selected cases of HOCM with 8 years follow up.

## 2. Materials and methods

From Jan 1997 to Dec 2011 fifty-three patients underwent TASH procedure for symptomatic HOCM at our center. Their ages ranged from 20 to 68 yrs with a mean age of 48 ± 7.2 yrs. There were 43 men and 10 females. The diagnosis was based on clinical findings and echocardiographic evidence of disproportionate hypertrophy of the interventricular septum compared to posterior LV wall associated with LV outflow tract (LVOT) gradient.

### 2.1. Symptoms

Details are as shown in Table 1. Majority were in NYHA class III (77.4%) or class IV (9.5%) symptoms. One patient had undergone TASH procedure as an emergency on ventilatory support. Prior dual chamber pacemaker was implanted in one case and one case had undergone surgical myectomy 6 years prior to TASH without much improvement in symptoms or LVOT gradient.

### 2.2. Medications

Thirty seven (69.8%) were on betablockers, 11 (20.7%) were receiving calcium channel blockers, amiodarone in 8 (15%) and only 2 (3.7%) patients were on disopyramide.

### 2.3. Procedure

TASH procedure was performed as per the procedural details published by us earlier.[5] The inclusion and exclusion criteria followed at our center were described in our earlier publication.[5] Drugs like betablockers were stopped 24 h before the procedure. Temporary pacing wire was inserted routinely and kept for 48 h. Weight adjusted heparin was given to all of them.

Left coronary artery was cannulated using 6F/7F guiding catheter. High torque floppy guide wire was used to enter the target septal branch (TSB). Over the wire balloon 1.5–2 mm and lengths 10–12 mm was positioned in TSB and inflated to 4–6 atms. 0.5–1 ml of nonionic contrast was injected through the central lumen to verify the balloon position in the desired septal branch and also to ensure that no contrast leakage into the left anterior descending artery. Temporary occlusion of TSA should result in significant fall in resting or provocable gradient and portends good response to TASH.[6] After identifying the culprit septal branch 2 ml of absolute alcohol was injected into the TSB, 1 ml as bolus followed by 0.2 ml every 2 min as described by Kuhn et al.[2] Intravenous analgesia was administered routinely before injecting alcohol. In 46 cases 2 ml or less was injected and in 7 cases more than 2 ml alcohol was injected. Mean amount of alcohol injected was 1.92 ± 1.8 ml. The culprit septal branch was first septal in 47 cases and second septal in 6 cases.

### 2.4. Echocardiographic guidance

Echo guidance is an integral part of TASH procedure. Echocardiographic Levovist contrast was used by earlier workers.[7–10] We routinely used diluted nonionic contrast to identify TSB and also to ensure that unwanted areas like papillary muscles or ventricular free walls were not opacified. Basal septal brightening after contrast injection is confirmatory.

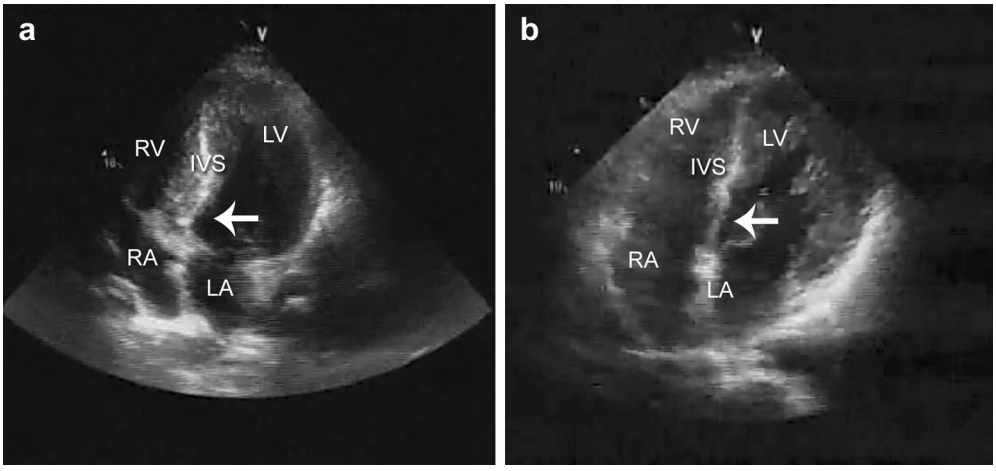



**Fig. 1 – a: Interventricular septal hypertrophy before TASH. b: Interventricular septum thinned out 6 months post-TASH in same patient.**

Echocardiograms were needed during follow up to confirm reduction of gradient to measure septal thickness and also to assess mitral regurgitation. Echocardiographic follow up at 6 months revealed septal remodelling in the form of scooped out septal area (Fig. 1a and b).

### 2.5. *Successful ablation*

Final angiogram performed 10 min after alcohol injection invariably shows completely occluded TSB. But this is not a must, sometimes there can be TIMI I flow. Fig. 2a, b and c shows TSB before and after TASH. When there is either complete abolition of gradient or more than 50% reduction in either resting or provocable LVOT gradient after TASH, it was concluded as successful procedure.[11] In some cases there will be total disappearance of gradient soon after procedure, followed by reappearance of 50% preprocedural gradient after 48 h. During follow up at 6 months, the gradient falls again, termed biphasic response[12,13] and was noted in 7 of our patients. The reduction in gradient and septal thickness was assessed at the end of 6 months and yearly thereafter as recommended by earlier workers.[11,14]

### 2.6. *Follow up*

Creatine Phospokinase(CPK), CPKMB were measured soon after, 6, 24 and 48 h after the procedure. The maximum level of CPK and CPKMB was taken as a representation of quantum of myocardial necrosis. ECG and echocardiograms were repeated 24 h, 48 h, pre-discharge, at 3 months, 6 months and yearly thereafter. The follow up pattern is as shown in Table 2. There were 2 in-hospital deaths and 51 of them could be followed for 6 months. There were 2 late deaths and 4 cases were lost to follow up. Forty-five (85%) of them were followed up to a mean period of 96 ± 9.2 months.

Statistical analysis was done using Modified students 'T' test and unpaired 't' test for independent samples.

## 3. Results

### 3.1. *Symptoms*

Symptomatic improvement at the end of 6 months is shown in Table 3. Forty six patients were in class III or IV before TASH and only 4 remained in class III or IV after the procedure.

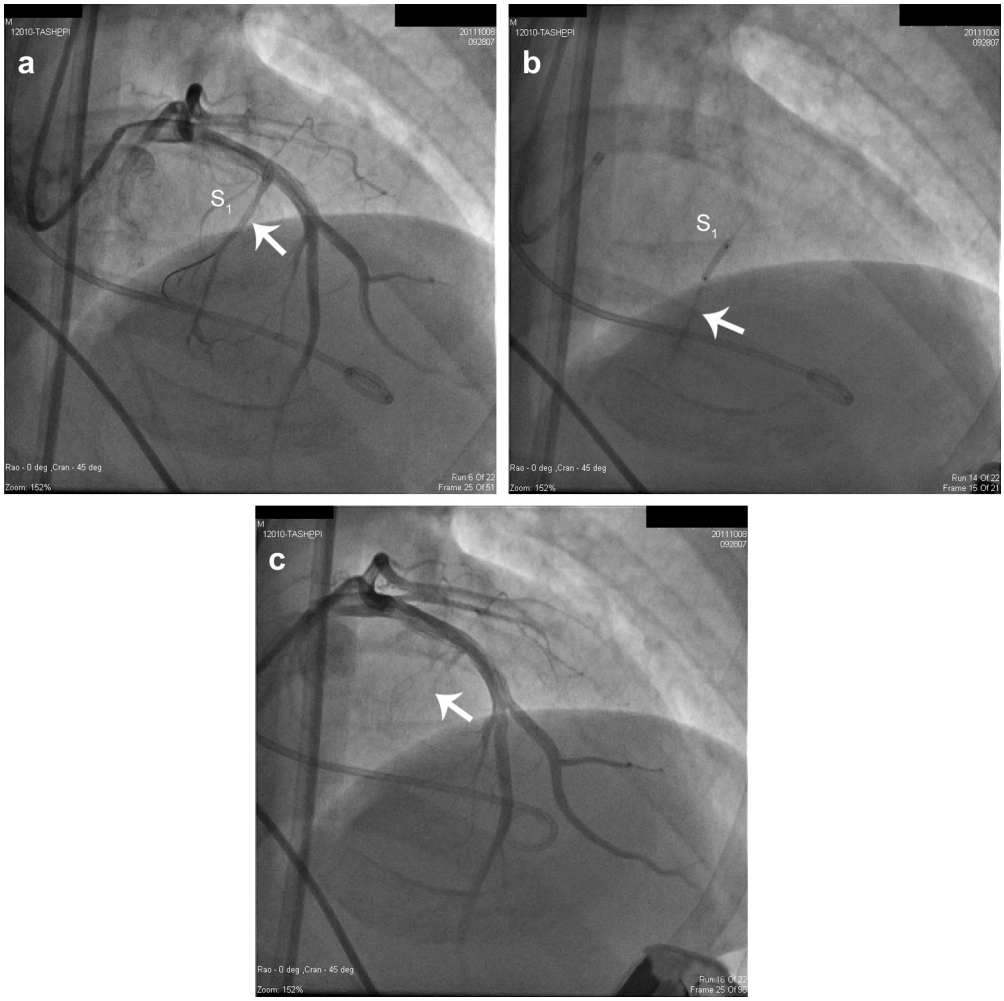



**Fig. 2 – a: contrast injection in to LAD showing first septal artery (S1) and the guide wire in the target septal branch. b: Balloon inflated in S1 and injection of contrast in to the central lumen opacifying the target area. c: Post-TASH -arrow showing obliteration of the S1.**

### 3.2. Septal thickness

(Table 4) Pre-TASH the mean septal thickness was 23 ± 4.7 mm and 6 months Post-TASH it came down to 19 ± 3 mm and the difference were found to be statistically significant. Beyond 6 months the reduction was minimal and was not significant and thereafter no further reduction in septal thickness noted during 8 years follow up.

### 3.3. LVOT gradient (Table 4)

The mean LVOT gradient was 79 ± 35 mmHg before the procedure and at 6 months it came down to 34 ± 23 mmHg which was statistically significant. Beyond 6 months the reduction was not significant during the follow up period of 8 years.

LVOT gradient reduction was not dependent upon the magnitude of CPKMB elevation (Table 5). CPKMB elevation was more than 5 times the normal value in 30 cases, 3 to 5 times elevation in 9 cases and less than 3 times elevation in 12 cases. Mean gradient reduction was different between these groups and was no correlation found between CPKMB elevation and LVOT gradient reduction 6 months after TASH. LVOT gradient reduction at 6 months was complete in 8 cases and 50% or more reduction in 40 cases. Of the 51 cases followed upto 6 months, 48 (94%) revealed successful ablation manifested by LVOT gradient reduction (Table 6).

### 3.4. Conduction disturbances

Forty two patients (79%) developed RBBB and 3 developed complete heart block (CHB) immediately after TASH.

### 3.5. Pacemaker implantation

One patient had dual chamber pacemaker (DDD) before the procedure and 4 more patients after the procedure. One patient who had pre-existing LBBB and Non-sustained VT developed complete heart block soon after the procedure and was implanted with a dual chamber cardiac defibrillator. Of the 52 patients (excluding the one with prior DDD pacer), 5 patients (10%) were implanted with pacemakers.

### 3.6. Follow up

Two of our cases died within a week after TASH, one due to cerebrovascular accident and the other due to pulmonary edema secondary to complete heart block. Both of them received more than 2 ml of alcohol. One patient underwent mitral valve replacement surgery 1 year after the procedure and died due to fungal endocarditis. Another patient died of anterior wall MI resulting in cardiogenic shock and ventricular arrhythmias, 3 years after the procedure. During mean follow up of 8 years the survival was 92%.

**Table 2 – Duration of follow up.**

| Duration | No of patients | Percentages |
|---|---|---|
| Death | 4 | 7.5% |
| Lost to follow up | 4 | 7.5% |
| 6 months to 1 year | 3 | 5.6% |
| 1 to 5 years | 8 | 15.1% |
| 5 to 10 years | 14 | 26.4% |
| Above 10 years | 20 | 37.7% |
| Total | 53 | 100.0% |

**Table 3 – Symptomatic improvement.**

| Class | Pre-TASH | 6 months post-TASH |
|---|---|---|
| No of cases | 53 | 51 |
| I | 0% | 36 (70.5%) |
| II | 7 (13%) | 11 (21.5%) |
| III | 39 (74%) | 2 (3.9%) |
| IV | 7 (13%) | 2 (3.9%) |

## 4. Discussion

TASH has emerged as an effective and acceptable therapeutic procedure for the treatment of symptomatic HOCM patients who are refractory to medical therapy. This is less invasive compared to surgical myectomy and it is practiced widely. We are reporting our experience of TASH at a tertiary referral hospital.

Symptomatic improvement after TASH was found to be excellent in our series. Only 4 cases continued to be class III or class IV NYHA (Table 3). The gratifying results could be because of proper selection of cases. Similar results were reported by Kuhn et al,[2] Seggewiss et al[14] and recently by Malak et al.[15] In a systematic review of 42 studies involving 2959 patients, Alam et al[13] reported significant reduction in symptoms with mean NYHA class coming down from 2.9 to 1.2 after TASH.

To predict the long term outcomes it is essential to do echocardiographic assessment at the end of 6 months as shown by us. Sigwart et al[1] observed complete septal remodelling occurring upto 6 months and in some rare cases even upto one year post-TASH. Ruzyllo et al[16] also observed that LV remodelling reaches a plateau by 6 months. Even in our study of 8 years follow up we did not observe any further reduction of LVOT gradient or septal thickness beyond 6 months as shown in Table 4. Biphasic response reported[12] earlier was observed in 14% of our cases and was thought to be due to stunned myocardium immediate post procedure.

CPKMB elevation is a direct evidence of myocardial necrosis. Fivefold increase in CPKMB approximately suggests 20% of myocardial necrosis.[17,18] Peak CPKMB elevation has been shown to predict magnitude of LVOT gradient reduction and also procedure related complications in one of the studies.[19] However we did not find any correlation between CPKMB elevation and LVOT gradient reduction (Table 5).

Ten percent of our patients have undergone pacemaker implantation including the one who had dual chamber ICD. Seggewiss et al[15] reported 20% incidence of pacemaker implantation in his initial series of 25 cases. By properly selecting TSB and limiting the amount of alcohol to less than 2 ml the need for pacemaker implantation can be minimized. Variability in the size and distribution of first septal perforator has been evaluated and reported by Mandeep Singh et al[20] from

**Table 4 – Effect of TASH on septal thickness & LVOT gradient.**

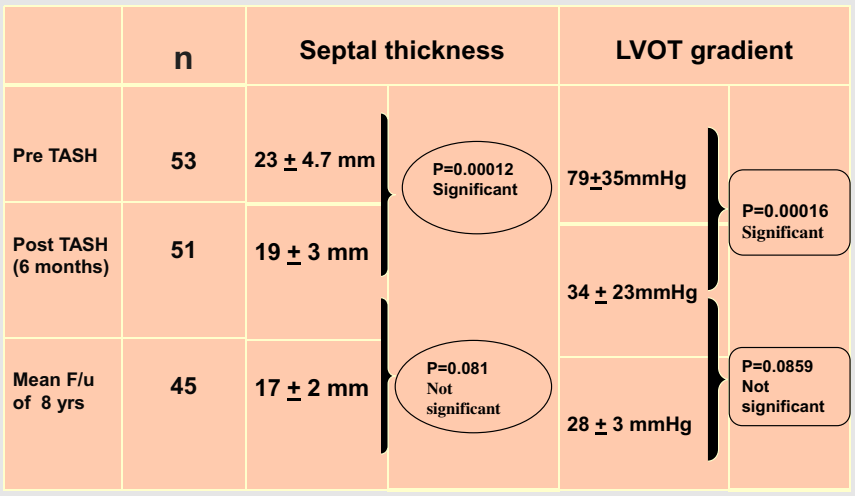
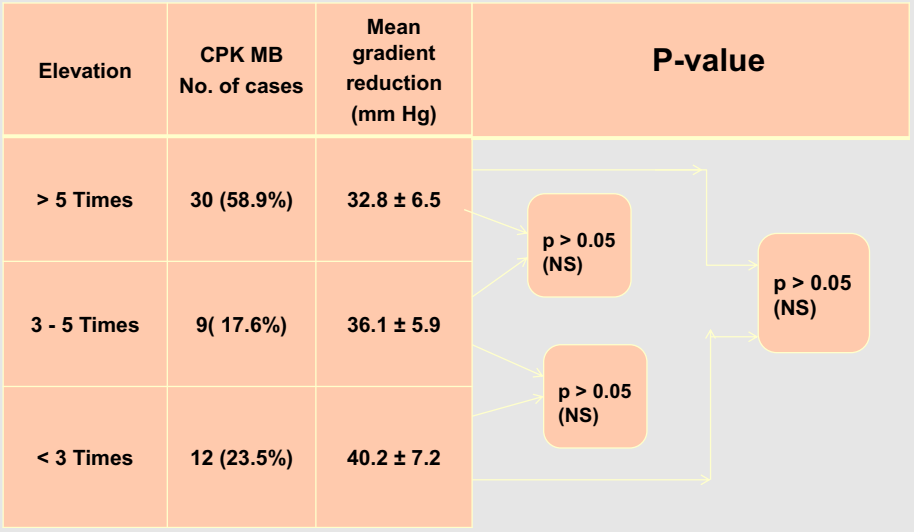



**Table 5 – CPKMB elevation Vs LVOT gradient at 6 months.**




Mayo clinic. Identifying the ideal TSB is the key to success of the procedure.

Early mortality occurring within first 30 days after TASH was reported[14] to be 1.5 percent of cases. In our initial 6 cases there were 2 deaths as the amount of alcohol injected was more than 2 ml. One of our early mortality was due to CHB occurring 7 days after the procedure. CHB may be transient phenomena in 10–46% of patients with recovery within the first 24 h.[21,22] Delayed occurrence of CHB upto 9 days after TASH has been reported earlier.[23,24] From our seventh case the maximum amount of alcohol injected was 2 ml or less. Kuhn et al[23] reported 644 patients followed upto 10 years and noticed significant decrease of in-hospital mortality from 1.8% to 0.6% when the mean amount of alcohol injected was reduced from 2.9 ml to 0.8 ml. Similar observations were reported by Veselka et al.[25,26] We strongly recommend to limit the amount of alcohol to 2 ml to reduce the incidence of CHB and also to reduce mortality.

**Table 6 – LVOT gradient reduction 6 months after TASH.**

| | *n* | % |
|---|---|---|
| Complete reduction | 8 | 15.7% |
| >50% | 40 | 78.4% |
| <50% | 3 | 5.9% |

LVOT gradient reduction 6 months after TASH was total in 16% of our series, in the majority (78%) of our cases there was more than 50% reduction of LVOT gradient. Seggewiss et al[27] reported complete elimination of gradient after a mean follow up of 58 ± 14 months in most of his patients. Similar observation was reported by Kuhn et al.[28] Even partial

reduction of gradient was reported to show good symptomatic improvement during long term follow up.[12,16,29] Another potential beneficial mechanism of TASH was through its effect on autonomic dysfunction. The adrenergic and cholinergic nerves as well as ganglions present in large numbers in basal septal region get ablated due to alcohol induced necrosis.[30]

At the end of 6 months 48 out of 51 (94%) of our cases, TASH was found to be successful. As regards symptoms, improvement was noted in 92% of our cases. As regards long term follow up, we observed excellent 92% survival at the end of 8 years. Seggewiss et al[27] showed 96% survival in his 100 patients followed up for 8 years. Recently published data from a large cohort of 347 patients showed a survival of 94% after 5 years and 87% after 10 years.[31] Our results are in agreement with those reported earlier.

## 5. Limitation of the study

It is a retrospective analysis, myocardial contrast was not used to delineate the supply of target septal branch. LVOT area was not measured as an end point. None of our patients needed redo TASH probably due to proper selection of cases.

### 5.1. *Conclusions*

TASH is a promising nonsurgical technique to reduce septal thickness, LVOT gradient and there by results in symptomatic improvement. The maximum septal remodelling and improvement occurs in 6 months time beyond which there won't be any further reduction in gradients. The key to success is proper selection of cases and also in identifying the target septal branch. One can avoid complications and need for pacemaker implantation if the amount of alcohol is limited to 2 ml or less. Long term survival is excellent. TASH procedure needs expertise and experience and this procedure should be restricted to tertiary care centers with sufficient experience.

## Conflicts of interest

All authors have none to declare.

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