Comparison of Clinical Effects between Percutaneous Transluminal Septal Myocardial Ablation and Modified Morrow Septal Myectomy on Patients with Hypertrophic Cardiomyopathy

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Abstract

Background: Percutaneous transluminal septal myocardial ablation (PTSMA) and modified Morrow septal myectomy (MMSM) are two invasive strategies used to relieve obstruction in patients with hypertrophic cardiomyopathy (HCM). This study aimed to determine the clinical outcome of these two strategies.

Methods: From January 2011 to January 2015, 226 patients with HCM were treated, 68 by PTSMA and 158 by MMSM. Both ultrasonic cardiograms and heart functional class were recorded before, after operations and in the follow-up. Categorical variables were compared using Chi-square or Fisher's exact tests. Quantitative variables were compared using the paired samples *t*-test.

Results: Interventricular septal thickness was significantly reduced in both groups $(21.27 \pm 4.43 \text{ mm vs.} 18.72 \pm 4.13 \text{ mm for PTSMA}$, t = 3.469, P < 0.001, and $21.83 \pm 5.03 \text{ mm vs.} 16.57 \pm 3.95 \text{ mm for MMSM}$, t = 10.349, P < 0.001, respectively). The left ventricular outflow tract (LVOT) pressure gradient (PG) significantly decreased after the operations in two groups (70.30 ± 44.79 mmHg vs. $39.78 \pm 22.07 \text{ mmHg for PTSMA}$, t = 5.041, P < 0.001, and $74.58 \pm 45.52 \text{ mmHg vs.} 13.95 \pm 9.94 \text{ mmHg for MMSM}$, t = 16.357, P < 0.001, respectively). Seven patients (10.29%) in the PTSMA group required a repeat operation in the follow-up. Eight (11.76%) patients were evaluated for New York Heart Association (NYHA) III/IV in the PTSMA group, which was significantly more than the five (3.16%) in the same NYHA classes for the MMSM group at follow-up. Less than 15% of patients in the PTSMA group and none of the patients in the MMSM group complained of chest pain during follow-up.

Conclusions: Both strategies can not only relieve LVOT PG but also improve heart function in patients with HCM. However, MMSM might provide a more reliable reduction in gradients compared to PTSMA.

Key words: Hypertrophic Cardiomyopathy; Myectomy; Percutaneous Transluminal Septal Myocardial Ablation

INTRODUCTION

Hypertrophic obstructive cardiomyopathy (HCM) is a disease characterized by hypertrophy of the interventricular septum, obstruction of left ventricular outflow tract (LVOT), and frequently, systolic anterior motion (SAM) of the mitral valve.^[1-3] Although medical intervention can provide relief of symptoms, a considerable number of patients with hypertrophic obstructive cardiomyopathy remain symptomatic, and in these participants, invasive interventions such as percutaneous transluminal septal myocardial ablation (PTSMA) and modified Morrow

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septal myectomy (MMSM) are established treatment options.^[4,5] Extended septal myectomy can significantly relieve obstruction of LVOT and improve main complaints.^[6-8]

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PTSMA, regarded as a less invasive treatment than surgical procedure, is considered as an alternative to myectomy and is usually performed on patients who are not optimal surgical candidates or have a strong desire to avoid surgery.^[9,10] However, previous studies have also reported a greater need for pacemaker implantation and a higher rate of re-interventions after PTSMA compared to myectomy.^[11]

Handbook released by the American College of Cardiology/American Heart Association supplies a Class I recommendation to myectomy for patients with severe drug-refractory symptoms and LVOT obstruction in experienced centers with comprehensive hypertrophic cardiomyopathy (HCM) clinical program (Level of Evidence: C). PTSMA has been given a Class IIa recommendation for adult patients with an unacceptable surgical risk (Level of Evidence: B) in an experienced center.^[9] However, data on the effectiveness of these two septal reduction therapies in China are lacking. We report our experience in a comprehensive study of both procedures including periprocedural complications, re-interventions, long-term symptomatic status, and clinical outcome.

Methods

Ethical approval

The study was conducted in accordance with the *Declaration* of *Helsinki* and was approved by the Ethics Committee of Anzhen Hospital (No. AZ00305). Informed written consent was obtained from all patients or their guardians (in the case of children) before their enrollment in this study.

Patients

Two-hundred and twenty-six patients with HCM (aged >18 years) with significant LVOT obstruction were selected who first visited the Department of Cardiac Surgery of Beijing Anzhen Hospital, Beijing, China, between January 2011 and January 2015. The following exclusion criteria included (1) concomitant moderate or greater aortic/mitral stenosis; (2) maximal (including provokable) LVOT pressure gradient (PG) <50 mmHg(1 mmHg=0.133 kPa); (3) apical HCM variant;and (4) hypertensive heart disease in elderly patients. HCM was diagnosed by experienced cardiologists based on typical features, with ventricular myocardial hypertrophy (LV wall thickness >15 mm) in the absence of any other disease responsible for the hypertrophy.^[9,10] Resting/provokable LVOT obstruction (LVOT gradient >50 mmHg) was also included in the study.

Clinical data collection

The clinical data and demographic information were taken from the medical records of each patient including demographics, clinical outcomes, and echocardiographic parameters. Complications including the need for permanent pacing between two groups were recorded. The echocardiographic parameters were analyzed before and after the operation.

Percutaneous transluminal septal myocardial ablation

PTSMA was performed using previously described techniques.^[12] Different catheters were inserted in the LV and aorta to measure pressures and PG of LV tract. Then, another catheter was placed in the selected branch of the left anterior descending artery. After balloon inflation, angiographic contrast was injected through the balloon catheter together with simultaneous transthoracic two-dimensional myocardial contrast echocardiography to determine the extent of the myocardium supplied by the selected septal artery. After delineation of the size of targeted myocardium, 1–4 ml of alcohol was slowly (1 ml/min) injected. The balloon was left inflated for 10 min after alcohol injection to prevent a retrograde spill of alcohol. During the procedure, patients without permanent pacemakers received a temporary pacemaker.

Modified Morrow myectomy

Standard cardiopulmonary bypass and myocardial preservation techniques were used. After aortotomy, the resection was started by making two parallel longitudinal incisions in the septum, the first beneath the nadir of the right coronary cusp and the second beneath the commissure between the right and the left coronary cusps. The classic incision was extended with a midventricular resection, beginning with continued resection leftward toward the mitral valve annulus and apically to the bases of the papillary muscles. All areas of papillary muscle fusion to the septum or ventricular free wall were divided, and anomalous chordal structures, muscle bundles, and fibrous attachments of the mitral leaflets to the ventricular septum or free wall were divided or excised.^[13]

PTSMA was usually selected in elderly patients who have a high risk of surgical therapy. When patients need receive valvular surgery or coronary artery bypass operation, they were excluded from the study. All patients gave informed consent before these respective procedures.

Follow-up study

Physical examination including assessment of New York Heart Association (NYHA) functional class and echocardiography was recommended during follow-up. The follow-up was carried out by subsequent clinic visits to the outpatient departments and telephone interviews with the patients and their relatives.

Statistical analysis

Continuous variables were expressed as mean \pm standard deviation (SD), and categorical variables were expressed as frequencies or percentages. SPSS V.22 (SPSS, Inc., IBM, Chicago, IL, USA) was used for the statistical analysis. Categorical variables were compared using Chi-square or Fisher's exact tests. Quantitative variables were compared using the paired samples *t*-test. A value of P < 0.05 was considered statistically significant for comparison of clinical outcomes.

RESULTS

Baseline clinical profiles

Of the 226 HCM patients, 68 (31.1%) patients were treated with PTSMA and 158 (69.9%) with MMSM. The patients in the PTSMA group were older than those in the MMSM group. A significantly higher proportion of patients in the MMSM group had hypertension as a presenting feature. No significant differences of other baseline clinical or echocardiographic profiles were observed between the two groups [Table 1].

Echocardiographic outcomes

The ejection fraction pre- and postprocedure was within normal ranges for both groups [Table 2]. The mean of the LV outflow gradient decreased from 70.30 ± 44.79 mmHg to 39.78 ± 22.07 mmHg in the PTSMA group (t = 5.041, P < 0.001) and from 74.58 ± 45.52 mmHg to 13.95 ± 9.94 mmHg in the MMSM group (t = 16.357, P < 0.001), indicating a significant hemodynamic improvement with both procedures. The residual PGs at rest were significantly reduced in the MMSM group than that in the PTSMA group after the operation. The septal thickness reduced from 21.27 ± 4.43 mm to 18.72 ± 4.13 mm in the PTSMA group (t = 3.469, P < 0.001) and from 21.83 ± 5.03 mm to 16.57 ± 3.95 mm (t = 10.349, P < 0.001) in the MMSM group. There was a significant difference in the absence of SAM between the two groups. SAM decreased from 91.18% to 45.59% in the PTSMA group ($\chi^2 = 32.682$, P < 0.001) and from 93.67% to 5.06% in MMSM group ($\chi^2 = 248.141$, P < 0.001; Table 2).

Procedural, clinical outcomes, and follow-up

Four patients in the PTSMA group failed to complete the procedure, two for multiple side branches, one for a severe blood pressure drop after balloon inflation, and one for acute left heart failure in operation. The mean duration of hospitalization was shorter in the PTSMA group (t = -4.462, P < 0.001). Two patients in the MMSM group needed extracorporeal membrane oxygenation (ECMO) for postoperative low cardiac output. Forty (58.82%) patients in the PTSMA group had a right bundle branch block, compared with 22 (13.92%) of the patients in the MMSM group ($\chi^2 = 48.142$, P < 0.001). Interestingly, left bundle branch blocks were more common in the MMSM group ($\chi^2 = 13.182, P < 0.001$). Permanent pacemakers because of complete heart block were required in five patients (7.35%) of the PTSMA group and in four patients (2.53%) of the MMSM group $(\gamma^2 = 2.809, P = 0.089; Table 3).$

The mean follow-up was 44.19 ± 15.19 months for the PTSMA group and 38.48 ± 15.93 months for the MMSM group. Six (8.8%) patients in the PTSMA group and 12 (7.6%) patients in the MMSM group died before long-term follow-up. Two patients in the PTSMA group

Table 1: Baseline characteris				
Parameters	$PTSMA\ (n=68)$	MMSM ($n = 158$)	Statistics	Р
Age (years)	52.59 ± 10.54	49.20 ± 12.30	1.978†	0.049
Male	43 (63.24)	94 (59.49)	0.279*	0.597
Syncope	22 (63.24)	53 (33.54)	0.030*	0.862
Angina	29 (32.35)	76 (48.10)	0.569*	0.451
NYHA (III/IV)	55 (80.88)	112 (70.89)	2.463*	0.117
Medical history				
Hypertension	37 (54.41)	43 (27.22)	15.377*	< 0.001
Diabetes	5 (7.35)	7 (4.43)	0.808*	0.369
Coronary artery disease	10 (14.71)	17 (10.76)	0.704*	0.402
Family history of HCM	4 (5.88)	8 (5.06)	0.063*	0.801
History of radiofrequency	2 (2.94)	3 (1.90)	0.239*	0.625
Arrhythmias				
Atrial fibrillation	11 (16.18)	18 (11.39)	0.973*	0.324
Right bundle branch block	4 (5.88)	7 (4.43)	0.216*	0.642
Left bundle branch block	1 (1.47)	7 (4.43)	1.220*	0.269
Preoperative echocardiogram				
Septal thickness (mm)	21.27 ± 4.43	21.83 ± 5.03	-0.793^{\dagger}	0.429
PW thickness (mm)	12.29 ± 2.47	12.75 ± 2.95	-1.115^{\dagger}	0.266
LA (mm)	41.23 ± 5.56	42.94 ± 6.78	-1.831*	0.068
LVOT PG (mmHg)	$70.30 \pm 44.79^{\ddagger}$	$74.58 \pm 45.52^{\$}$	-0.650^{\dagger}	0.516
SAM	62 (91.18)	148 (93.67)	0.450*	0.503
MR Grade 1	31	44	6.748*	0.009
MR Grade 2	30	73	0.803*	0.773
MR Grade 3	7	41	6.965*	0.008

Data are presented as mean \pm SD or *n* (%). $*\chi^2$ values; $^{\dagger}t$ values; $^{\dagger}The$ LVOT PG of 12 patients over 100 mmHg; $^{\$}The$ LVOT PG of 32 patients over 100 mmHg. PTSMA: Percutaneous transluminal septal myocardial ablation; MMSM: Modified Morrow septal myectomy; NYHA: New York Heart Association; HCM: Hypertrophic cardiomyopathy; PW: Posterior wall; LA: Left atrium; LVOT: Left ventricular outflow tract; PG: Pressure gradient; SAM: Systolic anterior motion of mitral leaflet; MR: Mitral valve regurgitation; SD: Standard deviation. 1 mmHg = 0.133 kPa.

Table 2: Clinical outcome	s and	hemodynamic	results	of	the study
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Parameters	ameters $PTSMA (n = 68)$			MMSM ($n = 158$)				Outcomes		
	Pre	Post	Statistics	Р	Pre	Post	Statistics	Р	Statistics	P**
Septal thickness (mm)	21.27 ± 4.43	18.72 ± 4.13	3.469*	0.001	21.83 ± 5.03	16.57 ± 3.95	10.349*	< 0.001	3.710*	< 0.001
LVOT PG (mmHg)	$70.30\pm44.79^{\ddagger}$	$39.78 \pm 22.07^{\S}$	5.041*	< 0.001	$74.58\pm45.52^{\parallel}$	$13.95\pm9.94^{\mathrm{e}}$	16.357*	< 0.001	12.146*	< 0.001
LA (mm)	41.23 ± 5.56	39.94 ± 4.71	1.461*	0.146	42.94 ± 6.78	37.31 ± 6.59	7.491*	< 0.001	2.982*	0.003
LVEF	69.28 ± 7.66	64.16 ± 5.33	4.523*	< 0.001	67.65 ± 7.09	61.10 ± 7.46	8.011*	< 0.001	3.069*	0.002
SAM	62 (91.18)	31 (45.59)	32.682 [†]	< 0.001	148 (93.67)	8 (5.06)	248.141 [†]	< 0.001	54.678†	< 0.001

Data are presented as mean \pm SD or *n* (%). **t* values; [†] χ^2 values; [‡]The LVOT PG of 12 patients over 100 mmHg; [§]The LVOT PG of 15 patients over 50 mmHg; [¶]The LVOT PG of 32 patients over 100 mmHg; [¶]The LVOT PG of two patients over 30 mmHg. **: Compared post-operations parameters between two methods. PTSMA: Percutaneous transluminal septal myocardial ablation; MMSM: Modified Morrow septal myectomy; LA: Left atrium; LVOT: Left ventricular outflow tract; PG: Pressure gradient; SAM: Systolic anterior motion of mitral leaflet; LVEF: Left ventricular eject fraction; SD: Standard deviation. 1 mmHg = 0.133 kPa.

Table 3: Complications and follow-up data of the study								
Parameters	$PTSMA\ (n=68)$	MMSM ($n = 158$)	Statistics	Р				
Mitral valve replacement	0 (0)	15 (9.49)	_	_				
Right bundle branch block	40 (58.82)	22 (13.92)	48.142*	< 0.001				
Left bundle branch block	10 (14.71)	62 (39.24)	13.182*	< 0.001				
Permanent pacemaker insertion due to heart block from procedure	5 (7.35)	4 (2.53)	2.809*	0.089				
Repeat procedure	7 (10.29)	0 (0)	16.785*	< 0.001				
Mortality postprocedure (<30 days)	2 (2.94)	2 (1.27)	0.767*	0.381				
Late mortality (>1 year)	1 (1.47)	2 (1.27)	0.015*	0.902				
Follow-up data								
NYHA (III, IV)	8 (11.76)	5 (3.16)	6.486*	0.011				
Angina	10 (14.71)	0 (0)	24.311*	< 0.001				
Ventricular septal thickness (mm)	18.13 ± 4.14	16.47 ± 5.28	2.304 [†]	0.022				
LVOT PG (mmHg)	$33.51 \pm 24.08^{\ddagger}$	$15.82 \pm 27.20^{\$}$	4.639†	< 0.001				
SAM	34 (50.00)	8 (5.06)	63.447*	< 0.001				
LVEF	62.49 ± 5.88	64.96 ± 7.29	-2.451†	0.015				

Data are presented as mean \pm SD or *n* (%). * χ^2 values; [†]*t* values; [‡]The LVOT PG of 19 patients over 50 mmHg; [§]The LVOT PG of 9 patients over 30 mmHg. PTSMA: Percutaneous transluminal septal myocardial ablation; MMSM: Modified Morrow septal myectomy; NYHA: New York Heart Association; LVOT: Left ventricular outflow tract; PG: Pressure gradient; SAM: Systolic anterior motion of mitral leaflet; LVEF: Left ventricular eject fraction; SD: Standard deviation. –: No applicable. 1 mmHg = 0.133 kPa.

died of acute heart failure in the early postoperative period (<1 month). Two patients died of low cardiac output in the MMSM group. There was one later death (>12 months) in the PTSMA group with the patient dying of chronic heart failure. Two patients died 1 year after the procedure in the MMSM group; one of noncardiac cause and one of stroke. There was no significant difference between groups in the level of survival. Kaplan-Meier Curves demonstrated no difference in long-term survival between the PTSMA and MMSM groups ($\chi^2 = 0.190$, P = 0.663 by log-rank test). Seven patients received PTSMA required a repeat operation after the procedure; two of whom received second septal myocardial ablation and five patients received MMSM. Echocardiography examination demonstrated that the MMSM group had a lower LVOT PG 1 year after the operation [Table 3]. Eight (11.76%) patients were evaluated for NYHA III/IV in the PTSMA group, which was significantly more than 5 (3.16%) in the MMSM group at the latest follow-up. Less than 15% of patients in the PTSMA group and none of the patients in the MMSM group complained of any chest pain during follow-up.

DISCUSSION

Hypertrophic cardiomyopathy (HCM) is characterized by hypertrophy of the myocardium and is associated with various clinical presentations ranging from complete absence of symptoms to sudden, unexpected death. LVOT obstruction is present in 20-30% of HCM patients and a number of patients remain symptomatic despite optimal medical therapy, and surgical myectomy is usually recommended for HCM patients. Myectomy procedures were first reported by Morrow in 1975, and many variations of this procedure have been reported with varied efficacies since.^[14,15] Myectomy reduces or eliminates LVOT obstruction in most individuals, and its effects are usually sustained.^[15,16] Sigwart reported that inflating an angioplasty balloon catheter in the septal perforator resulted in a significant decrease in LVOT obstruction.^[17] Subsequently, intracoronary alcohol injection gained popularity in treating patients with HCM who are refractory to medical therapy. In this study, we report our experience of two strategies for treating refractory HCM.

The two groups of patients involved in this investigation had identical baseline gradients and achieved a similar hemodynamic improvement after both procedures. This might be related to the similar mechanisms for eliminating obstructions that are common to both procedures. As noted in the previously, a similar reduction in basal septal thickness was noted after both MMSM and PTSMA. These observations are similar to the mechanisms by which successful septal myectomy relieves LVOT obstruction.

The two patient groups had similar baseline NYHA and Canadian Cardiovascular Society classes, and a similar number in each group suffered from syncope at baseline examination. After surgery, nearly 97% of the patients were in NYHA Class I or II, and after PTSMA, 88% of the patients were in these two classes. Angina disappeared in the MMSM group after surgery; however, 10 (14.71%) patients in the PTSMA group still suffered relevant symptoms. Complete heart block necessitating permanent pacing occurred in 7.35% of patients in the PTSMA group, which was higher than the MMSM group (2.53%), but the data are not statistically significant.

Two deaths occurred in the PTSMA group, both of them suffering acute left heart failure after balloon inflation. This may have been because of heart failure after extensive myocardial infarction. As expected, percutaneous interventions in older patients carry more risk due to the presence of atherosclerotic lesions. Two deaths were observed in the MMSM group because of low cardiac output syndrome postoperatively.

Seven patients suffered second interventions because of recurrent symptoms after the procedure in the PTSMA group, but none required it in the MMSM group. Two patients chose repeated PTSMA because they refused the thoracotomy operation, and five patients received the MMSM procedure. The results showed that MMSM was a more reliable strategy for treating LVOT obstruction.

Like most studies on HCM, this was a retrospective, nonrandomized study, with the common limitations inherent in this type of study. Although the PTSMA and MMSM groups were well matched in terms of baseline clinical profiles, there may have been bias that led patients to select MMSM instead of PTSMA. We just recorded the NYHA class and angina of patients in the follow-up.

In conclusion, both the PTSMA procedure and the MMSM procedure can reduce LVOT obstruction and alleviate symptoms in patients with HCM. However, the MMSM is superior to the PTSMA in reducing the LVOT gradient and alleviating the symptoms associated with HCM.

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Conflicts of interest

There are no conflicts of interest.

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经皮酒精消融术与改良Morrow手术治疗肥厚性梗阻性心 肌病临床疗效的单中心比较研究

摘要

背景: 经皮酒精消融术和改良Morrow手术是针对肥厚性梗阻性心肌病左心室流出道梗阻的两种不同的治疗方法。本项研究旨 在比较这两种治疗方法的疗效。

方法: 选取2011年到2015年226例在我院住院的肥厚型梗阻性心肌病患者,其中68患者接受经皮酒精消融术,168例患者接受 改良Morrow手术。患者在术前,术后和随访过程中接受超声心动图检查采集相关数据并记录心功能分级。

结果: 两组患者术后室间隔厚度显著减少,经皮酒精消融:术前21.27±4.43 mm,术后18.72±4.13 mm(*t*=3.469,*p*<0.001),改良 Morrow组:术前21.83±5.03 mm,术后16.57±3.95 mm(*t*=10.349,*p*<0.001)。两组患者术后左心室流出道压差均显著降低,经 皮酒精消融:术前70.30±44.79 mmHg,术后39.78±22.07 mmHg (*t*=5.041,*p*<0.001),改良Morrow组:术前21.83±5.03 mm,

术后16.57±3.95 mm (*t*=16.357, *p*<0.001)。有7例接受经皮酒精消融患者接受再次外科手术治疗。随访期间,8例接受经皮酒 精消融手术的患者心功能分级为III级以上,接受改良Morrow手术有5人。其中14.71%接受经皮酒精消融的患者术后仍有胸痛 的症状发作。

结论: 经皮酒精消融术和改良Morrow术都可以显著改善患者心功能及缓解左室流出道梗阻,然而改良Morrow术缓解更加彻底。