Long-Term Outcome of Percutaneous Transluminal Septal Myocardial Ablation in Hypertrophic Obstructive Cardiomyopathy
A Scandinavian Multicenter Study

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Background—Single-center reports on percutaneous transluminal septal myocardial ablation (PTSMA) in patients with hypertrophic obstructive cardiomyopathy have shown considerable differences in outcome.

Methods and Results—We report the long-term outcome of 313 PTSMA procedures performed in 279 patients with hypertrophic obstructive cardiomyopathy aged 59 ± 14 years from 1999 to 2010 in 4 Scandinavian centers. Sixty-nine percent of patients had ≥1 comorbidity at baseline. The median (interquartile range) of left ventricular outflow tract gradient at rest was reduced from 58 mm Hg (34 to 89 mm Hg) at baseline to 12 mm Hg (8 to 24 mm Hg) at 1-year (P < 0.001) and during Valsalva maneuver from 93 mm Hg (70 to 140 mm Hg) to 21 mm Hg (11 to 42 mm Hg) (P < 0.001). The proportion of patients with syncope was reduced from 18% to 2% (P < 0.001), and the proportion in New York Heart Association class III/IV was reduced from 94% to 21% (P < 0.001). All treatment effects remained stable during the follow-up. New York Heart Association class III/IV at the most recent follow-up (2.9 ± 2.6 years) was associated with diabetes mellitus (P = 0.03), chronic obstructive pulmonary disease (P = 0.02), and valve disease unrelated to hypertrophic cardiomyopathy (P < 0.01). In-hospital mortality was 0.3%. The 1-, 5- and 10-year survival rates were 97%, 87%, and 67%, respectively (P = 0.06 versus an age- and sex-matched background population) in all patients and 99%, 94%, and 88%, respectively (P = 0.12) in patients aged < 60 years (48 ± 9 years, n = 141). Age (hazard ratio, 1.07; 95% CI, 1.03 to 1.1) was the only predictor of survival.

Conclusions—in this multicenter study, the in-hospital mortality after PTSMA was low despite considerable comorbidities. The hemodynamic and symptomatic effects were sustained long term. The long-term symptomatic outcome was associated with baseline comorbidities. The 10-year survival rate was comparable to that in an age- and sex-matched background population, and age was the only predictor of survival. (Circ Cardiovasc Interv. 2011;4:256-265.)

Key Words: percutaneous transluminal septal myocardial ablation ■ cardiomyopathy hypertrophic ■ left ventricular outflow obstruction ■ survival ■ treatment outcome ■ multicenter study

Left ventricular outflow tract obstruction (LVOTO) is present in up to two thirds of patients with hypertrophic cardiomyopathy (HCM).1 The obstructive form of HCM (HOCM) is associated with increased morbidity and mortality.2 The long-term symptomatic effectiveness of myectomy has been proven in patients with HOCM with severe drug refractory symptoms and possibly improves survival.3-7 Percutaneous transluminal septal myocardial ablation (PTSMA) was introduced in 1995 as an alternative to myectomy and has been shown to reduce the LVOTO and associated symptoms.8-10 Myectomy has been the gold standard for septal reduction therapy because of solid long-term results (eg, survival comparable to the background population).11 The favorable outcome of myectomy reported from high-volume centers has been matched by a few high-volume PTSMA centers.12-13 However, single-center reports on annual mortality rates after PTSMA ranges considerably,14 with high mortality rates in some reports contributing to keep myec-
tomy the gold standard. Direct comparisons between such studies may be misleading. Multicenter studies may add to our knowledge of PTSMA outcome. Therefore, in the present multicenter study, we analyzed the short- and long-term outcome of PTSMA performed in 4 Scandinavian heart centers.

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Methods

The Scandinavian HOCM Database (www.scand-hocm.org) was established in collaboration among heart centers at Oslo University Hospital, Rikshospitalet, Oslo, Norway; Copenhagen University Hospital, Gentofte Hospital, Gentofte, Denmark; Karolinska University Hospital, Stockholm, Sweden; and Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark. PTSMA was introduced independently in these centers from 1999 to 2001. The aim of the collaboration is to evaluate the long-term outcome of PTSMA in a clinical multicenter setting. The database complies with data registry regulations within the European Union and Norway and was approved by relevant data authorities and committees for ethics in medicine.

The participating heart centers are based in public university hospitals. All PTSMA operators had a record of >1000 percutaneous coronary interventions before their first PTSMA. Patients with HOCM were followed by subspecialized HCM cardiologists and examined by experts in echocardiography.

Patients

All patients treated with PTSMA in the 4 centers from 1999 to 2010 were included. The patients were referred from a geographically defined background population of approximately 10 million citizens, which is ~50% of the Scandinavian population. Retrospective data for this study were merged in the database in 2007. Since 2007, new patients and follow-up data have been included prospectively. Data were retrieved from patient files, echocardiography reports, and survival registries and registered at baseline and annually during follow-up. Data were withdrawn from the Scandinavian HOCM Database on April 1, 2010.

HCM/HOCM was diagnosed in accordance with the American College of Cardiology/European Society of Cardiology consensus document,11 and arterial hypertension, to an extent, that could not explain the degree of myocardial hypertrophy was not considered an obstacle for establishing the diagnosis. The indication for PTSMA was HOCM with severe drug refractory, New York Heart Association (NYHA) class III/IV symptoms and a resting LVOT gradient of >30 mm Hg (1 center), >50 mm Hg (3 centers), or >100 mm Hg during provocaction. Since its introduction in the 4 centers, PTSMA has been the primary treatment of choice. Myectomy was considered in patients with midventricular obstruction or in patients needing valve, coronary artery bypass graft, or other kinds of cardiac surgery. A high perioperative risk was considered in favor of PTSMA, and multivessel coronary artery disease was considered in favor of myectomy. Finally, patient preferences were taken into account. The ratio between PTSMA procedures and myectomies was ~7:1.

The PTSMA procedures were guided by transthoracic or transesophageal echocardiography. In all cases, intracoronary echocardiography contrast was used according to previous descriptions.8,15,16 The alcohol was injected slowly during a period of 5 to 10 minutes, and then the balloon was kept inflated for 10 minutes. The volume of injected alcohol was reduced during the first years after implementation of PTSMA and, subsequently, 0.1 mL alcohol per millimeter septum thickness per septal branch has been used as guidance.

According to our protocols, patients were monitored (including telemetry) in coronary care units for 7 days after the PTSMA procedure. After 48 hours, the temporary pacemaker was removed if the patient seemed to have normal cardiac conduction. If high-grade atrioventricular (AV) conduction disturbances were seen during the following days, a permanent pacemaker (PPM) implantation was offered. Patients were discharged to follow-up in our outpatient clinics.

Treatment Effects

The hemodynamic effects of PTSMA were evaluated by changes in echocardiographically obtained LVOT gradients.17 The symptomatic effects were evaluated by changes in NYHA class and Canadian Cardiovascular Society class scores. The proportion of patients with ≥1 syncope (abrupt transient loss of consciousness and spontaneous awakening not explained by emotional, neurological, environmental, or other noncardiac causes) within 1 year of assessment was registered. Palpitations were registered similarly.

Complications

Complications during PTSMA procedures and in-hospital monitoring were registered. Events were acute heart failure and death, and arrhythmic events were bradycardia, asystole, and sustained and nonsustained ventricular tachycardia and ventricular fibrillation (VF). Coronary artery complications were coronary dissection, coronary perforation, acute pericardial effusion, pericardial tamponade, and alcohol displacement. Bundle branch block and AV block, including advanced heart block, leading to PPM implantation were registered. Advanced heart block was defined as bifascicular block, second- or third-degree AV block. Asystole due to third-degree AV block was classified as third-degree AV block (ie, advanced heart block).

Background Population

The expected age- and sex-matched survival rates were calculated for each patient on the basis of survival in the Danish population (5.4 million citizens).18 On the basis of these survival rates, survival of a fictive age- and sex-matched background population of average Danes in a 20:1 ratio to the PTSMA cohort was constructed. We used the Danish background population (2001 to 2005) for these calculations, ignoring possible minor differences in life expectancy among Scandinavian populations.19

Statistical Analysis

Data were analyzed using the SAS version 9.1 statistical software. Baseline refers to pre-PTSMA data, and most recent follow-up refers to the most recently available data after PTSMA. Data are presented as mean±SD when normally distributed or median (interquartile range [IQR]) when nonnormally distributed. Proportions are presented as percentages (%). Student t test was used for paired comparisons of continuous variables. Unpaired comparisons were performed with the Student t test or Wilcoxon rank sum test, depending on the data distribution. Proportions were compared with χ2 test or Fisher exact test when unpaired and McNemar test when paired.

All patients treated with PTSMA (alcohol injection performed) entered the survival analysis at the date of their first PTSMA. Patients were censored if they were still alive when survival status was obtained from the survival registries. Death of all causes was considered an event. No patients were censored for other cardiovascular events or interventions such as myocardial infarction, valvular surgery, and coronary bypass because such patients were still considered to be at risk of developing adverse events related to PTSMA. Kaplan-Meier estimates of survival were calculated, and time-to-event curves were compared using the log-rank test. Predictors of death were analyzed in a univariable Cox regression model, and continuous variables (excluding age) were log transformed as appropriate. The assumption of proportional hazards, linearity of continuous variables, and lack of interactions were found to be valid without transformation. Results are presented as hazard ratio (HR).
Comorbidity

Hypertension. In 95% of the procedures, 1 septal branch was ablated, and in the rest, 2 septal branches were ablated.

Table 1. Baseline Characteristics of 279 Patients Treated With PTSMA

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic</td>
<td></td>
</tr>
<tr>
<td>Age at first PTSMA, y</td>
<td>59±14</td>
</tr>
<tr>
<td>Female sex, %</td>
<td>46</td>
</tr>
<tr>
<td>Clinical follow-up, y</td>
<td>2.9±2.5</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
</tr>
<tr>
<td>Obesity (BMI ≥30 kg/m²)</td>
<td>80 (32)</td>
</tr>
<tr>
<td>COPD</td>
<td>18 (6)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19 (7)</td>
</tr>
<tr>
<td>History of arterial hypertension</td>
<td>123 (44)</td>
</tr>
<tr>
<td>Cerebrovascular events</td>
<td>15 (5)</td>
</tr>
<tr>
<td>Heart valve disease (not related to HCM)</td>
<td>22 (8)</td>
</tr>
<tr>
<td>Previous invasive treatment</td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>19 (7)</td>
</tr>
<tr>
<td>Pacemaker (total)</td>
<td>45 (16)</td>
</tr>
<tr>
<td>Pacemaker (LVOT gradient)</td>
<td>40 (14)</td>
</tr>
<tr>
<td>Pacemaker (other)</td>
<td>5 (1.8)</td>
</tr>
<tr>
<td>ICD</td>
<td>4 (1.4)</td>
</tr>
<tr>
<td>Myectomy</td>
<td>4 (1.4)</td>
</tr>
<tr>
<td>Heart surgery (other)</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>Echocardiography</td>
<td></td>
</tr>
<tr>
<td>IVSd, mm</td>
<td>19±4</td>
</tr>
<tr>
<td>LVEDd, mm</td>
<td>43±6</td>
</tr>
<tr>
<td>LVPWd, mm</td>
<td>13±3</td>
</tr>
<tr>
<td>Maximal wall thickness, mm</td>
<td>20±4</td>
</tr>
<tr>
<td>Left atrial dimension, mm</td>
<td>45±7</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>59±7</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD or n (%), unless otherwise indicated. BMI indicates body mass index; COPD, chronic obstructive pulmonary disease; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; IVSd, interventricular septum diastolic dimension; LVEDd, left ventricular diastolic dimension; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; LVPWd, left ventricular posterior wall diastolic dimension; PCI, percutaneous coronary intervention; PTSMA, percutaneous transluminal septal myocardial ablation.

and 95% CI. A 2-sided P<0.05 was considered significant. Repeated-measures ANOVA and generalized estimating equation analyses were used to account for multiple observations per patient during follow-up as appropriate.

Results

From 1999 to 2010, 313 PTSMA procedures were performed in 279 patients (age, 59±14 years) (Table 1). Symptoms and functional class were assessed at 1033 time points (1 to 8 follow-up assessments per patient), and 594 echocardiography examinations were performed at baseline and during 2.9±2.6 years of follow-up. The prevalences of comorbidities are listed in Table 1. The proportions of patients with 0, 1, 2, 3, and 4 comorbidities were 31%, 35%, 27%, 7%, and 0.4%, respectively. Forty-four percent of patients (range, 37% to 48% between centers) had a history of some degree of arterial hypertension. In 95% of the procedures, 1 septal branch was ablated, and in the rest, 2 septal branches were ablated.

Within 2 years after the first PTSMA, 14% of patients were treated with another septal reduction therapy (6 myectomy, 26 PTSMA) (Figure 1).

Hemodynamic and Symptomatic Effects

There were no differences in baseline LVOT gradients at rest between the center using a resting LVOT gradient ≥30 mm Hg as a criterion for performing PTSMA (median, 55 mm Hg; IQR, 38 to 70 mm Hg) and the centers using the >50 mm Hg as a criterion (median, 59 mm Hg; IQR, 33 to 90 mm Hg; P=0.5). The LVOT gradients at rest were reduced from 58 mm Hg (IQR, 34 to 89 mm Hg) at baseline to 12 mm Hg (IQR, 8 to 24 mm Hg) at 1-year follow-up (P<0.001) and with a small further decrease (0.9 mm Hg per year) during the follow-up period (P=0.03) (Figure 2). The LVOT gradients during Valsalva maneuver were reduced from 93 mm Hg (IQR, 70 to 140 mm Hg) at baseline to 21 mm Hg (IQR, 11 to 42 mm Hg) at 1-year follow-up (P<0.001) and remained stable during the follow-up period (P=0.14) (Figure 2).

The proportion of patients in NYHA class III/IV was reduced from 94% at baseline to 21% at 1-year follow-up (P<0.001) and remained stable during the follow-up period (P=0.99) (Figure 3). The proportion of patients in Canadian Cardiovascular Society class III/IV was reduced from 16% at baseline to 3% at 1-year follow-up (P<0.001) and remained stable during the follow-up period (P=0.5) (Figure 3). The proportion of patients with syncope or palpitations were 18% and 34%, respectively, at baseline compared to 2% and 13% (P<0.001) at 1-year follow-up and remained stable during the follow-up period (P=0.35 and P=0.45, respectively) (Figure 3). Left ventricle ejection fraction was 59±7% at baseline and 58±9% at 1-year follow-up (P=0.08) and remained stable during the follow-up period (P=0.2).

In patients in NYHA class III/IV at most recent follow-up (21%), LVOT gradients at rest (median, 13 mm Hg; IQR, 10 to 30 mm Hg) and during Valsalva-manuever (median, 21 mm Hg; IQR, 14 to 47 mm Hg) were not significantly different from LVOT gradients in patients in NYHA class III/IV at most recent follow-up and tended to be older (61±15 years versus 57±13 years, respectively, P=0.17). NYHA class III/IV at most recent follow-up was associated with diabetes mellitus (P=0.03), chronic obstructive pulmonary disease (P=0.02), and valve disease not related to HCM (P<0.01). Ninety-one percent of patients without comorbidities at baseline were in NYHA class III/IV at most recent follow-up compared to 72% (P<0.01) of the patients with ≥1 comorbidity. Symptomatic improvement defined as decreased NYHA or Canadian Cardiovascular Society class or disappearance of syncope was evident in 88% of patients at most recent follow-up.
Complications

The in-hospital mortality was 0.3% (n=1), and the 30-day mortality was 0.6%. The patient who died in the hospital was a 72-year-old woman with left bundle branch block. The PTSMA procedure was performed without complications, but 8 hours later, she developed acute heart failure with advanced heart block (treated with pacing) and refractory hypotension. In the autopsy report, myocardial changes typically seen in HCM were described, but no evidence of unintentional coronary lesions, ischemic heart disease, or any other explanation for the fatal outcome was disclosed.

In-hospital VF occurred in 9 (2.8%) patients during the PTSMA procedure (n=4) or during the in-hospital monitoring (n=5) (Table 2). All patients with VF were defibrillated using external defibrillators and had immediate complete recovery. The volume of alcohol injected during procedures complicated by in-hospital VF tended to be lower (1.7±0.3 mL) than the volume injected during procedures not complicated by VF (2.2±0.7 mL, P=0.08). In 2 patients, VF was related to injection of contrast (ie, before alcohol injection). Implantable cardioverter-defibrillators were not used in case of per- or periprocedural VF, and there was no association between VF and long-term survival (Table 3).

Episodes of third-degree heart block were seen in 36% of patients during the PTSMA procedures and in 23% during the postprocedural observation (Table 2). Sixteen percent (45/279) of patients had a PPM before the first PTSMA, and 20% (45/230) without a PPM or an implantable cardioverter-defibrillator (n=4) before PTSMA had a PPM implanted within 30 days after PTSMA (ie, in total, 32% [90/279] had a PPM 30 days after the first PTSMA). The indication for PPM implantation after PTSMA was advanced heart block in 98% of cases. In patients requiring PPM implantation, the injected alcohol volume was 2.3±0.7 mL compared to 2.2±1.0 mL (P=0.006) in the remaining patients. The pacemaker implantation rate of 30% from 1999 to 2004 was reduced to 17% (P=0.01) in the following period. This reduction may be related to a reduction in the volume of injected alcohol from 2.6±0.9 mL until 2004 to 2.0±0.6 mL in the following period (P=0.001).

Bradycardia or asystole occurred during in-hospital monitoring after 12 (3.9%) PTSMA procedures and were related to
failure of temporary pacemakers or late-occurring (>48 hours after PTSMA) advanced heart blocks. In 2 patients, pericardial effusions causing tamponade were evacuated by acute sternotomy. In 1 patient, a pericardial effusion was evacuated by pericardiocentesis, and in 1 patient, an effusion (9 mm) was treated conservatively (Table 2). No other complications led to acute surgery. Two cases of thrombosis in the left anterior descending artery during the PTSMA procedure were observed (1 in-stent). Both cases were successfully treated, and coronary flows were normalized.

Survival
The median observational time (April 4, 2010) used in the survival analysis was 3.7 years (IQR, 1.4 to 6.3 years). Thirty-four deaths occurred during 1142 patient-years (ie, an overall mortality rate of 3% per year). The 1-, 5-, and 10-year survival rates after PTSMA were 97% (95% CI, 95% to 99%), 87% (95% CI, 81% to 92%), and 67% (95% CI, 53% to 80%), respectively, compared to 98%, 90%, and 78% in the age- and sex-matched background population (HR, 1.4; 95% CI, 0.9 to 2.1; log-rank \( P=0.06 \)) in the age- and sex-matched background population (Figure 5). In patients aged ≥60 years (70±7 years, n=138) the 1-, 5-, and 10-year survival rates were 95% (95% CI, 93% to 97%), 79% (95% CI, 70% to 88%), and 46% (95% CI, 35% to 57%) compared to 97%, 83%, and 63% (HR, 1.4; 95% CI, 0.96 to 2.1; log-rank \( P=0.09 \)) in the age- and sex-matched background population (Figure 5). Eleven percent of patients had an implantable cardioverter-defibrillator at most recent follow-up. There were no differences in survival among the 4 heart centers (log-rank \( P=0.9 \)).

Age at baseline, sex, chronic obstructive pulmonary disease, and sum of arrhythmic events during in-hospital monitoring were univariably associated \( (P≤0.1) \) with reduced survival. These parameters were analyzed in a multivariable Cox regression model (Table 3). There were no interactions among these 4 variables. Age at baseline showed significant association to survival (HR, 1.07; 95% CI, 1.03 to 1.1; \( P=0.001 \)), and there was a nonsignificant association between chronic obstructive pulmonary disease (HR, 2.4; 95% CI, 0.9 to 5.7; \( P=0.06 \)) and survival, whereas female sex (HR, 1.09; 95% CI, 0.5 to 2.3; \( P=0.9 \)) and the sum of
Table 2. Complications After 313 PTSMA Procedures in 279 Patients

<table>
<thead>
<tr>
<th>Complication</th>
<th>During PTSMA</th>
<th>In-Hospital Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injected volume of alcohol, mL</td>
<td>2.2 ± 0.8</td>
<td></td>
</tr>
<tr>
<td>CKMB max, µg/L</td>
<td>. . .</td>
<td>152 ± 104</td>
</tr>
<tr>
<td>TNT max, µg/L</td>
<td>. . .</td>
<td>3.26 ± 1.76</td>
</tr>
<tr>
<td>TNI max, µg/L</td>
<td>. . .</td>
<td>22 ± 16</td>
</tr>
<tr>
<td>Coronary artery perforation</td>
<td>3 (1.0)</td>
<td>. . .</td>
</tr>
<tr>
<td>Coronary artery spasm</td>
<td>4 (1.3)</td>
<td>. . .</td>
</tr>
<tr>
<td>Wire/balloon failure</td>
<td>3 (0.9)</td>
<td>. . .</td>
</tr>
<tr>
<td>Alcohol displacement</td>
<td>5 (1.6)</td>
<td>. . .</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>2 (0.6)</td>
<td>. . .</td>
</tr>
<tr>
<td>Hemopericardium/tamponade/effusion</td>
<td>0 (0)</td>
<td>4 (1.3)</td>
</tr>
<tr>
<td>Femoral hematoma</td>
<td>0 (0)</td>
<td>19 (6)</td>
</tr>
<tr>
<td>Cerebrovascular events</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Arrhythmia (n = 313)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td>5 (1.6)</td>
<td>5 (1.6)*</td>
</tr>
<tr>
<td>Asystole</td>
<td>4 (1.3)</td>
<td>9 (2.9)*</td>
</tr>
<tr>
<td>Sustained ventricular tachycardia</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>4 (1.3)</td>
<td>5 (1.6)</td>
</tr>
<tr>
<td>Conduction disturbances (n = 230)†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First-degree AVB</td>
<td>6 (2.6)</td>
<td>9 (3.9)</td>
</tr>
<tr>
<td>Second-degree AVB</td>
<td>2 (0.9)</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>Third-degree AVB</td>
<td>82 (36)</td>
<td>54 (23)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or n (%). AVB indicates atrioventricular block; CKMB, creatinine kinase MB; PTSMA, percutaneous transluminal septal myocardial ablation; TNI, troponin I; TNT, troponin T.

*Two (0.6%) patients experienced both asystole and bradycardia.
†Conduction disturbances only evaluated in patients without permanent pacemakers and implantable cardioverter-defibrillators at baseline.

Arrhythmic events during in-hospital monitoring (HR, 1.2; 95% CI, 0.8 to 1.7; P = 0.5) were not associated with survival. Adding postprocedural advanced heart block (univariably associated with increased survival) to the multivariable Cox analysis did not disclose any association to survival (HR, 1.4; 95% CI, 0.7 to 2.8; P = 0.4).

Discussion

Considering the observational time of 1142 patient-years, this first multicenter study reporting long-term outcome of PTSMA is among the largest studies of PTSMA.14 The main findings included a low in-hospital mortality and a low complication rate. Survival after PTSMA was only predicted by age and was comparable to the survival in an age- and sex-matched background population. Additionally, the hemodynamic and symptomatic benefits were sustained, but in 21% of the patients, dyspnea (NYHA class III/IV) persisted despite successful reduction of the LVOTO. Persistence of NYHA class III/IV at follow-up was associated with noncardiac or cardiac comorbidities.

Our in-hospital mortality was 0.3% compared to 1.0% (n = 611) reported by Fernandes et al.12 Comorbidities tend to increase the surgical mortality,20 but in the present cohort with considerable comorbidity, the 30-day mortality was 0.6% compared to 0.8% (n = 289) after myectomy reported by Omnen et al.4 The survival in the present PTSMA-treated cohort (87% at 5 years) was not significantly reduced compared to survival in an age- and sex-matched background population (90% at 5 years, P = 0.06). Five-year survival reported from other PTSMA centers have been higher than the survival in our background population (97% [n = 100]13 and 92% [n = 611]12). In contrast, Sorajja et al.21 reported a 4-year survival rate of 88% (n = 138) after PTSMA, which seems to be lower than the 4-year survival rate in the present study (92%). Kuhn et al.10 reported a mortality rate of 4.3% per year after PTSMA (n = 644) compared to 3.0% per year in the present study. Thus, the survival in this study seems to be in the midrange of reported survival rates after PTSMA.

In addition to the value of increased total number of patients in a multicenter study, the effects of differences in local routines (eg, referral routines, case selection [age, sex, HCM phenotype, methods for gradient measurements, presence of comorbidities, previous treatment], operator skills, minor differences in procedures, differences in postprocedure care, medication and recommendations for PPM or implantable cardioverter-defibrillator, follow-up routines) may have been leveled out and had a reduced effect on the overall results. Thus, the results of our multicenter study may be more generalizable than those from single-center studies.

The size of our cohort and the death rate limit the analysis of differences in survival between patients and the age- and sex-matched background population, but it should be noted that there was a trend toward a reduced survival in the PTSMA-treated patients with HCM. However, this trend might be explained to some extent by a generally higher mortality caused by the presence of HCM per se.

We found age to be the sole predictor of survival in the present study. Generally, reported myectomy cohorts have been younger (mean age, 45 to 50 years)4,6,7,22 than PTSMA cohorts (mean age, 54 to 64 years).9,10,12,14,21,23 In a recent meta-analysis of outcome after PTSMA versus myectomy, Leonardi et al.14 reported that odds ratios for treatment effect on all-cause mortality as well as sudden cardiac death were in favor of PTSMA after adjustment for available baseline characteristics, including age. Our finding of an 88% survival 10 years after PTSMA in patients aged <60 years, compared to the 10-year survival rate of 83% reported by Omnen et al.4 in a slightly younger myectomy population (age, 45 ± 20 years; n = 289) seems to confirm the more favorable survival after PTSMA compared to myectomy as reported by Leonardi et al.14 However, such comparisons of survival estimates between studies have statistical limitations and are affected by a number of confounding factors. Taken together, it is likely that age to a considerable extent explains the reported differences in survival between PTSMA- and myectomy-treated patients.

Several reports have documented the hemodynamic and symptomatic effects of PTSMA in the short and intermediate term.9,10,21,24–27 In the present study, the resting
LVOT gradient was 12 mm Hg (IQR, 8–24 mm Hg) at 1-year follow-up. This finding matches that of resting LVOT gradients of 22 mm Hg (IQR, 15–23 mm Hg) after PTSMA in a meta-analysis by Leonardi et al.14 Furthermore, this hemodynamic effect and the symptomatic improvements after PTSMA were sustained in the long term (Figures 2 and 3).

At most recent follow-up, 21% of the patients in the present study were in NYHA class III/IV. This subgroup had no increased LVOT gradients at rest or during Valsalva maneuver compared to patients in NYHA class I/II. Olivotto et al.28 reported an increasing proportion of patients in NYHA class III/IV (n=237) from 10% to 23% during 12±7 years follow-up.
(age, 56±23 years at follow-up), although only 3% had significant LVOTO. Thus, persistent dyspnea after PTSMA is not necessarily due to a failure of the procedure but may be caused by other HCM-related pathophysiologic factors, such as diastolic dysfunction, atrial fibrillation, or reduced stroke volume. We did, however, also find that cardiac and noncardiac comorbidities were associated with persistent NYHA class III/IV symptoms. Functional impairment due to concomitant comorbidity can only partly be differentiated from impairment caused by intrinsic HCM.

We found a high prevalence of a history of arterial hypertension. Our cohort had mainly asymmetrical hypertrophy (septum, 19±4 mm; posterior wall, 13±3 mm), and previous mild to moderate hypertension was not considered to be the etiology of the observed degree of hypertrophy. We have no data allowing us to dissect the time relationship between the development of hypertension and the development of LVOTO. However, as in patients with hypertension in general, it is likely that arterial hypertension also is a trigger for development of more severe hypertrophy in patients with HCM, which may increase the likelihood for developing LVOTO and need for PTSMA when hypertension and HCM coexist.

Advanced heart block occurred during 34% of procedures (Table 2). This finding was comparable to incidences of 46%\textsuperscript{29} and 38%\textsuperscript{30} reported from other PTSMA centers. Twenty percent of the patients in the present study had a PPM implanted as a complication to PTSMA compared to 5%\textsuperscript{29} and 18%\textsuperscript{30} in the other centers. The reduction of the volume of injected alcohol seemed to be associated with a reduction in the need for PPM implantations in the present study. However, the high rate of PPM implantations we saw emphasizes the need to look carefully into our routines to lower the PPM implantation rate to the 5% to 10% reported in other centers.

![Figure 4. Survival after PTSMA in 279 patients in 4 Scandinavian heart centers (1999 to 2010). Background indicates age- and sex-matched background population; PTSMA, percutaneous transluminal septal myocardial ablation.](image)

![Figure 5. Survival after percutaneous transluminal septal myocardial ablation stratified by age in 4 Scandinavian heart centers (1999 to 2010). Solid line indicates age <60 years (mean, 48±9 years); thin solid line, age- and sex-matched background population; dashed line, age >60 years (mean, 70±7 years); and thin dashed line, age- and sex-matched background population. P values represent comparisons between each group and its age- and sex-matched background population.](image)
of some PTSMA centers.23,29,31 Conduction disturbances also are seen after myectomy, necessitating PPM implantation in up to 8% of patients.7 Reports of in-hospital VF in relation to PTSMA have attracted considerable attention.23,31 We found 9 (2.8%) cases of in-hospital VF (4 procedural and 5 postprocedural). Other centers have reported an in-hospital incidence of ventricular tachycardia, VF, or sudden death of 2% to 3% during or after PTSMA.21,23 According to our experience, in-hospital ventricular arrhythmia can be handled safely but warrants careful monitoring.

In the present study, 14% of the patients had a reintervention (myectomy or PTSMA) within 2 years, which is comparable to an 83% success rate (no reintervention) after PTSMA reported by Sorajja et al.21 but seems higher than reintervention rates of 5% to 10% reported by others.23,31,32

Conclusion

In this long-term multicenter study, PTSMA-treated patients had sustained hemodynamic and symptomatic effects, and the survival was comparable to that in the background population, with age as the only predictor of survival. The in-hospital mortality was low despite significant comorbidity. The long-term symptomatic outcome was significantly affected by baseline comorbidities.

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Disclosures

None.

References


**CLINICAL PERSPECTIVE**

Left ventricular outflow tract obstruction in patients with hypertrophic obstructive cardiomyopathy can be reduced by an alcohol-induced septal infarct, that is, by selective injection of alcohol in a proximal septal perforator (percutaneous transluminal septal myocardial ablation [PTSMA]). Single-center reports on outcome of PTSMA treatment have shown marked differences, and there have been considerable theoretical concerns of potentially malignant arrhythmia in the border zone of the alcohol-induced infarct. Therefore, surgical myectomy has remained the gold standard. The Scandinavian hypertrophic obstructive cardiomyopathy database was established to evaluate the long-term outcome of PTSMA in an international clinical multicenter setting. In 279 patients treated with PTSMA between 1999 and 2010, the left ventricular outflow tract gradients were reduced to a median (interquartile range) of 12 mm Hg (8 to 24 mm Hg) at rest and 21 mm Hg (11 to 42 mm Hg) during Valsalva maneuver at 1-year follow-up, and these effects remained stable during long-term follow-up (2.9±2.6 years). The proportion of patients with syncope was reduced from 18% to 2%, and the proportion in New York Heart Association class III/IV was reduced from 94% to 21%. Persistent New York Heart Association class III/IV was associated with diabetes mellitus, chronic obstructive pulmonary disease, and valve disease unrelated to hypertrophic cardiomyopathy. Ninety-one percent of patients without comorbidities at baseline were in New York Heart Association class I/II at follow-up. The in-hospital mortality was 0.3% despite considerable comorbidities, and the long-term survival was comparable to that in an age- and sex-matched background population. However, a small tendency toward a reduced survival in the PTSMA-treated patients may have been related the presence of hypertrophic cardiomyopathy per se. PTSMA may become the treatment of choice in hypertrophic obstructive cardiomyopathy in the near future.
Long-Term Outcome of Percutaneous Transluminal Septal Myocardial Ablation in Hypertrophic Obstructive Cardiomyopathy: A Scandinavian Multicenter Study
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