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# Long-Term Survival in Patients With Resting Obstructive Hypertrophic Cardiomyopathy

## Comparison of Conservative Versus Invasive Treatment

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**Objectives** The aim of this study was to compare the survival of patients with hypertrophic cardiomyopathy (HCM) and resting left ventricular outflow tract (LVOT) obstruction managed with an invasive versus a conservative strategy.

**Background** In patients with resting obstructive HCM, clinical benefit can be achieved after invasive septal reduction therapy. However, it remains controversial whether invasive treatment improves long-term survival.

**Methods** We studied a consecutive cohort of 649 patients with resting obstructive HCM. Total and HCM-related mortality were compared in 246 patients who were conservatively managed with 403 patients who were invasively managed by surgical myectomy, septal ethanol ablation, or dual-chamber pacing.

**Results** Multivariable analyses (with invasive therapy treated as a time-dependent covariate) showed that an invasive intervention was a significant determinant of overall mortality (hazard ratio: 0.6, 95% confidence interval: 0.4 to 0.97, $p = 0.04$). Overall survival rates were greater in the invasive (99.2% 1-year, 95.7% 5-year, and 87.8% 10-year survival) than in the conservative (97.3% 1-year, 91.1% 5-year, and 75.8% 10-year survival, $p = 0.008$) cohort. However, invasive therapy was not found to be a significant independent predictor of HCM-related mortality (hazard ratio: 0.7, 95% confidence interval: 0.4 to 1.3, $p = 0.3$). The HCM-related survival was 99.5% (1 year), 96.3% (5 years), and 90.2% (10 years) in the invasive cohort, and 97.8% (1 year), 94.6% (5 years), and 86.9% (10 years) in the conservative cohort ($p = 0.3$).

**Conclusions** Patients treated invasively have an overall survival advantage compared with conservatively treated patients, with the latter group more likely to die from noncardiac causes. The HCM-related mortality is similar, regardless of a conservative versus invasive strategy. (J Am Coll Cardiol 2011;58:2313–21) © 2011 by the American College of Cardiology Foundation

Hypertrophic cardiomyopathy (HCM) is a genetic disorder of the cardiac sarcomere (1–3). Asymmetric septal hypertrophy is the most common manifestation of this condition, and a significant number of patients have associated left ventricular outflow tract (LVOT) obstruction (4–6). The long-term prognosis of patients with HCM and LVOT obstruction in the contemporary era remains unclear. Patients with New York Heart Association (NYHA) functional class III/IV symptoms are generally started on pharmacotherapy (5). In patients who remain symptomatic or who become intolerant of medications, an invasive intervention is warranted. Invasive therapeutic options include surgical myectomy, dual-chamber (DDD) permanent pacing, or septal ethanol ablation (SEA) (5). Although significant hemodynamic and clinical benefit can be achieved after invasive relief of the LVOT obstruction, it remains controversial whether abolition of the LVOT gradient actually improves long-term survival (7).

One large observational study has demonstrated that patients with HCM and LVOT obstruction have a worse long-term prognosis when compared with patients without obstruction (6). However, there are no randomized trials of medical versus invasive therapy, and the majority of retrospective cohort studies were done before the modern era. Another study suggested that patients with LVOT obstruction managed with surgical myectomy

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**Abbreviations and Acronyms**

**CI** = confidence interval
**DDD** = dual-chamber
**HCM** = hypertrophic cardiomyopathy
**LVOT** = left ventricular outflow tract
**NYHA** = New York Heart Association
**SCD** = sudden cardiac death
**SEA** = septal ethanol ablation
**TGH** = Toronto General Hospital

have better survival than conservatively treated patients (8). However, in this study, the medically and surgically managed patients were treated at different institutions, raising issues of referral bias. Therefore, we sought to compare the survival of patients with obstructive HCM who were treated conservatively with those treated invasively at a single tertiary care referral center. We also evaluated the factors predicting long-term survival in patients with resting obstructive HCM.

## Methods

**Study population and data collection.** This study included consecutive adult patients (≥18 years of age at initial presentation to the Toronto General Hospital [TGH]) with resting obstructive HCM who were referred to our institution between 1986 and 2007. Some of these patients were included in previous publications from our institution (9,10), but clinical and echocardiographic follow-up were updated from the time of completion of these studies. The diagnosis of HCM was established by the presence of asymmetric septal hypertrophy (septum ≥13 mm), in the absence of another condition that could account for the degree of hypertrophy observed (5). Echocardiographic data were obtained, as described previously (11), and LVOT gradients were determined by continuous wave Doppler assessment (11,12). Only patients with resting LVOT obstruction, defined as a resting gradient of ≥30 mm Hg, were included. The following conditions excluded patients from this study: other congenital syndromes (e.g., Noonan's), a fibrous subaortic membrane, significant aortic stenosis (defined as an aortic valve area <1.2 $cm^2$ or peak gradient ≥30 mm Hg across aortic valve), HCM with midventricular obstruction, HCM with pure provocable LVOT obstruction (i.e., LVOT gradient <30 mm Hg at rest but ≥30 mm Hg only after provocation), significant valvular lesions (other than mitral regurgitation due to systolic anterior motion), and significant epicardial coronary artery disease (coronary stenosis [>70%] on coronary angiography, previous bypass surgery, or percutaneous coronary intervention). Finally, we excluded patients who had previously undergone invasive procedures to treat their LVOT obstruction at other institutions.

**Management of patients with obstructive HCM: conservative and invasive management.** Over the course of the study period, the approach to the management of patients with obstructive HCM adhered to the following principles. Symptomatic patients were typically initially treated with medications (beta blockers, disopyramide, and/or calcium channel blockers). Patients were referred for invasive management in the presence of unacceptable symptoms despite maximally tolerated medical therapy. The choice of invasive procedure (myectomy, SEA, or DDD pacing) was determined by the managing physician, taking into account the clinical profile of the patient, presence of comorbid conditions, and his/her individual preferences.

**Classification of patients.** Patients were classified into 2 groups: 1) the conservative group, comprising those patients who received only medications (or no therapy) throughout the entire follow-up period; and 2) the invasive group, comprising patients who underwent (at any point during the follow-up period) any of the following procedures for management of their LVOT obstruction: 1) surgical myectomy; 2) SEA; or 3) DDD pacing. Patients in the conservative group were subclassified according to clinical status. Patients in the invasive group might have received medical therapy at the time of presentation but were subsequently referred for an invasive procedure. If patients underwent more than 1 procedure to treat their LVOT obstruction, they remain categorized according to the initial invasive treatment. Although DDD pacing has largely fallen out of favor as a treatment strategy in patients with HCM and LVOT obstruction (5), we included patients who underwent DDD pacing in the invasively managed cohort, because pacing was considered a reasonable therapeutic option for much of the 1990s.

**Invasive procedures.** Surgical myectomy was performed, as previously described, throughout the study period (10). Dual-chamber pacing has been offered at TGH since the 1990s (13). Septal ethanol ablation has been available at our institution since 1998 (9).

**Follow-up and definition of outcomes.** The status of patients was determined by cross-sectional follow-up, with the most recent evaluation available in the last 2 years. We classified deaths as HCM-related or noncardiovascular. Deaths were considered to be HCM-related in the presence of 1 of the following: 1) death within 30 days of an invasive procedure; 2) sudden cardiac (nontraumatic) death (SCD); 3) heart failure-related death; or 4) stroke-related death. For our survival analyses, resuscitated cardiac arrest and appropriate implantable cardioverter-defibrillator discharges were treated as HCM-related and sudden deaths. Patients who underwent cardiac transplantation were censored at the time of transplantation. In instances when the cause of death could not be determined, an HCM-related cause of death was ascribed.

**Ethics.** This study was approved by the Research Ethics Board of our institution.

**Statistical analysis.** Continuous and categorical data were analyzed with *t* tests, Wilcoxon rank-sum tests, chi-square tests, or McNemar's test, where appropriate.

MULTIVARIABLE MODELS. The primary survival analyses were performed with the Cox proportional hazards model (14). Univariate and multivariable models were developed to