Do myocardial perfusion SPECT and radionuclide angiography studies in adult patients with hypertrophic cardiomyopathy have prognostic implications?

Guillermo Romero-Farina, PhD,[a] Jaume Candell-Riera, PhD, FESC,[a] Enrique Galve, PhD,[a] Lluís Armadans, PhD,[b] Francisca Ramos, MD,[b] Joan Castell, PhD,[c] Santiago Aguadé, MD,[c] Juan M. Nogales, MD,[a] and Jordi Soler-Soler, PhD, FESC, FACC[a]

Background. **Some myocardial perfusion single photon emission computed tomography (SPECT) and radionuclide ventriculography studies have suggested that the presence of regional perfusion defects and diastolic abnormalities could have prognostic implications in patients with hypertrophic cardiomyopathy (HC). The aim of this prospective study was to analyze the prognostic value of these techniques in adult patients with HC.**

Methods and Results. **One hundred one patients with HC (44 women; mean age, 54 ± 16 years; 55% obstructive) were prospectively studied by means of myocardial perfusion SPECT and radionuclide angiography. Of these patients, 55 (54.4%) had an abnormal myocardial perfusion SPECT study: 28 (27.7%) had fixed defects and 41 (40.6%) had reversible defects; 15 (14.8%) of these patients had both types of defect. Of the patients, 16% had left ventricular ejection fraction lower than 60%, 25.7% had an abnormal peak filling rate, and 51% had an abnormal time to peak filling rate. During 5.6 ± 2.7 years of follow-up, 13 patients (12.8%) died (heart failure 8 and sudden death in 5) and 14 had one or more severe complications develop (syncope in 6, angina III-IV in 4, dyspnea III-IV in 10, and acute myocardial infarction in 3). The summed difference score was higher in patients with cardiac death (2.2 ± 2.3 vs 1.1 ± 1.3, $P = .008$), and fixed defects were more prevalent in patients with severe complications (57% vs 21%, $P = .01$). In the Kaplan-Meier survival plot analysis, severe complications were more likely in patients with fixed defects ($P = .01$) or ejection fraction lower than 60% ($P = .01$).**

Conclusions. **Prognostic information from myocardial perfusion SPECT and radionuclide angiography has limited clinical significance with regard to cardiac death in adult patients with HC. However, the presence of fixed defects and lower ejection fraction in these patients has an adverse prognostic meaning for severe complications. (J Nucl Cardiol 2004;11:578-86.)**

Key Words: Hypertrophic cardiomyopathy • myocardial perfusion single photon emission computed tomography • radionuclide ventriculography • prognosis

Hypertrophic cardiomyopathy (HC) is a genetically determined disorder that is caused by mutations in genes that encode sarcomeric contractile proteins, with a variable clinical and morphologic expression and which is characterized by unexplained left ventricular hypertrophy.[1-4] The most frequent causes of death in patients with this disease are sudden cardiac death, progressive heart failure, and stroke associated with atrial fibrillation.[5] Risk factors associated with cardiac death are syncope, a family history of sudden cardiac death in young patients, nonsustained ventricular tachycardia, hypotension during exercise, induced ventricular tachycardia, high degree of hypertrophy, severity of obstruction, mitral insufficiency, atrial fibrillation, and coronary microvascular dysfunction.[4-16]

Ischemia and diastolic abnormalities are common in patients with HC, but some myocardial perfusion scintigraphic[17-19] and radionuclide ventriculographic[20] studies have shown controversial results with regard to their

From the Departments of Cardiology,[a] Preventive Medicine and Epidemiology,[b] and Nuclear Medicine,[c] Hospital Universitari Vall d'Hebron, Barcelona, Spain.

Received for publication March 11, 2004; final revision accepted May 13, 2004.

Reprint requests: Jaume Candell-Riera, PhD, FESC, Servei de Cardiologia, Hospital Universitari Vall d'Hebron, P. Vall d'Hebron, 119-129, 08035 Barcelona, Spain; *jcandell@vhebron.net.*

1071-3581/$30.00

doi:10.1016/j.nuclcard.2004.05.008

prognostic significance. The aim of this study was to prospectively analyze the prognostic value of myocardial perfusion single photon emission computed tomography (SPECT) and radionuclide angiography in adult patients with HC.

MATERIAL AND METHODS

Patients

Between 1990 and 2001, 125 patients with HC were consecutively studied at a tertiary hospital. The diagnosis of HC was based on echocardiographic evidence of myocardial hypertrophy (anterior septum or posterior free wall thickness >15 mm and posterior septum or lateral free wall thickness >17 mm) in the absence of another cardiovascular or systemic disease that could produce left ventricular hypertrophy.[21] No patient had previous cardiac arrest. Coronary angiography was performed in 53 patients (42%), and only 7 patients had significant coronary lesions. Patients with previous myocardial infarction (n = 7), myotomy-myectomy (n = 5), pacemaker (n = 13), and coronary artery disease (n = 7) were excluded. Therefore 101 patients were included in the study (44 women; mean age, 54 ± 16 years). Of these patients, 72 (71.2%) were symptomatic at the time of diagnosis; 10 of these patients were hospitalized (6 with angina grade III-IV, 2 with heart failure, and 2 with syncope). Asymptomatic patients were studied to evaluate a systolic murmur (n = 15), abnormal electrocardiogram (n = 11), or family history of sudden cardiac death (n = 3). After the diagnosis was confirmed, these patients were prospectively studied by means of myocardial perfusion SPECT and radionuclide angiography.

Myocardial Perfusion SPECT

Exercise-rest myocardial perfusion SPECT with technetium 99m tetrofosmin was performed in 101 patients; all patients underwent a maximal symptom-limited exercise electrocardiographic test on a bicycle ergometer with an initial workload of 50 W and with subsequent 25-W increments every 3 minutes. A 12-lead electrocardiogram was recorded every third minute, at the end of the test, and at 1, 3, and 5 minutes after exercise. The test was stopped when the patient had any symptom precluding the continuation of exercise (angina, dizziness, or muscular fatigue), ST-segment depression greater than 0.2 mV appearing 0.08 seconds after the J point, or arterial hypotension. Patients whose peak heart rate was lower than 80% of the predicted value and whose oxygen consumption was less than 5 metabolic equivalents, without symptoms, received intravenous dipyridamole (0.14 mg/kg body weight per minute for 4 minutes) while they continued to exercise at the maximal tolerated load until 2 minutes after the end of dipyridamole administration.[22]

An intravenous dose of Tc-99m tetrofosmin (296-370 MBq) was administered 30 to 60 seconds before the end of exercise, and stress images were acquired 15 to 30 minutes later. An intravenous dose of 740 to 925 MBq was administered immediately after acquisition of stress images, and rest images were acquired 15 to 30 minutes later. Acquisition was performed with a Siemens ECAM scintillation camera (Siemens, Hoffman Estates, Ill) with a high-resolution collimator and a semicircular orbit starting at 30° right anterior oblique, with detection being carried out every 3°. Reconstruction was performed (Butterworth filter; order, 5; section frequency, 0.4), and short-axis, horizontal long-axis, and vertical long-axis sections were obtained.

The left ventricle was divided into 17 segments.[23] Each segment was scored based on a 5-point scoring system (0, normal; 1, mild defect; 2, moderate defect; 3, severe defect; and 4, absence of radioactive uptake). The apical region includes anteroapical, septoapical, inferoapical, lateroapical, and apical segments.

All studies were evaluated by consensus between 3 experienced observers. A reversible defect was defined as a mild, moderate, or severe defect or absence of uptake on stress with improvement on rest images. A fixed defect was defined as a mild, moderate, or severe defect or absence of radioactive uptake on stress without any improvement on rest images (Figure 1). A summed stress score, summed rest score, and summed difference score were calculated.

Radionuclide Angiography

Between days 1 and 10 of the myocardial perfusion SPECT study, all patients underwent equilibrium radionuclide angiography at rest with in vivo–in vitro labeling of erythrocytes with Tc-99m. At the time of ventriculography, 10 patients had atrial fibrillation. The same scintillation camera with the parallel-hole collimator was used, and imaging was performed in the left anterior oblique projection, which permits a better separation between the right and left ventricles. The information was collected as a histogram, by use of synchronization with the R wave on the electrocardiogram, and was stored on a computer in studies of 20 images/cardiac cycle and a minimal number of 200,000 counts/image or 300 cycles in a 64 × 64 matrix. All cardiac cycles differing by greater than 10% from the average cycle were rejected. In case of atrial fibrillation, the duration of the acquisition was prolonged in the same proportion of the arrhythmia (50% increase for 50% of rejected cycles).

Left ventricular ejection fraction was computed on the basis of relative end-diastolic and end-systolic counts. In all patients the framing rate was sufficiently high to allow calculation of diastolic parameters. Accordingly, the peak filling rate was computed from the first derivative of a third-order polynomial function fitted to the first two thirds of the diastolic portion of the left ventricular time-activity curve by a least squares technique, normalized for end-diastolic volume and expressed as end-diastolic volume per second; the time to peak filling rate, relative to end systole, was also calculated. The peak filling rate and time to peak filling rate were considered normal when they were greater

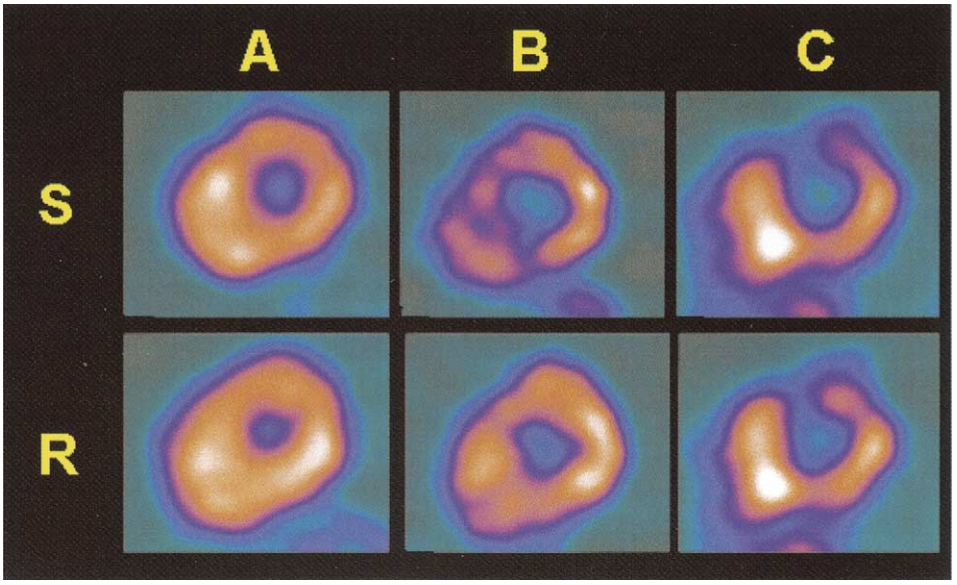

Figure 1. Examples of normal segment (**A**), anteroseptal and inferior reversible defect (**B**), and anterior fixed defect (**C**) in short-axis views of patients with HC. *S*, Stress; *R*, rest.

than 2.5 end-diastolic volume per second and less than 180 milliseconds, respectively.[24]

Follow-up

All patients were followed up for a minimum of 1 year or until death. Follow-up information was obtained by telephone contact with all patients. The data obtained during the follow-up and included in the statistical analysis were angina pectoris (Canadian Cardiovascular Society grade I, II, III, and IV), dyspnea (New York Heart Association functional class I, II, III, and IV), syncope, death (sudden cardiac death and heart failure death), and severe complications (myocardial infarction, syncope, angina III-IV, or dyspnea III-IV). Sudden cardiac death was defined as an unexpected nontraumatic event occurring less than 1 hour after the onset of symptoms in patients without previous severe symptoms.[25]

Statistical Analysis

Continuous variables are expressed as mean ± SD, and categoric data are expressed as percentages. Differences between groups were determined by unpaired Student *t* test for continuous variables and χ^2 test or Fisher exact test for categoric variables. To analyze the association between continuous variables and categoric variables, a nonparametric Mann-Whitney *U* test was used. To analyze cumulative survival and its relationship to scintigraphic variables, the Kaplan-Meier method was used, with death and severe complications as a composite outcome variable. Comparisons between groups were based on the log-rank test. Differences were considered statistically significant at $P <$ .05. All statistical analyses were performed with the SPSS statistical package.[26]

RESULTS

Of the patients, 56 (55.4%) had an obstructive dynamic gradient greater than 30 mm Hg. Of 101 patients, 54 (53.5%) had dyspnea and 10 (9.9%) had had one or more episodes of unexplained syncope. A history of exertional angina pectoris was present in 36 patients (35.6%). At the time of the SPECT study, 72 patients (71.3%) were receiving drug therapy (β-adrenergic–blocking agents in 45, calcium channel antagonists in 21, amiodarone in 6, and disopyramide in 5).

Myocardial Perfusion SPECT

Exercise stress testing was performed in all patients, and simultaneous dipyridamole was administered in 6 of these patients. The mean duration of the exercise test was 6.2 ± 2.5 minutes, with a peak achieved load of 80 ± 29 W and maximal oxygen uptake of 5.7 ± 1.3 metabolic equivalents. Peak heart rate was 119 ± 25 beats/min (70% ± 13% of the predicted value), peak systolic blood pressure was 164 ± 29 mm Hg, the peak heart rate × peak systolic blood pressure product was 19,567 ± 5,747. In 5.1% of patients, ST-segment depression of 1 mm or greater was observed. Reasons for termination of the test were fatigue (71 patients [70.2%]), dyspnea (31 [30.6%]), chest pain (7 [6.9%]), and hypotension (6

Table 1. Myocardial perfusion SPECT and radionuclide angiography results

	Data
Myocardial perfusion SPECT	
Fixed defects	28 (28.6%)
Reversible defects	41 (41.8%)
Fixed and/or reversible defects	55 (54.4%)
No. of fixed defects/patient	2.6 ± 1.6 (1-9)
No. of reversible defects/patient	2.1 ± 1.2 (1-7)
Summed stress score	2.6 ± 3.8 (0-24)
Summed rest score	1.5 ± 3.3 (0-24)
Summed difference score	1.1 ± 1.6 (0-7)
Radionuclide angiography	
Ejection fraction (%)	69.6 ± 10 (36-94)
End-diastolic volume (mL)	94.9 ± 32 (39-185)
End-systolic volume (mL)	28.8 ± 12 (13-74)
Stroke volume (mL)	61 ± 23 (14-115)
Peak filling rate (EDV/s)	3.2 ± 1 (1.6-7)
Time to peak filling rate (ms)	232.3 ± 155 (84-735)

EDV, End-diastolic volume.

[5.9%]). No complications were observed during exercise stress testing.

An abnormal myocardial perfusion SPECT study was found in 55 patients (54.4%). Of the patients, 28 (27.7%) had 1 or more fixed defects (2.6 ± 1.6 [range, 1-9]) and 41 (40.5%) had 1 or more reversible defects (2.1 ± 1.2 [range, 1-7]); 14 of these patients had both defects. The values of the summed stress score, summed rest score, and summed difference score are shown in Table 1. The most affected segments were apical (35 patients) and inferior (35 patients) segments, followed by anterior (23 patients), lateral (15 patients), and septal (3 patients) segments. There was no relationship between the results of myocardial perfusion SPECT and symptoms.

Radionuclide Angiography

Table 1 shows the results of radionuclide angiography. Sixteen percent of patients had left ventricular ejection fraction lower than 60%. There were no significant differences in summed stress score, summed rest score, and summed difference score between patients with ejection fraction of 60% or greater and those with ejection fraction lower than 60%. Twenty-six percent of patients had an abnormal peak filling rate, and fifty-one percent of patients had an abnormal time to peak filling rate. There was no relationship between the results of radionuclide angiography and symptoms.

Table 2. Clinical results at initial study and at end of follow-up

	Initial	Follow-up	*P* value
Dyspnea (NYHA)	54 (53.5%)	83 (82.2%)	.001
I	5 (9.3%)	8 (9.7%)	
II	37 (68.6%)	53 (63.9%)	
III	11 (20.3%)	20 (24%)	
IV	1 (1.8%)	2 (2.4%)	
Angina (CCS)	36 (35.6%)	47 (46.6%)	.07
I	9 (25%)	9 (19.2%)	
II	25 (69.4%)	32 (68%)	
III	1 (2.8%)	3 (6.4%)	
IV	1 (2.8%)	3 (6.4%)	
Syncope	10 (9.9%)	16 (9.9%)	NS

NYHA, New York Heart Association functional class; *CCS,* Canadian Cardiovascular Society; *NS,* not significant.

Follow-up

During 5.6 ± 2.7 years (range, 1-12 years) of follow-up, there was an increase in the number of symptomatic patients (Table 2). At the end of follow-up, a cardiac pacemaker was implanted in 24 patients, and myotomy-myectomy and transcoronary ablation of septal hypertrophy were performed in 5 patients and 4 patients, respectively. The annual cardiac mortality rate was 2.3%. Of 13 cardiac deaths, 8 were a result of heart failure (annual heart failure death rate, 1.4%) and 5 were sudden (annual sudden death rate, 0.9%). Heart failure death occurred more frequently in elderly patients (50 ± 21 years for sudden death vs 70 ± 8 years for heart failure, $P = .04$). In 14 patients, one or more severe complications developed (syncope in 6, angina III-IV in 4, dyspnea III-IV in 10, and acute myocardial infarction in 3). The annual rate of severe complications was 3.1%.

By bivariate analysis, the summed difference score was higher (2.2 ± 2 vs 1.1 ± 1.3, $P = .008$) in patients with cardiac death (Table 3) and fixed defects were more prevalent (57% vs 23.6%, $P = .013$) and the summed rest score was higher (3.5 ± 6.1 vs 1.2 ± 2.6, $P = .02$) in patients with severe complications (Table 4).

In the Kaplan-Meier survival plot analysis of myocardial perfusion SPECT and radionuclide angiography, significant differences were not observed for death, although patients with reversible defects and fixed defects tended to have an adverse prognosis. Severe complications were more likely in patients with fixed defects ($P = .01$) or ejection fraction lower than 60% ($P = .01$) (Figures 2-4).

Table 3. Bivariate analysis for patients with and without cardiac death

	Dead (n = 15)	Alive (n = 86)	*P* value
Myocardial perfusion SPECT			
Fixed defects	5 (33%)	23 (27%)	.42
Reversible defects	9 (60%)	32 (38%)	.09
No. of fixed defects/patient	2.6 ± 2 (1-5)	2.6 ± 1.6 (1-9)	.96
No. of reversible defects/patient	2.3 ± 2.1 (1-7)	2 ± 0.8 (1-5)	.56
Summed stress score	3.9 ± 5 (0-20)	2.4 ± 3.5 (0-24)	.17
Summed rest score	1.8 ± 3.7 (0-13)	1.4 ± 3.3 (0-24)	.68
Summed difference score	2.2 ± 2.3 (0-7)	1.1 ± 1.3 (0-8)	.008
Radionuclide angiography			
Ejection fraction (%)	69 ± 9 (54-87)	69 ± 10 (36-94)	.87
Ejection fraction <60%	3 (20%)	13 (15%)	.62
End-diastolic volume (mL)	112 ± 35 (65-168)	91 ± 30 (39-185)	.07
End-systolic volume (mL)	39 ± 17 (17-14)	27 ± 10 (13-63)	.09
Stroke volume (mL)	73 ± 21 (47-112)	62 ± 23 (14-115)	.19
Peak filling rate (EDV/s)	2.8 ± 0.7 (1.6-4)	3.2 ± 1 (2-7)	.29
Time to peak filling rate (ms)	221 ± 147 (108-561)	233 ± 157 (89-735)	.83

EDV, End-diastolic volume.

Table 4. Bivariate analysis for patients with and without severe complications

	Severe complications (n = 14)	No severe complications (n = 72)	*P* value
Myocardial perfusion SPECT			
Fixed defects	8 (57%)	15 (21%)	.01
Reversible defects	5 (43%)	27 (38%)	.79
No. of fixed defects/patient	3.3 ± 2 (1-9)	2.5 ± 1.2 (1-6)	.21
No. of reversible defects/patient	2 ± 1 (1-4)	2.2 ± 2 (1-7)	.63
Summed stress score	4.3 ± 6 (0-24)	2.2 ± 3.4 (0-20)	.07
Summed rest score	3.5 ± 6.1 (0-24)	1.2 ± 2.6 (0-13)	.02
Summed difference score	1.2 ± 1.6 (0-5)	1 ± 1.5 (0-7)	.70
Radionuclide angiography			
Ejection fraction (%)	65 ± 11 (36-81)	70 ± 10 (36-94)	.07
Ejection fraction <60%	5 (35.7%)	9 (12.5%)	.06
End-diastolic volume (mL)	88 ± 34 (58-144)	93 ± 30 (39-185)	.71
End-systolic volume (mL)	28 ± 7.4 (19-42)	27 ± 11 (13-63)	.79
Stroke volume (mL)	59 ± 30 (33-115)	63 ± 22 (14-112)	.68
Peak filling rate (EDV/s)	3.6 ± 1.5 (2-7)	3.2 ± 1 (2-6.9)	.33
Time to peak filling rate (ms)	148 ± 51 (84-231)	248 ± 165 (87-735)	.08

EDV, End-diastolic volume.

DISCUSSION

Myocardial Perfusion Defects in Patients With HC

Myocardial ischemia can occur in patients with HC in the absence of coronary artery disease.[27-29] Small vessel narrowing, raised intracavitary pressures, and the effects of left ventricular hypertrophy on metabolic demands and coronary vascular resistance are potential mechanisms. However, the correlation between angina and reversible perfusion defects is poor. This phenomenon can be explained in several ways: a relatively homogeneous reduction in coronary vasodilator reserve

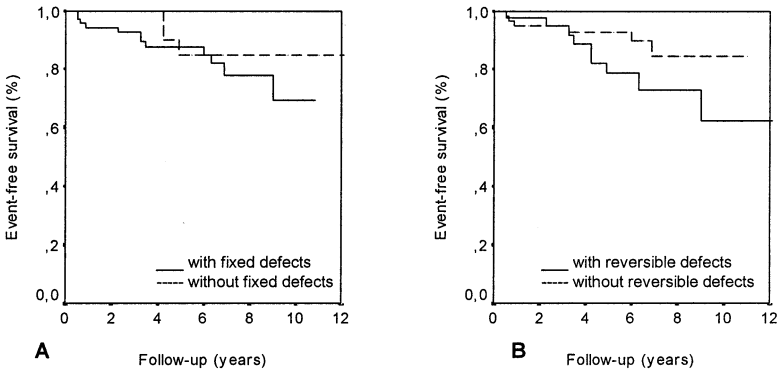

Figure 2. Kaplan-Meier analysis of survival free of cardiac death. **A**, Survival plot indicating the cumulative event-free survival rates in patients with (*solid line*) and without (*dashed line*) fixed perfusion defects (log rank $P = .46$, Breslow $P = .43$). **B**, Survival plot indicating the cumulative event-free survival rates in patients with (*solid line*) and without (*dashed line*) reversible perfusion defects (log rank $P = .12$, Breslow $P = .22$).

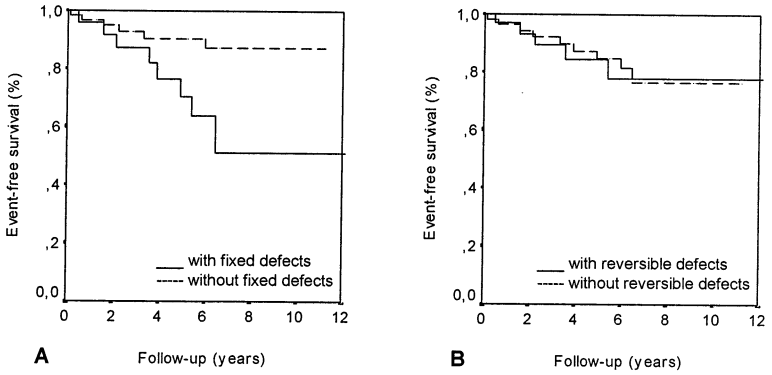

Figure 3. Kaplan-Meier analysis of survival free of severe complications. **A**, Survival plot indicating the cumulative event-free survival rates in patients with (*solid line*) and without (*dashed line*) fixed perfusion defects (log rank $P = .01$, Breslow $P = .05$). **B**, Survival plot indicating the cumulative event-free survival rates in patients with (*solid line*) and without (*dashed line*) reversible perfusion defects (log rank $P = .90$, Breslow $P = .84$).

and subendocardial hypoperfusion, known to be an important mechanism of ischemia in hypertrophic ventricles, might not be detected by perfusion scintigraphic studies. On the other hand, regional differences in tracer concentration resulting from factors such as variable myocardial thickness (ie, partial volume effect) are more likely in HC.

Tanaka et al[30] quantified the amount of myocardial scarring in a necropsy study of 10 patients with HC and found that patients who died suddenly had a larger amount of scarring than those who died from noncardiac causes. The demonstration of a relationship between fixed defects and left ventricular dimensions and ejection fraction supports the hypothesis that fixed perfusion abnormalities in patients with HC represent areas of myocardial fibrosis.[27,31-34] Choudhury et al[35] observed, in a magnetic resonance imaging study, that myocardial scarring is a common finding (80%) in patients with HC. In this study most defects were found in the septum. This finding suggests that SPECT is rather insensitive to detect myocardial scars in the septum because of the overdriving influence of the partial volume effect. The most affected segments in our series were apical and inferior. Decreased tracer uptake in apical areas where the myocardium is thin might be a result of insufficient thickness rather than myocardial scar. On the other hand, the inferior region of the left ventricle could be attenuated by the diaphragm in some patients.

The differences between the 54% positive rate (fixed and/or reversible defects) observed in our study and the wide range of positivity rates (39%-74%)[17-19,27,31,32,36,37] observed in other series may be attributed to differential

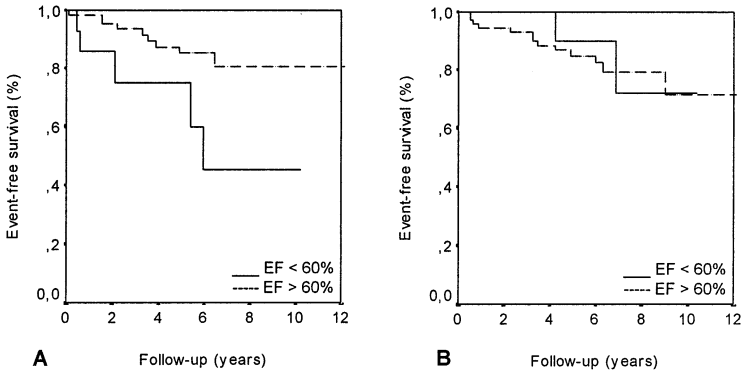

Figure 4. Kaplan-Meier analysis of survival free of severe complications (**A**) and cardiac death (**B**). **A**, Survival plot indicating the cumulative event-free survival rates in patients with (*solid line*) and without (*dashed line*) left ventricular ejection fraction (*EF*) lower than 60% (log rank $P = .01$, Breslow $P = .01$). **B**, Survival plot indicating the cumulative event-free survival rates in patients with (*solid line*) and without (*dashed line*) ejection fraction lower than 60% (log rank $P = .62$, Breslow $P = .42$).

referral patterns, continuation of β-blockers in some patients, and different interpretation criteria for fixed defects that were not interpreted as abnormal in some studies.

Prognostic myocardial perfusion studies in patients with HC are scarce (Table 5). von Dohlen et al[17] observed that thallium perfusion abnormalities were strongly associated with potentially lethal arrhythmias, Dilsizian et al[18] reported that reversible thallium defects were significantly more common in patients with a history of cardiac arrest or syncope, and Yamada et al[19] found that only fixed defects were significantly more common in patients with syncope.

In our series the summed difference score was significantly higher in patients with cardiac death and fixed defects and summed rest scores were more prevalent in patients with severe complications. Kaplan-Meier analysis showed a poor survival rate for patients with reversible defects, but this was not statistically significant. However, severe complications were more common in patients with fixed defects on Kaplan-Meier analysis.

The annual mortality rate in our series was 2.3%. There are several possible explanations for the relatively benign clinical course of the disease. Although the study was conducted in a tertiary medical center, patients were not selected on the basis of symptom severity or treatment needs. A family history of sudden death was rare, and all symptomatic patients and those with ventricular arrhythmias were receiving treatment with β-adrenergic receptors, verapamil, or amiodarone. The favorable survival data reported here can also be attributed to other particular therapeutic measures, such as pacemaker implantation and myectomy, that had been indicated during the follow-up period.

Systolic and Diastolic Function Abnormalities on Radionuclide Angiography

Systolic and diastolic abnormalities in HC have been characterized by radionuclide angiography. Patients with nonobstructive HC had significantly more fixed defects and decreased ejection fraction.[32,33] In our series patients with ejection fraction lower than 60% tended to have severe complications more likely on Kaplan-Meier analysis.

Prolonged isovolumetric period, time to peak filling rate, reduced relative filling volume during the rapid filling period, and increased atrial contribution have also been reported in patients with HC,[38,39] but the relationship of these parameters to prognostic features has not been extensively evaluated (Table 5). Chikamori et al[20] observed that patients with HC-related deaths had a reduced peak filling rate, but the overall positive predictive value of stepwise discriminant analysis was low. Furthermore, when analysis included established risk factors, the addition of radionuclide measurements did not improve overall predictability. In our study none of the diastolic radionuclide angiography parameters was predictive of death or severe complications.

Some limitations of our study must be considered. There were few younger patients, and our observations should be interpreted with caution, as they apply to an adult study cohort. Because of the low incidence of cardiac death in our population, we were unable to analyze sudden death and death related to heart failure as different endpoints. A longer follow-up period could be used to assess the incidence of several cardiovascular events, such as stroke, that increase in elderly patients. Nowadays, gated SPECT meth-

Table 5. Prognostic value of myocardial perfusion scintigraphy and radionuclide angiography in patients with HC

	N	Age (y)	Technique	Follow-up	Cardiac death	Prognostic variables	Event	Statistical analysis
Myocardial perfusion								
von Dohlen et al[17]	28	47 ± 16	Thallium 201 planar exercise or dipyridamole	No	No	Positive scans	Ventricular tachycardia	$P < .001$ (bivariate)
							Conduction disease	$P < .025$ (bivariate)
Dilsizian et al[18]	23*	6-23	Tl-201 SPECT exercise	3-6 mo	8 (34%)	Ischemia	Sudden death, syncope	$P < .01$ (bivariate)
Yamada et al[19]	216	36 ± 15	Tl-201 SPECT exercise	41 ± 21 mo	12 (5.5%)	Fixed defects	Syncope	$P = .03$ (bivariate and Kaplan-Meier)
Our series	101	54 ± 16	Tc-99m SPECT exercise	5.6 ± 2.7 y	13 (12.8%)	Summed stress score	Cardiac death	$P = .008$ (bivariate)
						Fixed defects	Severe complications	$P = .01$ (Kaplan-Meier)
Radionuclide angiography								
Chikamori et al[20]	161	Mean, 42 (range, 8-78)	Radionuclide angiography	3 ± 1.9 y	13 (8%)	Systolic and diastolic indexes	Cardiac death, electrical unstability	P = NS (bivariate and discriminant)
Our series	101	54 ± 16	Radionuclide angiography	5.6 ± 2.7 y	13 (12.8%)	Ejection fraction <60%	Severe complications	.01 (Kaplan-Meier)

NS, Not significant.
*With previous cardiac arrest, syncope, or family history of sudden cardiac death.

odology can be incorporated into the study of left ventricular perfusion and function in a unique scintigraphic test for patients with HC.

Conclusion

Prognostic information from myocardial perfusion SPECT and radionuclide angiography has limited clinical significance with regard to cardiac death in adult patients with HC. However, the presence of fixed defects and lower ejection fraction in these patients has an adverse prognostic meaning for severe complications.

Acknowledgment

We thank Dr G. Permanyer-Miralda for critical review of the manuscript.

The authors have indicated they have no financial conflicts of interest.

References

1. Chien KR. Genomic circuits and the integrative biology of cardiomyopathies. Eur Heart J 2001;3(Suppl L):3-9.
2. Maron BJ, Bonow RO, Cannon RO, Leon MB, Epstein SE. Hypertrophic cardiomyopathy: interrelation of clinical manifestations, pathophysiology and therapy. N Engl J Med 1987;316: 780-9.
3. Wigle ED, Rakowski H, Kimball BP, Williams WG. Hypertrophic cardiomyopathy: clinical spectrum and treatment. Circulation 1995;92:1680-92.
4. Maron BJ, Casey SA, Poliac LC, Gohman TE, Almquist AK, Aeppli DM. Clinical course of hypertrophic cardiomyopathy in a regional United States cohort. JAMA 1999;281:650-5.
5. Maron JM, Olivotto I, Spirito P, Casey SA, Bellone P, Gohman TE, et al. Epidemiology of hypertrophic cardiomyopathy-related death. Revised in a large non-referral-based patient population. Circulation 2000;102:858-64.
6. McKenna WJ, Deanfield J, Faruqui A, England D, Oakley C, Goodwin J. Prognosis in hypertrophic cardiomyopathy: role of age

and clinical, electrocardiographic and hemodynamic features. Am J Cardiol 1981:47:532-8.
7. Monserrat L, Elliot PM, Gimeno JR, Sharma S, Penas-Lado M, McKenna WJ. Non-sustained ventricular tachycardia in hypertrophic cardiomyopathy: an independent marker of sudden death risk in young patients. J Am Coll Cardiol 2003;42:873-9.
8. Koga Y, Itaya K, Toshima H. Prognosis in hypertrophic cardiomyopathy. Am Heart J 1984;108:351-9.
9. Cecchi F, Olivotto I, Gistri R, et al. Coronary microvascular dysfunction and prognosis in hypertrophic cardiomyopathy. N Engl J Med 2003;349:1027-35.
10. Spirito P, Rapezzi C, Autore C, Bruzzi P, Bellone P, Ortolani P, et al. Prognosis in asymptomatic patients with hypertrophic cardiomyopathy and nonsustained ventricular tachycardia. Circulation 1994;90:2743-7.
11. Sadoul N, Prasad K, Elliott PM, Bannerjee S, Frenneaux MP, McKenna WJ. Prospective prognosis assessment of blood pressure response during exercise in patients with hypertrophic cardiomyopathy. Circulation 1997;96:2987-91.
12. Ikeda H, Maki S, Yoshida N, Murohara T, Adachi H, Koga Y, et al. Predictors of death from congestive heart failure in hypertrophic cardiomyopathy. Am J Cardiol 1999;83:1280-3.
13. Spirito P, Bellone P, Harris KM, Bernabo P, Bruzzi P, Maron BJ. Magnitude of left ventricular hypertrophy and risk of sudden death in hypertrophic cardiomyopathy. N Engl J Med 2000;342:1778-85.
14. Candell Riera J, Romero Farina G, Galve Basilio E, Palet Balart J, Armadans L, Dolores Reina M, et al. Value of Doppler-echocardiography in the prognosis and follow up of hypertrophic myocardiopathy [in Spanish]. Rev Esp Cardiol 2001;54:7-15.
15. Maron BJ, Olivotto I, Bellone P, Conte MR, Cecchi F, Flygenring BP, et al. Clinical profile of stroke in 900 patients with hypertrophic cardiomyopathy. J Am Coll Cardiol 2002;39:301-7.
16. Kofflard MJM, Ten Cate FJ, van der Lee C, van Domburg RT. Hypertrophic cardiomyopathy in a large community-based population: clinical outcome and identification of risk factors for sudden cardiac death and clinical deterioration. J Am Coll Cardiol 2003; 41:987-93.
17. von Dohlen TW, Prisant LM, Frank MJ. Significance of positive or negative thallium-201 scintigraphy in hypertrophic cardiomyopathy. Am J Cardiol 1989;64:498-503.
18. Dilsizian V, Bonow RO, Epstein SE, Fananapazir L. Myocardial ischemia detected by thallium scintigraphy is frequently related to cardiac arrest and syncope in young patients with hypertrophic cardiomyopathy. J Am Coll Cardiol 1993;22:796-804.
19. Yamada M, Elliot PM, Kaski JC, Prasad K, Gane JN, Lowe CM, et al. Dipyridamole stress thallium-201 perfusion abnormalities in patients with hypertrophic cardiomyopathy. Eur Heart J 1998;19:500-7.
20. Chikamori T, Shaughan D, Poloniecki JD, Myers MJ, Lavender JP, McKenna WJ. Prognosis significance of radionuclide-assessed diastolic function in hypertrophic cardiomyopathy. Am J Cardiol 1990;65:478-82.
21. Maron BJ, Gottdiener JS, Epstein SE. Patterns and significance of the distribution of left ventricular hypertrophy in hypertrophic cardiomyopathy: a wide angle, two-dimensional echocardiographic study of 125 patients. Am J Cardiol 1981;48:418-28.
22. Candell-Riera J, Santana-Boado C, Castell-Conesa J, Aguade-Bruix S, Olona M, Palet J, et al. Simultaneous dipyridamole/maximal subjective exercise with ^{99m}Tc-MIBI SPECT: improved diagnostic yield in coronary artery disease. J Am Coll Cardiol 1997;29:531-6.
23. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation 2002;105:539-42.
24. Zaret BL, Battler A, Berger HJ, Bodenheimer MM, Borer JS, Brochier M, et al. Report of the Joint International Society and Federation of Cardiology/World Health Organization Task Force on Nuclear Cardiology. Eur Heart J 1984;5:850-63.
25. Cecchi F, Olivotto I, Montereggi A, Santoro G, Dolara A, Maron BJ. Hypertrophic cardiomyopathy in Tuscany: clinical course and outcome in an unselected regional population. J Am Coll Cardiol 1995;26:1529-36.
26. SPSS: Base 7.5 for Windows. User's guide. Chicago: SPSS Inc; 1997.
27. Cannon RO III, Dilsizian V, O'Gara PT, Udelson JE, Schenke WH, Quyyumi A, et al. Myocardial metabolic, hemodynamic, and electrocardiographic significance of reversible thallium-201 abnormalities in hypertrophic cardiomyopathy. Circulation 1991;83:1660-7.
28. Elliot PM, Rosano GMC, Gill JS, Poole-Wilson PA, Kaski JC, McKenna WJ. Changes in coronary sinus pH during dipyridamole stress in patients with hypertrophic cardiomyopathy and chest pain. Heart 1996;75:179-83.
29. Romero-Farina G, Candell-Riera J, Pereztol-Valdś O, Aguade-Bruix S, Castell-Conesa J, Armadans L, et al. Myocardial SPET in hypertrophic cardiomyopathy [in Spanish]. Rev Esp Cardiol 2000; 53:1589-95.
30. Tanaka M, Fujiwara H, Onodera T, Wu DJ, Hamashima Y, Kawai C. Quantitative analysis of myocardial fibrosis in normals, hypertensive hearts, and hypertrophic cardiomyopathy. Br Heart J 1986;55:575-81.
31. Rubin KA, Morrison J, Padnick MB, Binder AJ, Chiaramida S, Margouleff D, et al. Idiopathic hypertrophic subaortic stenosis: evaluation of anginal symptoms with thallium-201 myocardial imaging. Am J Cardiol 1979;44:1040-5.
32. Pitcher D, Wainwright R, Maisey M, Curry P, Sowton E. Assessment of chest pain in hypertrophic cardiomyopathy using exercise thallium-201 myocardial imaging. Br Heart J 1980;44:650-6.
33. O'Gara PT, Bonow RO, Maron BJ, Damske BA, Van Lingen A, Bacharach SL, et al. Myocardial perfusion abnormalities in patients with hypertrophic cardiomyopathy: assessment with thallium-201 emission computed tomography. Circulation 1987;76:1214-23.
34. Romero-Farina G, Candell-Riera J, Pereztol-Valdés O, Castell J, Aguade S, Galve E, et al. Myocardial perfusion SPECT and isotopic ventriculography in obstructive and non-obstructive hypertrophic myocardiopathy [in Spanish]. Rev Esp Med Nucl 2001;20:530-6.
35. Choudhury L, Mahrholdt H, Wagner A, Choi KM, Elliott MD, Klocke FJ, et al. Myocardial scarring in asymptomatic or mildly symptomatic patients with hypertrophic cardiomyopathy. J Am Coll Cardiol 2002;40:2156-64.
36. Hanrath P, Mathey D, Montz R, Thiel U, Vorbringer H, Kupper W, et al. Myocardial thallium-201 imaging in hypertrophic obstructive cardiomyopathy. Eur Heart J 1981;2:177-85.
37. Udelson JE, Bonow RO, O'Gara PT, Maron BJ, Van Lingen A, Bacharach SL, et al. Verapamil prevents silent myocardial perfusion abnormalities during exercise in asymptomatic patients with hypertrophic cardiomyopathy. Circulation 1989;79:1052-60.
38. Bonow RO, Rosing DR, Bacharach SL, Green MV, Kent KM, Lipson LC, et al. Effects of verapamil on left ventricular systolic function and diastolic filling in patients with hypertrophic cardiomyopathy. Circulation 1981;64:787-96.
39. Betocchi S, Bonow RO, Bacharach SL, Rosing DR, Maron BJ, Green MV. Isovolumic relaxation period in hypertrophic cardiomyopathy: assessment by radionuclide angiography. J Am Coll Cardiol 1986;7:74-81.