

## Hypertrophic Cardiomyopathy

# Myocardial Scarring in Asymptomatic or Mildly Symptomatic Patients With Hypertrophic Cardiomyopathy

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<b>OBJECTIVES</b>	We sought to ascertain whether myocardial scarring occurs in living unselected patients with hypertrophic cardiomyopathy (HCM).
<b>BACKGROUND</b>	Myocardial scarring is known to occur in select HCM patients, who were highly symptomatic prior to death or who died suddenly. The majority of HCM patients, however, are minimally symptomatic and have not suffered sudden death.
<b>METHODS</b>	Cine and gadolinium-enhanced magnetic resonance imaging was performed in 21 HCM patients who were predominantly asymptomatic. Gadolinium hyperenhancement was assumed to represent myocardial scar, and the extent of scar was compared to left ventricular (LV) morphology and function.
<b>RESULTS</b>	Scarring was present in 17 patients (81%). Scarring occurred only in hypertrophied regions ( $\geq 10$ mm), was patchy with multiple foci, and predominantly involved the middle third of the ventricular wall. All 17 patients had scarring at the junction of the interventricular septum and the right ventricular (RV) free wall. On a regional basis, the extent of scarring correlated positively with wall thickness ( $r = 0.36$ , $p < 0.0001$ ), and inversely with wall thickening ( $r = -0.21$ , $p < 0.0001$ ). On a per patient basis, the extent of scarring (mean, $8 \pm 9\%$ of LV mass) was minimally related to maximum wall thickness ( $r = 0.40$ , $p = 0.07$ ) and LV mass ( $r = 0.33$ , $p = 0.15$ ), and correlated inversely with ejection fraction ( $r = -0.46$ , $p = 0.04$ ).
<b>CONCLUSIONS</b>	Myocardial scarring is common in asymptomatic or mildly symptomatic HCM patients who have not suffered sudden death. When present, scarring occurs in hypertrophied regions, is consistently localized to the junctions of the septum and RV free wall, and correlates positively with regional hypertrophy and inversely with regional contraction. (J Am Coll Cardiol 2002;40:2156-64) © 2002 by the American College of Cardiology Foundation

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It has recently been established that ventricular tachycardia or fibrillation is the principal mechanism of sudden death in patients with hypertrophic cardiomyopathy (HCM) (1). An important anatomic component of the arrhythmogenic substrate has been postulated to be myocardial replacement scarring (2,3). Several necropsy studies have demonstrated that myocardial scarring is common in patients with HCM, even in the absence of angiographically significant epicardial coronary disease (3-7). This finding, however, may not be applicable to the overall population with HCM since the patients assessed in these studies were generally highly selected with severe symptoms of heart failure prior to death, a group not representative of the majority of patients with HCM. It is now recognized that most individuals with HCM are asymptomatic or mildly symptomatic and have a predominantly benign clinical course (8-12). Notwith-

standing this overall favorable prognostic profile, a small subset of patients experience sudden death as the first manifestation of HCM (3,9,12,13). Limited data from post-mortem studies that have included subgroups of patients with HCM who were asymptomatic prior to death, suggest that scarring is common in these patients as well (3,13). It is unknown whether myocardial scarring occurs in unselected patients with HCM who have not experienced sudden death.

Gadolinium contrast-enhanced magnetic resonance imaging (MRI) is a new technique that allows visualization of both transmural and subendocardial myocardial scarring (14). This technique has been validated in patients with documented chronic myocardial infarction, as well as in animal models of infarct healing (14-16). Contrast MRI has the unique advantage of allowing visualization of even microinfarcts that cannot be detected by other noninvasive imaging techniques (17).

The aim of the present study was to determine whether myocardial scarring is present in HCM patients with mild or no symptoms who are representative of the majority of community patients with this disease.

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#### Abbreviations and Acronyms

CAD	= coronary artery disease
HCM	= hypertrophic cardiomyopathy
LV	= left ventricular
LVOT	= left ventricular outflow tract
MRI	= magnetic resonance imaging
RV	= right ventricular
SAM	= systolic anterior motion of the mitral valve

## METHODS

**Patient population.** Twenty-one patients with HCM were recruited between July 2000 and February 2001. All gave informed consent to the protocol, which was approved by the Northwestern Institutional Review Board. HCM was diagnosed by the presence of a nondilated and hypertrophied left ventricle on two-dimensional echocardiography (maximal wall thickness  $\geq 15$  mm in adult index patients or  $\geq 13$  mm in adult relatives of a HCM patient) in the absence of another disease that could account for the hypertrophy (9,18). Patients who were known to have aortic stenosis, amyloidosis, or systemic hypertension were not included. The median time between echocardiography and MRI was six months (longest interval, three years). Sixty-one consecutive patients were initially identified for enrollment, but patients were excluded if they had concomitant coronary artery disease (CAD) or history of myocardial infarction (n = 1), left ventricular (LV) systolic dysfunction (n = 1), implantation of a pacemaker or defibrillator (n = 23), refused to participate (n = 6), or were lost to follow-up (n = 9).

Of the 21 study patients, 4 were  $\geq 50$  years old. CAD was excluded by angiographically normal coronary arteries in 3 of these 4. The remaining patient did not have angina or other symptoms indicative of CAD. Of the 17 patients  $< 50$  years, none had CAD risk factors except 2 in whom CAD was excluded by angiography in 1 and stress nuclear imaging in the other.

**MRI protocol.** All images were acquired on a 1.5T scanner (Siemens Sonata) using a phased array receiver coil during breath-holds ( $\sim 8$  s) gated to the electrocardiogram. Cine images were acquired in multiple short-axis and 2 to 3 long-axis views using TrueFISP (19). Short-axis views were obtained every centimeter throughout the entire left ventricle (20). A gadolinium-based contrast agent (gadoteridol, 0.1 mmol/kg) (17) was then administered intravenously, and contrast-enhanced images were acquired in the same views used for cine MRI 10 min after contrast administration. Contrast-enhanced images were acquired using a segmented inversion-recovery sequence, which has been described previously (21). The examination time was 30 to 40 min.

**Analysis.** For all patients, the MRI scans were placed in random order after the identity markers were removed. The cine and contrast-enhanced images were evaluated separately by the consensus of two observers who were unaware

of the results of the other modality. Hyperenhanced tissue on the contrast-enhanced images was assumed to represent scarred myocardium (14).

**Global parameters.** The endocardial and epicardial borders of the myocardium were planimetered on the short-axis cine images. Volumes were derived by summation of discs and the ejection fraction calculated accordingly. The LV mass was calculated by subtracting endocardial from epicardial volume at end-diastole and multiplying by  $1.05 \text{ g/cm}^3$ . Systolic anterior motion of the mitral valve (SAM) was assessed visually using the long-axis cine images through the left ventricular outflow tract (LVOT) and graded as *mild* (approached septum without contact), *moderate* (brief septal contact), or *severe* (septal contact,  $> 30\%$  of systole) (22). The extent of hyperenhanced myocardium was planimetered on the short-axis contrast-enhanced images (Fig. 1) using an image intensity level  $> 2$  SD above the mean of remote myocardium to define hyperenhancement and threshold the image by computer (15).

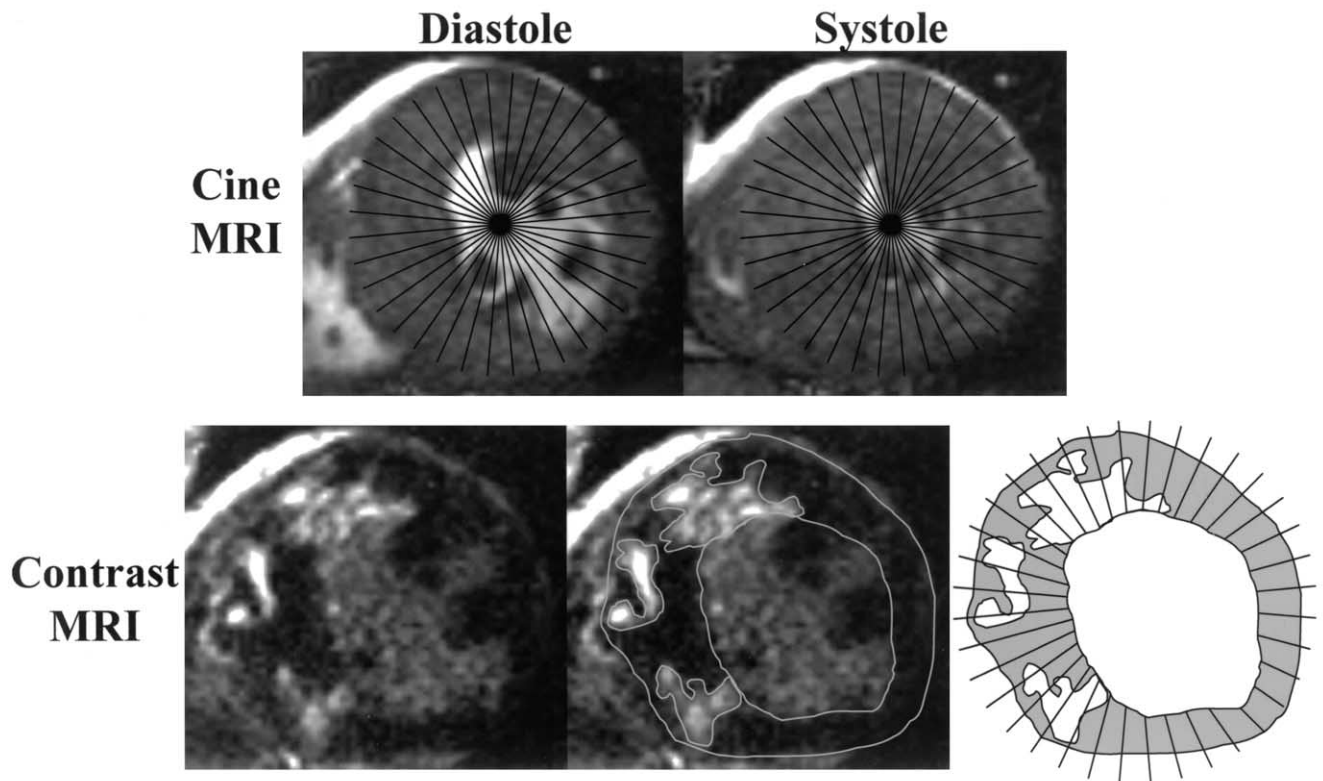
**Segmental model.** Regional parameters were assessed using a model in which each short-axis view (6 to 10 per patient) was divided into 36 circumferential segments (Fig. 1). For each segment on the cine images, LV end-diastolic wall thickness and systolic wall thickening were measured using the NIH Image program. For each segment on the contrast-enhanced images, the extent of scar was expressed as a percentage of the total segment area as well as a percentage of the area of the outer, middle, and inner third of the segment.

**Clinical indexes.** In all patients the peak instantaneous LVOT gradient (mm Hg) was measured by continuous-wave Doppler under basal conditions from the diagnostic echocardiogram. The QT interval was measured from the 12-lead electrocardiogram nearest in time to the MRI examination (median time difference, one month) and then corrected using Bazett's formula (23).

**Statistical analysis.** Continuous data are expressed as mean  $\pm$  SD except where specified. The relationships between continuous variables were examined by least-squares linear regression analysis. To account for the non-independence of the segmental data, a repeated-measures variable for the patient was added to the linear regression analysis using a mixed-effects model (S-PLUS 2000 software) (24). Comparisons in the extent of scar between segmental thickness and thickening subgroups were made using one-way ANOVA; the Tukey method was used for assessing pair-wise differences between the subgroups. All statistical tests were two-tailed;  $p < 0.05$  was regarded as statistically significant.

## RESULTS

**Patient characteristics.** The clinical features are summarized in Table 1. The age ranged from 18 to 76 years (median, 39 years). There were 12 men and 9 women. Of the 21 patients, 20 (95%) were asymptomatic or had only



**Figure 1.** Typical images obtained by magnetic resonance imaging (MRI) with superimposed segmental model. Segments were analyzed for diastolic wall thickness, systolic wall thickening, and the spatial extent of scar represented by hyperenhanced myocardium (outlined regions).

mild symptoms (New York Heart Association class I or II) at the time of enrollment. In the majority of patients (62%), the primary reason for the initial echocardiogram was family screening or the finding of an asymptomatic murmur on routine physical examination. Of the remaining patients, two underwent evaluation for chest pain, two for syncope, and four for exertional dyspnea. No patient had a family history of sudden cardiac death as defined previously (18). The pattern of LV hypertrophy by echocardiography was asymmetric septal hypertrophy (thickness of septum/free wall  $\geq 1.3$ ) (25) in 18 patients (86%), concentric in two and apical in one. Two patients had maximum wall thickness  $< 13$  mm by MRI. Both patients had maximum wall thickness  $> 13$  mm on their respective diagnostic echocardiograms (i.e., both met the entrance criteria in the Methods section). Resting LVOT obstruction (peak instantaneous gradient  $> 30$  mm Hg) was present in eight patients (38%). Of the 18 patients who had Holter monitoring, 4 had evidence of episodic ST segment depression (all asymptomatic), and none had evidence of supraventricular or ventricular tachycardia ( $\geq 3$  consecutive beats).

**MRI.** Figures 1 and 2 show typical examples of images obtained by MRI. For the full-motion cines video corresponding to Figure 2, please see the December 18th issue of *JACC* online at [www.cardiosource.com/jacc.html](http://www.cardiosource.com/jacc.html). The LV ejection fraction averaged  $70 \pm 11\%$  (range, 40% to 85%), the LV mass ranged from 95 to 427 g (mean,  $238 \pm 88$  g), and the maximal end-diastolic wall thick-

ness ranged from 11 to 37 mm (mean,  $25 \pm 8$  mm). Twelve patients exhibited SAM (Fig. 2 full-motion cine for Patient 19). The contrast images demonstrated myocardial hyperenhancement representing scar tissue in 17 of the 21 patients (81%). In general, scarring occurred in a patchy distribution with multiple discrete foci within hypertrophied regions of the interventricular septum and the anterior and posterior walls (Figs. 1 and 2). Scarring was not present in the lateral free wall. Of the 17 patients with scars, 16 (94%) had two or more foci of scarring. The mass of scar tissue ranged from 0 to 143 g (mean,  $22 \pm 31$  g), and was on average  $8 \pm 9\%$  of the LV mass.

**Regional scarring, wall thickness, and wall thickening.** In a total of 4,912 matched segments (no unmatched segments), the extent of scar tissue was compared to wall thickness at end-diastole. Scarring was present in 839 segments (17%). The average end-diastolic wall thickness was  $13.4 \pm 6.1$  mm (maximum, 37 mm). There was a modest but significant correlation between the extent of scarring and the end-diastolic wall thickness ( $r = 0.36$ ,  $p < 0.0001$ ). This relationship remained significant ( $p < 0.005$ ) when the data were reanalyzed with a separate parameter for "patient" to account for the nonindependence of segments. When the segments were divided into subgroups according to end-diastolic wall thickness (18,26), the mean scar extent increased significantly and progressively in direct relation to wall thickness ( $p < 0.05$  for every pair-wise comparison

**Table 1.** Clinical Characteristics

Patient	Age	Gender	NYHA	Symptoms	Pattern of Hypertrophy*	LVOT Gradient†	QTc (ms)	Holter	MRI Data		
									SAM	MWT (mm)	HE (%LV)
1	28	F	I	none	ASH	<25	412	STD	none	20	21
2	54	M	I	none	concentric	49	444	normal	mild	27	12
3	19	M	I	none	ASH	<25	462	normal	none	36	33
4	39	F	I	none	ASH	30	480	normal	none	26	22
5	76	F	II	D	ASH	36	505	STD	moderate	21	10
6	44	M	I	none	ASH	58	400	STD	moderate	33	4
7	47	M	I	none	ASH	<25	404	–	none	12	none
8	64	F	II	D	ASH	<25	413	normal	none	22	11
9	18	M	I	none	ASH	<25	413	normal	none	11	none
10	47	F	III	CP,D	ASH	<25	490	–	none	23	9
11	28	F	I	syncope	ASH	<25	445	–	mild	29	6
12	39	F	I	none	ASH	49	400	normal	moderate	27	6
13	72	M	II	D	ASH	41	408	normal	moderate	23	2
14	41	M	I	CP	Apical	<25	409	normal	none	18	none
15	38	F	I	none	ASH	36	440	normal	moderate	19	4
16	35	F	I	none	ASH	<25	380	normal	none	13	none
17	34	M	I	none	ASH	36	400	STD	mild	37	3
18	48	M	II	D	ASH	29	520	normal	mild	26	11
19	41	M	I	none	concentric	<25	447	normal	mild	27	8
20	22	M	I	none	ASH	48	429	normal	moderate	33	10
21	39	M	II	syncope,D	ASH	<25	416	normal	mild	32	4

\*From echocardiogram; †Peak instantaneous gradient (mm Hg) by continuous-wave doppler echocardiography under basal conditions.

ASH = asymmetric septal hypertrophy (thickness of septum/free wall  $\geq 1.3$ ); CP = chest pain; D = dyspnea; HE = hyperenhancement; LVOT = left ventricular outflow tract; MRI = magnetic resonance imaging; MWT = maximum wall thickness; NYHA = New York Heart Association functional class; %LV = percent left ventricular mass; QTc = corrected QT interval on 12-lead electrocardiogram; SAM = systolic anterior motion of mitral valve (see text for grading system); STD = ST-segment depression.

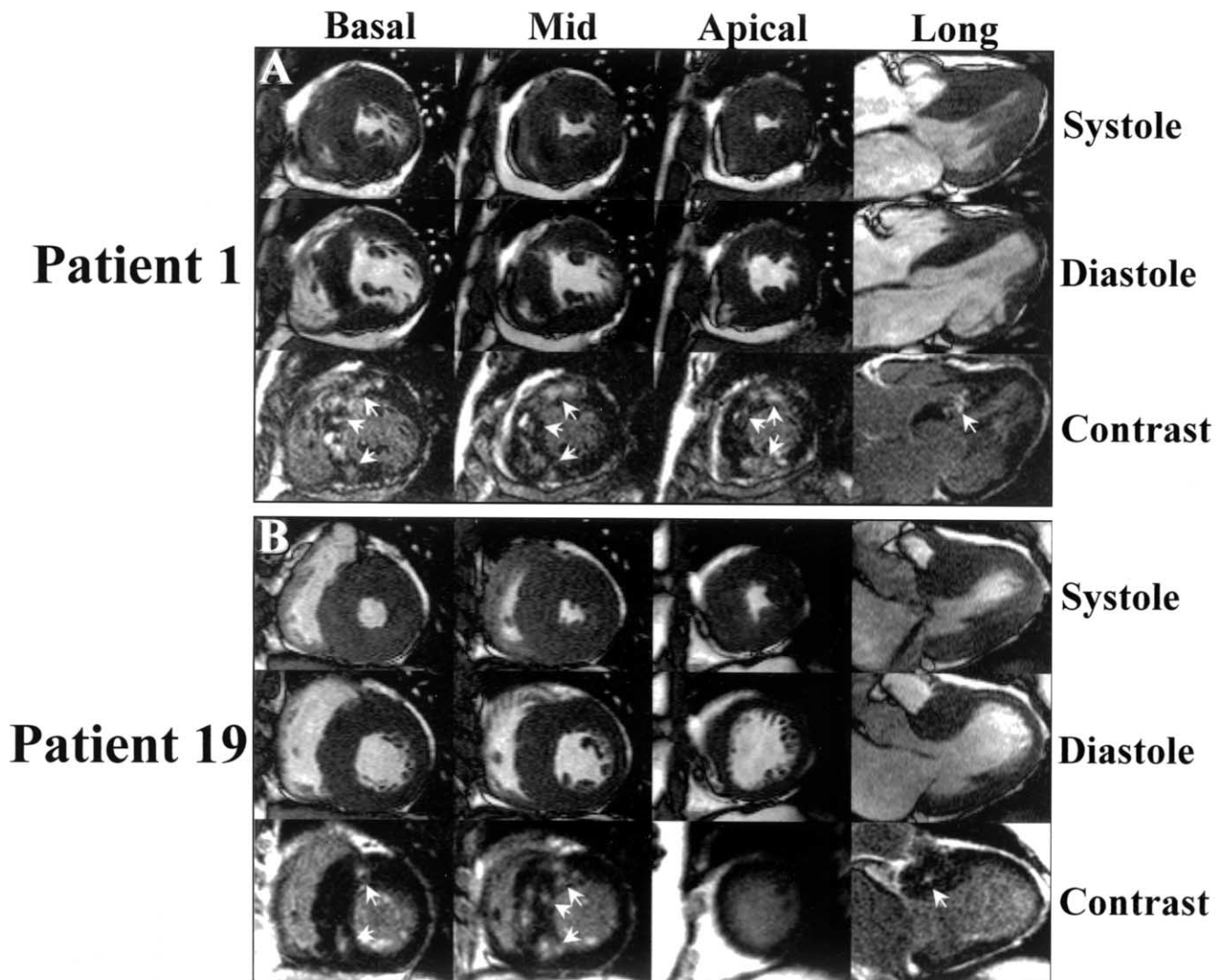
using the Tukey method, Fig. 3). None of the 1,638 segments <10 mm in thickness had any scarring.

The extent of scar tissue and the end-diastolic wall thickness were also compared to systolic wall thickening in 3,578 matched segments (fewer segments due to base-apex shortening). The average systolic thickening was  $77 \pm 63\%$  of the end-diastolic thickness. Both the extent of scar tissue and the end-diastolic thickness showed a negative correlation with systolic thickening ( $r = -0.21$ ,  $p < 0.0001$ , and  $r = -0.55$ ,  $p < 0.0001$ , respectively). These relationships remained significant ( $p < 0.05$  and  $p < 0.0001$ , respectively) when the data were reanalyzed to account for the nonindependence of segments. There was a progressive decrease in mean scar extent with each increment in systolic thickening ( $p < 0.05$  for every pair-wise comparison using the Tukey method, Fig. 3). When absolute rather than fractional thickening was considered, there was still a significant negative correlation with the extent of scar tissue and the end-diastolic thickness ( $r = -0.16$ ,  $p < 0.0001$  and  $r = -0.20$ ,  $p < 0.0001$ , respectively;  $p < 0.05$  and  $p < 0.0001$ , respectively, accounting for nonindependence of segments). The results were similar when the analysis was repeated using a 12-segment rather than a 36-segment model for the short-axis slices ( $r = -0.17$ ,  $p < 0.0001$ , and  $r = -0.18$ ,  $p < 0.0001$ , respectively;  $p = 0.07$  and  $p < 0.001$ , respectively, accounting for nonindependence of segments).

The mean values for end-diastolic wall thickness, wall thickening, and scar extent (hyperenhancement) are repre-

sented as grey-scale maps in Figure 4. These maps represent the averaged segmental data for all patients. For the map of scar tissue, segments were further divided into outer, middle, and inner thirds. Figure 4 demonstrates that the lateral free wall and the ventricular apex were least likely to be hypertrophied. These regions had the greatest amount of systolic thickening and the least amount of scar tissue. Hypertrophied regions did not have a uniform transmural distribution of scarring; the mid-myocardium had the greatest amount of scarring which consistently involved the junctions of the interventricular septum and the RV free wall. All 17 patients with scars had scarring of either the anteroseptal junction or the inferoseptal junction and 16 had scarring of both junctions.

**Extent of scarring related to global parameters.** Figure 5 demonstrates that the extent of scar (hyperenhancement) as a percentage of the left ventricle correlated poorly with the maximum LV end-diastolic wall thickness ( $r = 0.40$ ,  $p = 0.07$ ) and the LV mass ( $r = 0.33$ ,  $p = 0.15$ ), and modestly with the LV ejection fraction ( $r = -0.46$ ,  $p = 0.04$ ). When the patient with the depressed EF on MRI (Patient #18) was removed from the analysis the relationships did not change significantly (wall thickness:  $r = 0.40$ ,  $p = 0.08$ ; mass:  $r = 0.34$ ,  $p = 0.15$ ; EF:  $r = 0.55$ ,  $p = 0.01$ ). There was a positive correlation with the corrected QT-interval ( $r = 0.47$ ,  $p = 0.03$ ). No relation was observed to the LVOT gradient ( $p = 0.82$ ) or to the degree of SAM ( $p = 0.29$ ).



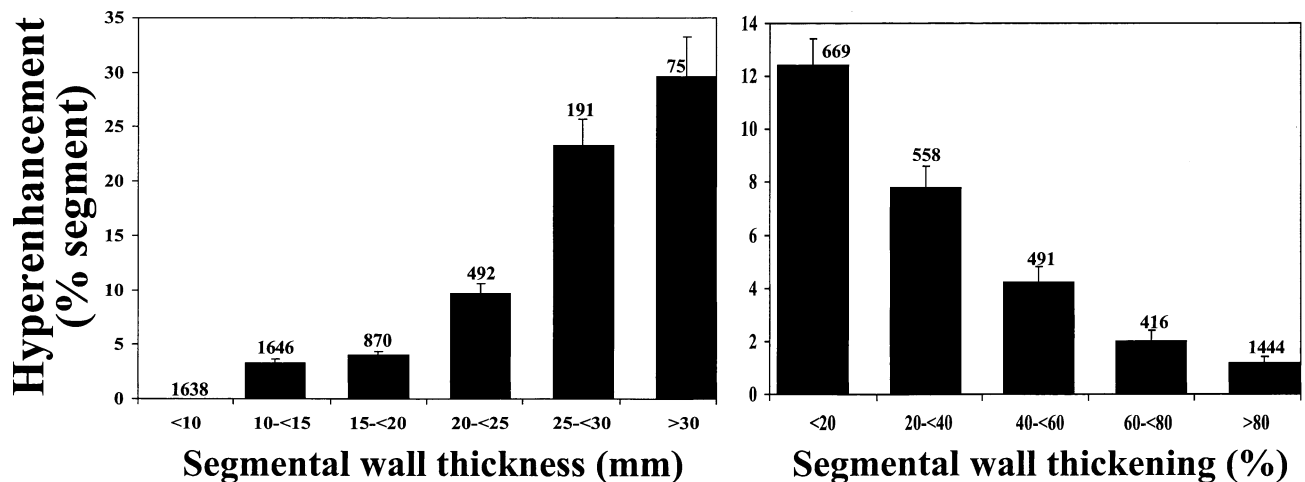
**Figure 2.** Representative patient images. (A) Patient with asymmetric septal hypertrophy, maximum wall thickness of 20 mm, normal ejection fraction, and marked myocardial scarring (hyperenhancement shown by **arrows**). (B) Patient with greater hypertrophy (maximum wall thickness, 27 mm) but with less scarring. In both patients, there are multiple foci of scar, which are predominantly mid-myocardial in location and are not present in the lateral free wall. The long-axis cines images of Patient 19 demonstrate systolic anterior motion of the mitral valve, systolic flow turbulence in the left ventricular outflow tract, and mitral regurgitation. For the accompanying full-motion cines video corresponding to Figure 2, please see the December 18 issue of *JACC* at [www.cardiosource.com/jacc.html](http://www.cardiosource.com/jacc.html).

## DISCUSSION

**Myocardial scarring in HCM.** In the present study, we observed that myocardial scarring is a common finding in patients with HCM. Prior studies have also documented scarring in vivo, but these were invasive, requiring tissue samples from myocardial biopsy or surgical myomectomy in patients with refractory symptoms (27,28). The remainder of the studies that have documented scarring were necropsy studies (3-7,29,30) or studies of explanted hearts (31). In comparison to previous studies reporting myocardial scarring, the patients in the present study are a unique population, in so far as they are predominantly asymptomatic, belong to an unselected community cohort and have not experienced sudden death. These patients are likely to be representative of the majority of patients with HCM.

We observed a peculiar pattern of myocardial scarring. The scarring occurred only in hypertrophied regions, was patchy with multiple foci, and predominantly involved the mid-ventricular wall (Figs. 2 and 4). The location of scarring did not correspond to the perfusion territories of the epicardial coronary arteries. Maron and coworkers (4) in a necropsy study, also noted that scarring did not correspond to any particular epicardial coronary artery distribution. In a follow up study (5), they reported increased numbers of structurally abnormal *intramural* coronary arteries within areas of scarred myocardium. They postulated a causal role for these intramural arteries in producing myocardial ischemia leading to scarring.

In our study, the pattern of scarring was also characterized by consistent involvement of the junctions of the



**Figure 3.** Relationship between amount of scarring (% hyperenhancement of segment) and segmental wall thickness and thickening. The amount of scarring increases progressively in direct relation to wall thickness and in inverse relation to wall thickening ( $p < 0.05$  for every pairwise comparison between increments in both thickness and thickening). **Error bars** represent standard error of the mean. The number of segments for each category are listed.

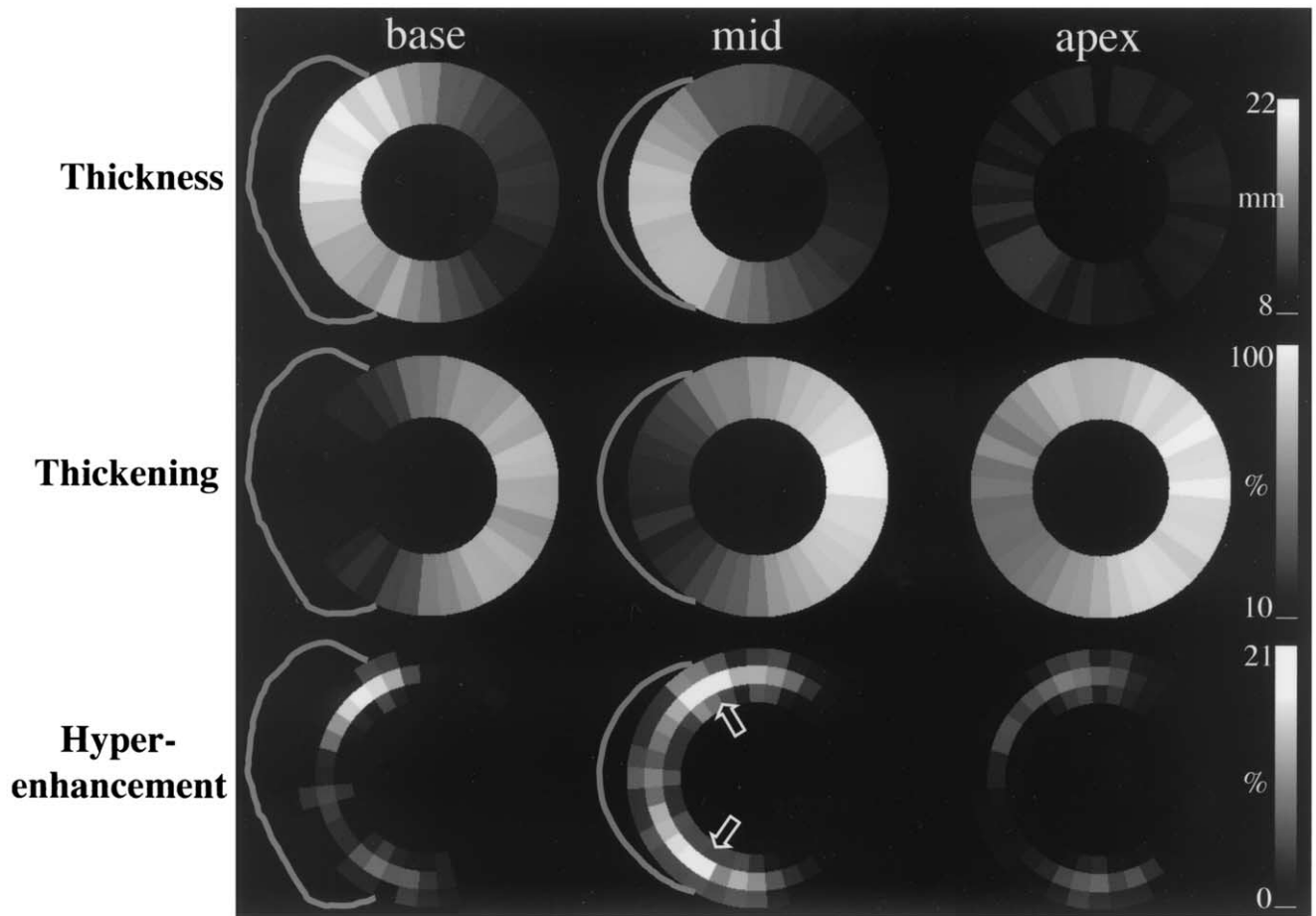
interventricular septum and the right ventricular free wall. All 17 patients with scars had scarring of either the anteroseptal junction or the inferoseptal junction, and 16 had scarring of both junctions. Although systematically examined in only one report (29), the presence of scarring in these particular junctional locations have been demonstrated incidentally in several necropsy studies (3,6,7). Kuribayashi and Roberts (29) demonstrated in a necropsy study of HCM that the junctions of the septum and RV free wall are also where myocardial fascicular disarray is maximal, associated with numerous deep tissue clefts, and destruction of the normal circular architecture of the midwall muscle layer. The current study demonstrates in living patients with HCM, a pattern of myocardial scarring that has been observed previously only in HCM patients after death.

**Correlates of scarring.** The only morphologic feature of HCM found to be predictive of future sudden death is the magnitude of LV hypertrophy (18,32). Recently Basso *et al.* (3) reported a positive correlation between the magnitude of septal hypertrophy and the extent of replacement scarring in young patients with HCM experiencing sudden death. They concluded that the presence of scarring supports the clinical evidence (33) that ischemia occurs in the natural history of HCM and may contribute to life-threatening electrical instability. Consistent with the findings of Basso *et al.* (3) the current study found that the extent of scar increased significantly and progressively in direct relation to wall thickness on a regional basis (Fig. 3). On a per patient basis, however, the extent of scarring was only minimally related to the maximum LV wall thickness (Fig. 5). Although it is possible that this relation may have reached statistical significance with a larger study population, it is clear from the current data that there is not a one-to-one relationship between scar extent and wall thickness. First, there is the predilection of scarring for the junctions of the septum and RV free wall. These regions, while hypertrophied, did not represent the location of maximum wall

thickness (Fig. 4). Second, there is a large variation in the amount of scarring in hypertrophied regions on both a regional and per patient basis. For example, among the five patients with maximum wall thickness  $>$ 30 mm, the amount of scar ranged from 3% to 33% of the total LV mass. Likewise, Figure 2 demonstrates a patient with a large amount of scarring and relatively less hypertrophy (Fig. 2A) in comparison to another patient with less scarring yet greater hypertrophy (Fig. 2B). Despite these observations, there is nonetheless an association between scar and wall thickness. None of the 1,638 segments that were less than 10 mm in thickness had any scarring, and the four patients who did not have any scarring, were those with the least maximum wall thickness of the entire cohort (Fig. 5).

In the current study, regional systolic dysfunction was observed (Fig. 4) despite overall normal to supranormal LV ejection fraction in the patient cohort. This finding is consistent with the results of several studies in patients with HCM (34–37). Potential mechanisms for regional systolic dysfunction in HCM that have been postulated include primary defects of the sarcomeric proteins leading to impaired myocyte contractility, increased interstitial fibrosis leading to impaired myocardial shortening, and disorganized arrangement of the myocytes leading to inefficient, nonuniform contraction (36,38). Our results indicate an additional possible mechanism. We found that the mean extent of scar increased significantly and progressively as wall thickening decreased (Fig. 3). This was observed for all regions of the left ventricle (Fig. 4). Accordingly, a causal role for myocardial scarring in producing regional dysfunction should be considered.

**Study limitations.** The use of gadolinium enhanced MRI to detect myocardial scarring has been validated in animal models of ischemic injury and in patients with coronary artery disease (14–16). However, the direct comparison of gadolinium MRI to the underlying histopathology has not yet been performed in the case of hypertrophic cardio-



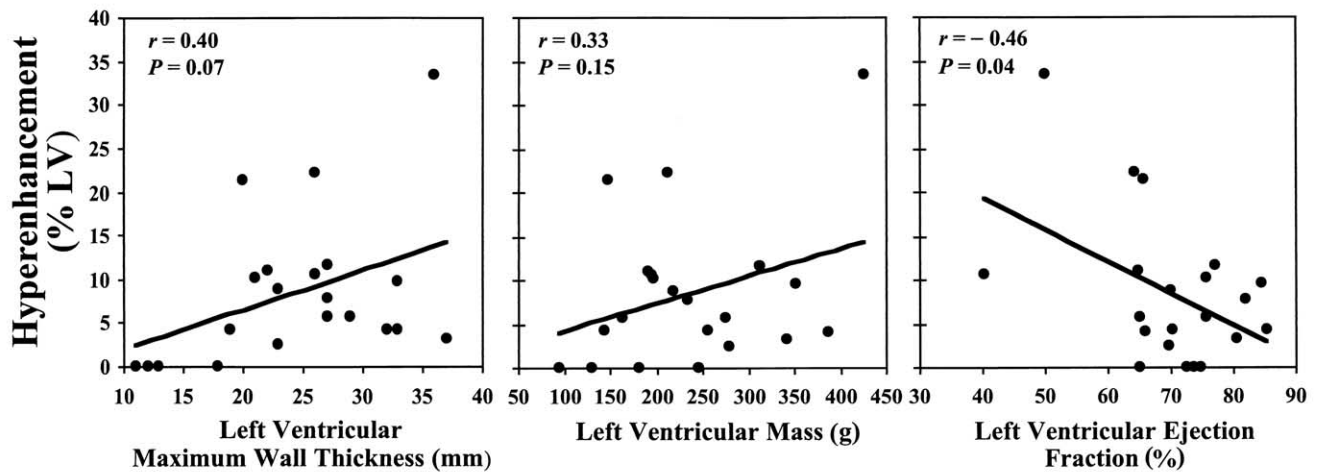
**Figure 4.** Spatial distribution of the mean values for segmental wall thickness, wall thickening and scar extent (hyperenhancement) represented as grey-scale maps in basal, mid, and apical short-axis slices in all patients. Note that the thicker walls (basal and mid septum) have the least thickening. Scarring predominantly involves the mid-wall myocardium at the junctions of the interventricular septum and the right ventricular free wall (**arrows**).

myopathy. The interpretation, therefore, that gadolinium hyperenhancement solely represents myocardial scarring is speculative. Other types of fibrosis such as interstitial fibrosis may also lead to an increased distribution volume of gadolinium within the myocardium and thus also produce hyperenhancement. Furthermore, the presence of hyperenhancement, even if scarring is verified, should not be equated with the process of ischemic myocardial necrosis as scarring may be due to a variety of mechanisms other than ischemia.

**Clinical implications.** Data from recent epidemiological studies indicate that the overall risk of sudden death in our patient population is likely to be  $\leq 1\%$  per year (8-12). Since scarring was present in over 80% of our patients, the presence of scarring in itself cannot be indicative of an adverse prognosis. However, the total amount of scarring may be a prognostic determinant. Tanaka *et al.* (39) quantified the amount of myocardial scarring in a necropsy study of 10 patients with HCM. Although the sample size was small, they found that all seven patients who died

suddenly had a larger amount of scarring ( $13 \pm 3\%$  of total area) than the three who died from noncardiac causes ( $6 \pm 3\%$ ,  $p < 0.05$ ). Additional evidence that suggests a relation between the amount of scarring and future adverse events is our finding of a positive correlation between the amount of scarring and the magnitude of hypertrophy, since it has been demonstrated that the magnitude of hypertrophy is related to the risk of sudden death (18,32). The mechanism by which LV hypertrophy relates to higher risk for malignant ventricular arrhythmias and sudden death is unknown. The results of the current study, however, raise the possibility that myocardial scarring is a potential link between LV hypertrophy and the occurrence of sudden death.

Using similar criteria as the study by Tanaka *et al.* (39), three of the patients in the present study would be deemed to be at higher risk ( $>15\%$  scar). However, extreme hypertrophy ( $\geq 30$  mm), which has been shown to be an important risk factor for sudden death (18), was present in only one of these three patients (Patient 3). Patients 1 and 4, who had significant scarring without extreme hypertrophy, high-



**Figure 5.** Relationship between total amount of myocardial scar (hyperenhancement) and the maximum left ventricular (LV) wall thickness, LV mass, and LV ejection fraction.

lights the important finding of Elliott et al. (26) who recently reported that most sudden deaths in HCM occur in patients with wall thickness <30 mm, and concluded that the presence of mild hypertrophy cannot be used to reassure patients that they are at low risk. Whether extreme myocardial scarring is an independent predictor of adverse prognosis or adds incremental prognostic information to the magnitude of LV hypertrophy remains to be determined.

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