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Differences in Myocardial Velocity Gradient Measured Throughout the Cardiac Cycle in Patients With Hypertrophic Cardiomyopathy, Athletes and Patients With Left Ventricular Hypertrophy Due to Hypertension

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Objectives. **We sought to compare the myocardial velocity gradient (MVG) measured across the left ventricular (LV) posterior wall during the cardiac cycle between patients with hypertrophic cardiomyopathy (HCM), athletes and patients with LV hypertrophy due to systemic hypertension and to determine whether it might be used to discriminate these groups.**

Background. **The MVG is a new ultrasound variable, based on the color Doppler technique, that quantifies the spatial distribution of transmyocardial velocities.**

Methods. **A cohort of 158 subjects was subdivided by age into two groups: Group I (mean [±SD] 30 ± 7 years) and Group II (58 ± 8 years). Within each group there were three categories of subjects: Group Ia consisted of patients with HCM (n = 25), Group Ib consisted of athletes (n = 21), and Group Ic consisted of normal subjects; Group IIa consisted of patients with HCM (n = 19), Group IIb consisted of hypertensive patients (n = 27), and Group IIc consisted of normal subjects (n = 33).**

Results. **The MVG (mean [±SD] s^{-1}) measured in systole was lower ($p < 0.01$) in patients with HCM (Group Ia 3.2 ± 1.1; Group IIa 2.9 ± 1.2) compared with athletes (Group Ib 4.6 ± 1.1), hypertensive patients (Group IIb 4.2 ± 1.8) and normal subjects (Group Ic 4.4 ± 0.8; Group IIc 4.8 ± 0.8). In early diastole, the MVG was lower ($p < 0.05$) in patients with HCM (Group Ia 3.7 ± 1.5; Group IIa 2.6 ± 0.9) than in athletes (Group Ib 9.9 ± 1.9) and normal subjects (Group Ic 9.2 ± 2.0; Group IIc 3.6 ± 1.5), but not hypertensive patients (Group IIb 3.3 ± 1.3). In late diastole, the MVG in patients with HCM (Group Ia 1.3 ± 0.8; Group IIa 1.4 ± 0.8) was lower ($p < 0.01$) than that in hypertensive patients (Group IIb 4.3 ± 1.7) and normal subjects (Group IIc 3.8 ± 0.9). An MVG ≤ 7 s^{-1}, as a single diagnostic approach, differentiated accurately (0.96 positive and 0.94 negative predictive value) between patients with HCM and athletes when the measurements were taken during early diastole.**

Conclusions. **In both age groups, the MVG was lower in both systole and diastole in patients with HCM than in athletes, hypertensive patients or normal subjects. The MVG measured in early diastole in a group of subjects 18 to 45 years old would appear to be an accurate variable used to discriminate between HCM and hypertrophy in athletes.**

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At present, standard M-mode and two-dimensional echocardiography are the most common techniques used to determine left ventricular (LV) hypertrophy (1–4). However, using these techniques alone, the precise cause of hypertrophy is sometimes difficult or impossible to determine (5,6). The diagnosis of hypertrophic cardiomyopathy (HCM) is currently based on combined information obtained from clinical history, ultrasound imaging and genetic investigations (6–9). Two ultrasound variables were reported to be particularly useful in diagnosing HCM: systolic anterior motion of the mitral valve (10,11) and asymmetric septal hypertrophy (1,2). However, other studies have shown that both these abnormalities also occur in other heart conditions (12). The analysis of ultrasound radiofrequency data was also used in an attempt to distinguish between HCM and secondary LV hypertrophy (13,14). Despite the diagnostic potential of the current ultrasound techniques, cases of ambiguous myocardial hypertrophy still exist (6). Therefore, an accurate clinical test that would further define patients of this group would be of great value.

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Abbreviations and Acronyms

DMI = Doppler myocardial imaging
ECG = electrocardiogram
HCM = hypertrophic cardiomyopathy
LV = left ventricle, left ventricular
MVG = myocardial velocity gradient

A new ultrasound technique, Doppler myocardial imaging (DMI), allows the quantification of intramural transmyocardial velocities by detecting consecutive phase-shifts of the ultrasound signal returning from the contracting myocardium (15–18). Based on the spatial distribution of these transmyocardial velocities, the myocardial velocity gradient (MVG) is measured, the new index of LV function (19–21). The aim of this study was to assess MVG in patients with HCM, highly competitive athletes and patients with LV hypertrophy due to systemic hypertension in order to determine whether this variable might be used to define these groups.

Methods

Subjects. Before the study, informed consent was obtained from all subjects. A cohort of 158 subjects was enrolled into the study: 44 patients with HCM, 21 highly competitive athletes, 27 patients with secondary LV hypertrophy due to systemic hypertension and 66 normal, sedentary subjects as a control group.

The inclusion criteria were HCM (small size or irregular shape of LV cavity, or both); unexplained focal or asymmetric LV hypertrophy (myocardial thickness ≥1.3 cm) on the transthoracic echocardiogram; abnormal results on the electrocardiogram (ECG); and a positive family history (6,7,22,23). For the purpose of the study, only asymptomatic or mildly symptomatic patients between 18 and 70 years old with diagnosed HCM were included in the study. Patients with HCM with moderate to severe symptoms (e.g., syncope or dyspnea, or both, with at least New York Heart Association functional class II symptoms) were excluded from the study. Also, patients with HCM with severe myocardial hypertrophy (myocardial thickness ≥2.0 cm), markedly increased mean LV outflow tract gradient ≥30 mm Hg or prolonged mitral-septal contact during systole (i.e., for >30% of systole), or a combination of these, or those with suspected HCM but with relatively dilated LV and/or decreased ejection fraction, were excluded (7,12). Finally, 44 patients with HCM (36 asymptomatic, 8 mildly symptomatic) met the inclusion criteria and were enrolled into the study. A positive family history or an abnormal ECG, or both, were present in 32 patients; LV outflow tract gradient ≥10 mm Hg was present in 10 patients; and systolic motion of the anterior mitral valve leaflet was present in 13 patients. All patients were free of medication during the examination, and in six patients treatment that included beta-blockers or calcium channel blockers was stopped 48 h before the study. All patients with HCM were normotensive. 2) Highly competitive athletes (age 18 to 45 years): cyclists, rowers, middle- and long-distance runners (24) who had trained for at least 16 h/week for the last 5 years. Twenty-one athletes were included in the study; all had at least mild LV posterior wall or interventricular septum hypertrophy (≥1.3 cm), or both. 3) Patients with systemic hypertension (age 46 to 70 years): rest diastolic blood pressure ≥100 mm Hg before treatment and presence of ECG and echocardiographic evidence of secondary LV hypertrophy (LV posterior wall or interventricular septum thickness ≥1.3 cm, or both). Medication was stopped 24 h before examination in all hypertensive patients.

No study patient had clinical evidence of coronary artery disease, valvular diseases or left or right ventricular heart failure. All subjects studied were in sinus rhythm and patients with left bundle branch block on the ECG were excluded. In our previous study (21), we showed that MVG is age related, so the study cohort was prospectively divided into two groups according to age. Subjects between 18 and 45 years old (mean 30 ± 7) comprised Group I, and those between 46 and 70 years old (mean 58 ± 8) comprised Group II. Thus, Group I consisted of patients with HCM (n = 25), highly competitive athletes (n = 21) and age-matched normal subjects (n = 33). Group II consisted of patients with HCM (n = 19), patients with secondary LV hypertrophy due to systemic hypertension (n = 27) and age-matched normal subjects (n = 33).

Standard echocardiographic study. This consisted of M-mode, two-dimensional and Doppler blood flow measurements. M-mode, two-dimensional directed measurements of the LV were taken at the level of the tips of the mitral valve leaflets in the parasternal long-axis view (25). The variables measured at end-diastole were LV posterior wall thickness with fractional thickness change, interventricular septal thickness, LV diameter and diameter of the aortic root; at end-systole the variable was diameter of the left atrium. Standard methodology was used to record pulsed wave Doppler transmitral velocity waveforms, with the interrogating sample volume being placed at the tips of the mitral valve leaflets (26). Recordings were made using a paper speed of 100 mm/s. The following Doppler indices were measured: peak E and A wave velocities, ratio of early transmitral flow velocity to atrial flow velocity (E/A ratio), E decleration time and isovolumic relaxation time. Cardiac cycles were excluded if either E-A fusion or curvilinear E wave descent was present (26). Standard methodology—the modified biplane Simpson method (27)—was used to measure the LV ejection fraction. All measurements were averaged over three cardiac cycles.

Digitized standard gray scale M-mode echocardiography. From each subject, standard gray scale M-mode echocardiography of the LV posterior wall was digitized and then subsequently analyzed. From manually traced endocardial and epicardial boundaries, using specially designed software, the normalized peak rate of systolic wall thickening and diastolic wall thinning was analyzed (28,29). This was calculated as

$$\frac{1}{PW} \times \frac{\Delta PW}{\Delta t},$$

Table 1. Clinical and Echocardiographic Data for Patients With Hypertrophic Cardiomyopathy, Athletes, Patients With Hypertension and Aged-Matched Normal Subjects

	Group I (age 18 to 40 years)			Group II (age 46 to 70 years)		
	HCM (n = 25)	Athletes (n = 21)	Normal (n = 33)	HCM (n = 19)	Hypertensive (n = 27)	Normal (n = 33)
Clinical						
Gender (F/M)	9/16	3/18	9/24	7/12	9/18	12/21
Age (yr)	31 ± 8	28 ± 7	30 ± 7	57 ± 7	58 ± 8	59 ± 8
Rest heart rate (beats/min)	66 ± 7*	54 ± 9†	64 ± 8	68 ± 11	70 ± 10	68 ± 11
Systolic blood pressure (mm Hg)	120 ± 9	122 ± 7	121 ± 8	129 ± 8‡	159 ± 17†	132 ± 9
Body surface area (m^2)	1.9 ± 0.2	1.9 ± 0.2	1.8 ± 0.2	1.8 ± 0.2	1.8 ± 0.2	1.9 ± 0.2
Echocardiographic						
Interventricular septum (cm)	1.5 ± 0.2†	1.3 ± 0.1‡	0.8 ± 0.1	1.7 ± 0.2†‡	1.5 ± 0.2†	0.9 ± 0.1
LV posterior wall (cm)	1.2 ± 0.2†	1.3 ± 0.1†	0.8 ± 0.1	1.4 ± 0.3†	1.4 ± 0.2†	0.9 ± 0.1
Fractional thickening (%)	63 ± 16	61 ± 13	58 ± 11	52 ± 11	56 ± 13	55 ± 14
Normalized peak rate of systolic thickening (s^{-1})	5.8 ± 1.3	6.3 ± 1.5	5.9 ± 1.5	5.3 ± 1.4	5.1 ± 1.6	5.4 ± 1.6
Normalized peak rate of diastolic thinning (s^{-1})	8.8 ± 1.8	8.7 ± 1.7	8.1 ± 2.0	7.6 ± 2.4	7.4 ± 2.3	7.9 ± 2.7
LV dimension (cm)	4.6 ± 0.6*	5.6 ± 0.6†	4.9 ± 0.4	4.7 ± 6	4.9 ± 0.7	4.8 ± 0.6
Aortic root dimension (cm)	2.9 ± 0.3	2.8 ± 0.3	2.9 ± 0.3	3.1 ± 0.4	3.2 ± 0.4	3.1 ± 0.4
Left atrial dimension (cm)	3.2 ± 0.5	2.9 ± 0.4	3.0 ± 0.4	3.4 ± 0.6	3.3 ± 0.6	3.2 ± 0.4
Peak E wave (cm/s)	73 ± 11	77 ± 9	74 ± 11	54 ± 9	60 ± 10	59 ± 9
Peak A wave (cm/s)	51 ± 16	45 ± 11	44 ± 9	65 ± 19	73 ± 11†	58 ± 10
E/A ratio (%)	1.5 ± 0.4	1.8 ± 0.4	1.7 ± 0.6	0.9 ± 0.2§	0.8 ± 0.1†	1.0 ± 0.3
Isovolumetric relaxation time (ms)	75 ± 14	69 ± 10	73 ± 11	97 ± 12	99 ± 18	91 ± 9
Ejection fraction (%)	69 ± 5†	67 ± 4†	61 ± 6	63 ± 6§	61 ± 6	59 ± 6

*$p < 0.01$ versus athletes' hearts. †$p < 0.01$ versus normal hearts. ‡$p < 0.01$ versus hypertensive hearts. §$p < 0.05$, analysis of variance with the Scheffé test. E/A = ratio of early transmitral flow velocity to atrial flow velocity; F = female; HCM = hypertrophic cardiomyopathy; LV = left ventricular; M = male. Data presented are mean value ± SD.

where ΔPW was the change in wall thickness that occurred during time Δt and PW was the average wall thickness during Δt.

Table 1 presents clinical and echocardiographic data from the study group.

Doppler myocardial imaging study. All M-mode DMI images taken from the LV posterior wall were recorded using an Acuson XP/10 ultrasound scanner with a 2.5-MHz phased array probe. The scanner modifications for DMI acquisition were described previously (17,19,21). Briefly, the velocity ranges used to encode myocardial velocities (0.2 to 24 cm/s) were lower than those conventionally used for blood flow. Throughout the study, the angle of interrogation of the M-mode beam was carefully aligned so that it was perpendicular to the LV posterior wall. The Doppler velocity range was set at the minimal value at which no aliasing occurred (21). The M-mode sweep rate was set to the maximal rate possible for the given Doppler velocity range. To eliminate the influence of respiration on myocardial velocities, cardiac cycles were stored at end-expiration (17). Images were obtained in the freeze-frame mode and digitally downloaded to a cardiac image capture system (Freeland/TomTec System, Munich, Germany). The ultrasound image was frozen on the monitor of the ultrasound machine and then downloaded with the DMI display turned first on and then off so that both DMI M-mode information and gray scale M-mode information were obtained from the same image frame. Doppler myocardial and standard gray scale images were acquired in the "mixed off" mode. This allowed the capture of separate information from DMI and gray scale data from the same M-mode image. After collection, the data were analyzed in blinded manner using specially designed PC software (17,19,21). Unlike currently available commercial DMI software that provides velocity information at single points but does not allow overall velocity analysis, the software designed for this study allowed a variety of quantified outputs based on the distribution of velocity estimates in the myocardium. In each stored DMI image, the MVG was calculated along each sequential scan line across the whole thickness of the myocardial wall. The computer program was used to convert color-coded velocities of the myocardium into velocity estimates using the color bar at the left side of the DMI image. Doppler myocardial images are constructed from 64 different colors, each of which represents a different velocity. Thirty-two colors represent positive velocities and the remaining 32 negatives velocities. The color bar consists of the same 64 colors. Therefore, a computer program operating on the digitized form of the images was programmed to use the color bar data as a look-up table for identifying colors in the DMI and to convert them into velocity estimates. This system was validated previously for the accuracy of measurements (17,19,21,30,31). The peak values of the MVGs were determined for three standard phases of the cardiac cycle: in systole,

during early ventricular ejection; in early diastole, during rapid ventricular filling; and in late diastole, during atrial contraction (17,21). For statistical analysis, the peak values of the MVGs in each of these three predetermined phases of the cardiac cycle were averaged from three consecutive cardiac cycles.

Myocardial velocity gradients. The MVG was defined as the slope of a linear regression of the myocardial velocity estimates along each M-mode scan line throughout the myocardium (19,20,30). A plot was then drawn of the velocity gradients against time during the cardiac cycle. In the normal healthy heart, in all but one phase of the cardiac cycle—namely, isovolumetric relaxation—the subendocardium rather than subepicardium is moving faster (21). Therefore, to illustrate this observation in the measurement of MVG rather than the overall motion of the myocardium, the MVG was expressed as a positive value when the subendocardium was moving faster than the subepicardium and as a negative value when the subepicardium was moving faster than the subendocardium (21).

Statistical analysis. The data are expressed as mean value ± SD. Analysis of variance, with the Scheffé F adjustment for multiple comparison, was used to assess the differences between each group of subjects in both Group I and Group II. An unpaired *t* test was used to compare the differences in MVG between age groups. The potential influence of patient gender, age, heart rate, systolic blood pressure and standard echocardiographic variables, which include regional and global LV hypertrophy, transmitral waveforms and normalized peak rate of systolic thickening and diastolic thinning on the MVG, was analyzed using stepwise multivariate regression analysis. Sensitivity and specificity were assessed in the standard manner. Positive predictive and negative predictive values were calculated using Bayes' theorem, which makes allowance for the influence of prevalence (32). Reproducibility was assessed according to Bland and Altman (33). A probability value <0.05 was considered significant.

Interobserver and intraobserver variability. The MVGs were measured by two independent observers in 10 randomly selected subjects in each study group. Analysis of variance was used to assess the differences between the measurements of MVG obtained by two observers and between the measurements taken from the same subject in different cardiac cycles. The interobserver variability was low at (mean ± SD) 0.1 ± 0.2 s^{-1}. The difference between the MVG obtained from the same subject but during different cardiac cycles (intraobserver variability) was low at 0.2 ± 0.2 s^{-1}.

Results

Myocardial velocity gradient comparisons between study groups. Figure 1 presents a summary of the data from MVG measurements.

Group I. In systole, during early ventricular ejection, MVG was significantly ($p < 0.01$) lower in patients with HCM (3.2 ± 1.1 s^{-1}) than in both athletes (4.6 ± 1.0 s^{-1}) and normal subjects (4.4 ± 0.8). Also in early diastole, during rapid ventricular filling, MVG was significantly ($p < 0.01$) lower in HCM hearts (3.7 ± 1.5 s^{-1}) than in athletes' (9.9 ± 1.9 s^{-1}) and normal subjects' (9.2 ± 2.0 s^{-1}) hearts. However, in late diastole, during atrial contraction, the differences in MVG between the groups of subjects under investigation were not significant (1.3 ± 0.8, 0.9 ± 0.9 and 1.0 ± 0.9 s^{-1}, respectively). The differences in MVGs between athletes and normal, untrained subjects in both systole and diastole were not significant.

Group II. The MVG measured in systole, during early ventricular ejection, was significantly ($p < 0.01$) lower in HCM hearts (2.9 ± 1.2 s^{-1}) than in both hypertensive hearts (4.2 ± 1.8 s^{-1}) and normal hearts (4.8 ± 0.8 s^{-1}). In both diastolic phases of the cardiac cycle, significant differences occurred. In early diastole, during rapid ventricular filling, MVG was significantly ($p < 0.05$) lower in HCM hearts (2.6 ± 0.9 s^{-1}) than in normal hearts (3.6 ± 1.5 s^{-1}). The difference in MVG taken during rapid ventricular filling between patients with HCM and hypertensive patients (3.3 ± 1.3 s^{-1}) was not significant. In late diastole, during atrial contraction, MVG measured in HCM hearts (1.4 ± 0.8 s^{-1}) was significantly ($p < 0.01$) lower than that in hypertensive hearts (4.3 ± 1.7 s^{-1}) and normal hearts (3.8 ± 0.9 s^{-1}). The differences between hypertensive hearts and normal hearts in MVG measured in systole and in both diastolic phases of the cardiac cycle were not significant.

Group I versus Group II. Analysis of age-related changes in MVG in HCM hearts showed that, unlike in healthy hearts, MVG changes were less significant (Fig. 1).

Multivariate analysis of MVG. *Systole.* The MVG measured in systole was significantly dependent on LV posterior wall thickness but not on other ultrasound variables, including normalized peak rate of systolic LV posterior wall thickening and degree of LV outflow tract obstruction.

Diastole. The MVGs measured in patients with HCM, athletes and hypertensive patients during both diastolic phases of the cardiac cycle were independent of transmitral waveform pattern and normalized peak rate of diastolic posterior wall thickening. Moreover, in all studied groups of subjects, early and late diastolic MVGs were independent of other clinical and ultrasound variables such as heart rate, blood pressure, LV dimension or myocardial hypertrophy (Fig. 2).

Sensitivity, specificity and predictive values of MVG for diagnosis of HCM. Calculations of accuracy in the diagnosis of HCM, based on assessment of the MVG measured in systole and diastole, are shown in Table 2. In Group I, MVG ≤ 7 s^{-1}, taken in early diastole during rapid ventricular filling, was the most accurate criterion for distinction between pathologically hypertrophied myocardium in patients with HCM and physiologic hypertrophy in highly competitive athletes (Fig. 3). In Group II, systolic or both early and late diastolic MVG measurements were less accurate for the diagnosis of HCM.

Discussion

Over the past 20 years, the peak rate of wall thickening and thinning has been recognized as the most accurate echocardio-

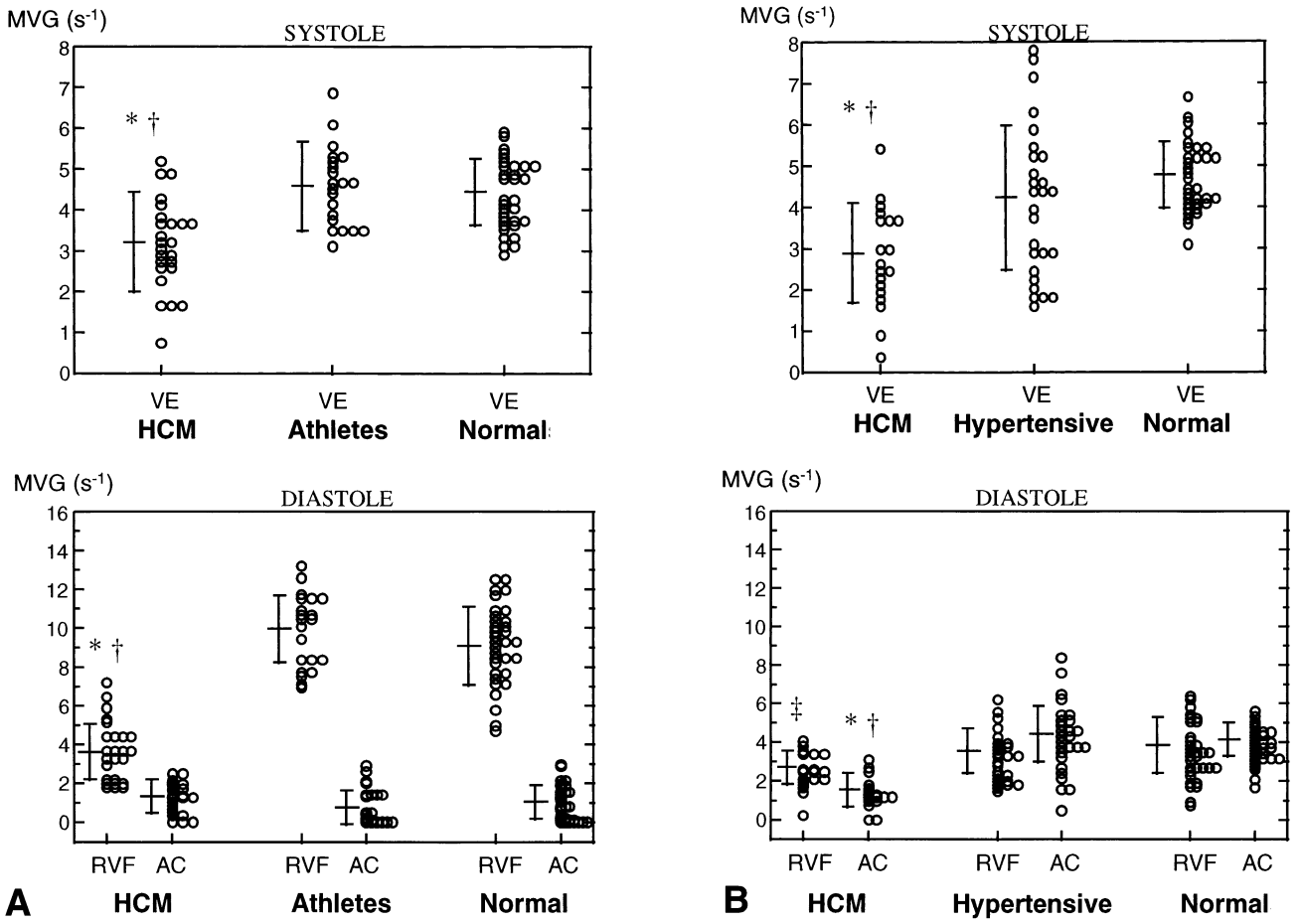

Figure 1. Comparison of MVG measurements in Group I (**A, top and bottom**) and in Group II (**B, top and bottom**) taken in systole and diastole between the groups of study patients. Comparison of MVG (mean [±SD] s^{-1}) measurements between the two age groups (Group I vs. Group II)—in patients with HCM: VE 3.2 ± 1.1 vs. 2.9 ± 1.2, p = 0.3191; RVF 3.7 ± 1.5 vs. 2.6 ± 0.9, p = 0.0034; and AC 1.3 ± 0.8 vs. 1.4 ± 0.8, p = 0.7033; in normal subjects: VE 4.4 ± 0.8 vs. 4.8 ± 0.8, p = 0.0684; RVF 9.2 ± 2.0 vs. 3.6 ± 1.5, p < 0.0001; and AC 1.0 ± 0.9 vs. 3.8 ± 0.9, p < 0.0001—by the unpaired *t* test. *p < 0.01 compared with athletes or hypertensive patients; †p < 0.01 compared with normal subjects; and ‡p < 0.05 compared with normal subjects—by analysis of variance with the Scheffé F adjustment. AC = atrial contraction; Normals = normal subjects; RVF = rapid ventricular filling; VE = ventricular ejection.

graphic variable of regional myocardial function (28,29). With this technique, the information is obtained from digitized, standard M-mode images and thus is more accurate than that obtained from standard gray scale video M-mode images. However, despite the fact that M-mode images are digitized, the endocardial and epicardial boundaries need to be traced manually. The peak rate of wall thickening and thinning is then calculated according to the wall thickness changes between these two lines. Most of the reported studies validating this technique were based on children (29,34,35). This is important, as the accuracy of the digitized M-mode–derived information is directly related to the quality of the analyzed images. Therefore, although accurate in children, this technique may not be as accurate in adults, in whom the quality of standard gray scale images is often poor. The error of the reading will increase according to the error in traces of endocardial and epicardial boundaries.

Myocardial velocity gradient. The MVG was introduced by Fleming et al. (19) and Uematsu et al. (20) as a new ultrasound index of myocardial function. The information on myocardial contraction and relaxation performance is derived from each pixel and from each ultrasound line, across the myocardium and between the endocardium and epicardium, as opposed to two values being taken into account in digitized gray scale M-mode images. This variable therefore has advantages over the digitized gray scale M-mode, as its accuracy is less dependent on the accuracy of endocardial and epicardial boundary traces (31). It also includes information on transmyocardial function, as opposed to the information obtained from digitized gray scale M-mode images, where only the motion of speckle lines of the endocardium and epicardium is being analyzed. Changes in MVG have been analyzed in both healthy hearts during systole and diastole (21) and in patients with impaired LV systolic function (20). It has also been shown that the endocardial boundary is more reliably displayed and

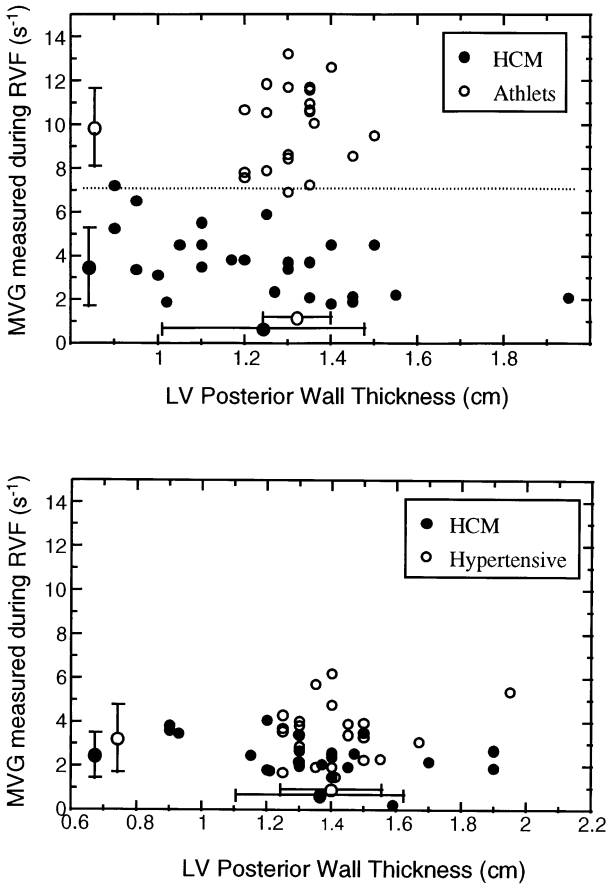

Figure 2. Relation between regional LV hypertrophy and diastolic MVG measured during rapid ventricular filling in Group I (18 to 45 years old [**top**]) and in Group II (46 to 70 years old [**bottom**]). RVF = rapid ventricular filling.

visually easier to detect using DMI than the standard gray scale imaging technique (36). In this study, we sought to determine whether MVG measurements can distinguish myocardial hypertrophy of different etiologies. The MVG was measured in three groups of patients with either generalized or focal LV hypertrophy—patients with HCM, athletes and hypertensive patients—and the results were compared with those of age-matched normal subjects. Because of physiologic age-related changes in diastolic MVG (decrease in early diastole and increase in late diastole), the study group was prospectively subdivided into two age subgroups (21).

Findings of present study. As expected, in healthy subjects, MVG measurements taken during diastole were age related (21). In the "old" group of healthy subjects, MVG measured during rapid ventricular filling decreased by 2.5 times compared with the "young" group. Also, as expected, MVG measured during atrial contraction increased with age. The situation was different in patients with HCM. The observed age-related changes in MVG were significantly less pronounced, and the MVG measured during rapid ventricular filling decreased only 0.5 times. In systole, in both HCM age groups, MVG was significantly lower than that in age-matched

Table 2. Accuracy of Diagnosis of Patients With Hypertrophic Cardiomyopathy Based on Measurement of Myocardial Velocity Gradient

Phase	MVG (s^{-1})	Sensitivity	Specificity	PPV	NPV
HCM vs. athlete hearts					
VE	≤4	0.80	0.62	0.71	0.72
RVF	≤7	0.96	0.95	0.96	0.95
AC	N/A	—	—	—	—
HCM vs. hypertensive hearts					
VE	≤4	0.89	0.52	0.57	0.88
RVF	≤3	0.68	0.52	0.50	0.70
AC	≤2	0.84	0.85	0.80	0.88

AC = atrial contraction; HCM = hypertrophic cardiomyopathy; MVG = myocardial velocity gradient; NPV = negative predictive value; PPV = positive predictive value; RVF = rapid ventricular filling; VE = ventricular ejection.

normal subjects, athletes and hypertensive patients. This was a particularly interesting finding because in the studied patients with HCM, all standard M-mode and two-dimensional ultrasound variables of systolic function, including normalized peak rate of systolic thickening and diastolic thinning, were either normal or elevated. Also, the ejection fraction measured in patients with HCM was similar to that in the athletes and higher than that in age-matched normal subjects. This increased ejection fraction at rest in athletes was rather surprising, as it has been previously described that the ejection fraction in this group of subjects is normal or decreased (37,38). However, that information was based on the assessment of LV shortening changes from M-mode parasternal images rather than on the assessment of LV cavity changes obtained in this study from the biplane apical window.

When comparing the groups with myocardial hypertrophy of different etiology, we found a characteristic pattern of MVG. In early diastole, during rapid ventricular filling, MVG was lower in HCM hearts compared with athletes' hearts, and was also lower in late diastole, during atrial contraction, when compared with hypertensive hearts. This decrease in diastolic MVG in patients with HCM is probably related to a known characteristic of diastolic dysfunction in HCM, namely, a decrease in LV compliance and prolonged (or incomplete) LV relaxation (39–41). It is mainly due to morphologic changes in HCM (i.e., cellular disorganization, myocardial scarring and abnormalities of the small intramural coronary arteries) (40). These features of myocardial morphologic changes may also occur in the LV myocardium of patients with secondary LV hypertrophy due to systemic hypertension, but will occupy significantly smaller areas of myocardium (11,40,42). Therefore, it is possible that the differences in MVG between the older group of patients with HCM and hypertension were not as distinct as the differences found between the younger group of patients with HCM and highly competitive athletes. Importantly, these abnormal MVGs measured in diastole were not dependent on the degree of both regional and global LV hypertrophy and normalized peak rate of diastolic wall thickening. These measurements were also independent of other

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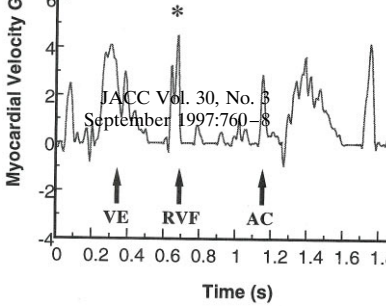

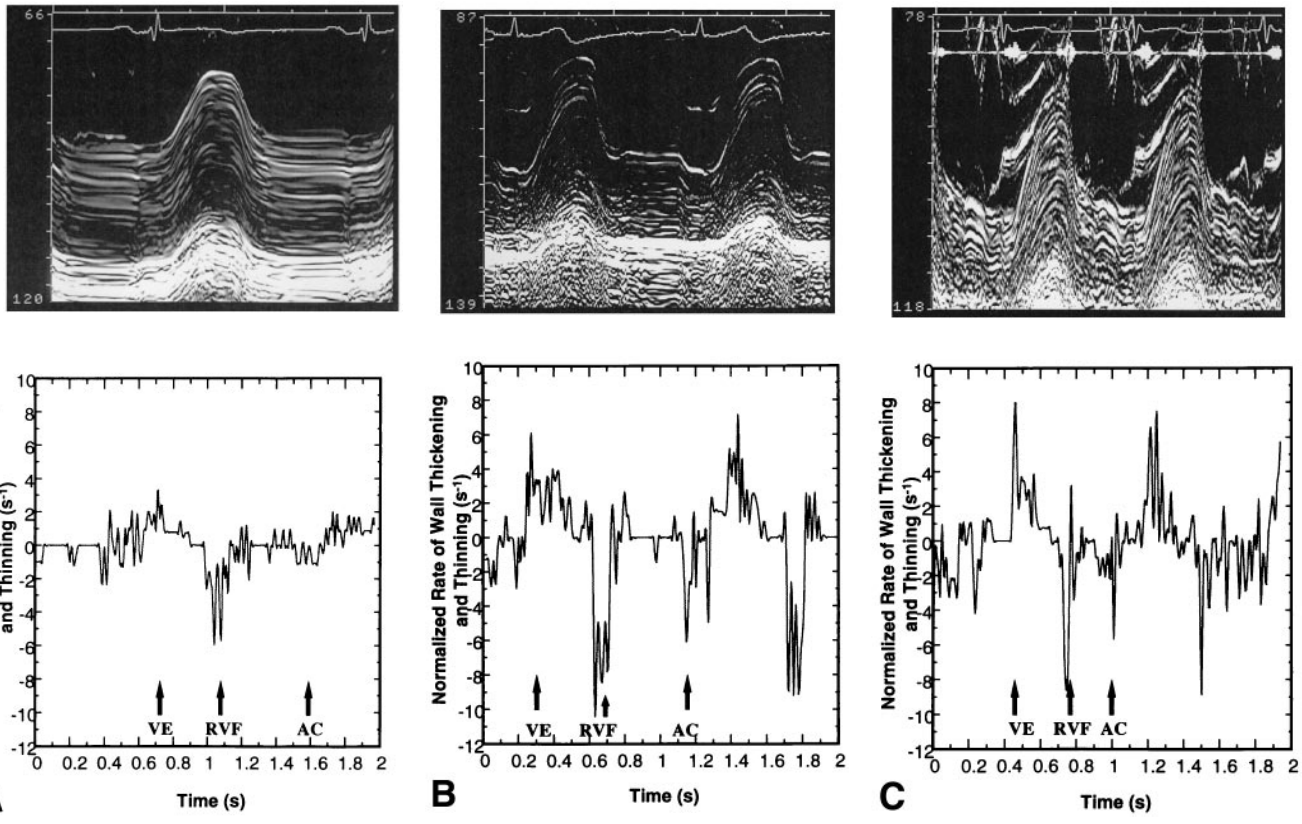

Figure 3. Examples of Doppler myocardial M-mode images taken from the LV posterior wall with calculated MVG (**top**), and corresponding gray scale image with calculated normalized rate of myocardial wall thickening and thinning (**bottom**). **A,** Male patient with HCM (age 36 years) with markedly hypertrophied LV posterior wall (1.9 cm). **B,** Male patient with HCM (age 23 years) with borderline LV posterior wall thickness (1.2 cm). **C,** Male athlete's heart (age 25 years) with mild LV posterior wall hypertrophy (1.3 cm). **Arrows** show the peak values of the MVG and the normalized rate of the LV posterior wall systolic thickening during phases of the cardiac cycle. **Asterisks** indicate that MVG measured during right ventricular filling was markedly decreased in both HCM hearts (**A** and **B**) compared with the athlete's heart (**C**). In contrast, the peak rate of wall thinning, assessed from a digitized gray scale M-mode image, did not show significant changes during right ventricular filling between the patient with HCM with borderline hypertrophy (**B**) and the athlete (**C**). Abbreviations as in Figure 1.

clinical factors such as heart rate and blood pressure, which were significantly different in the groups of patients studied.

Study limitations. In our clinical group, we did not have access to either sufficient numbers of young hypertensive patients with LV hypertrophy or elderly athletes who would meet the inclusion criteria. However, both these groups are relatively rare and thus present infrequently as a clinical problem. Although patients with HCM with substantial LV outflow tract obstruction were excluded from this study, approximately a quarter of the patients with HCM studied had a mild degree of LV outflow tract obstruction, and this potentially may have influenced MVG measurements. To assess how big an impact it might have on our measurements, a study with a group of patients with LV hypertrophy due to aortic stenosis would be of interest.

The main technical limitation of this study was that our measurements were restricted to M-mode tracings. Because of the angle dependence of Doppler information, we could only accurately measure LV posterior wall velocities derived from the parasternal long-axis view in which the interrogating beam was perpendicular to the myocardium. However, based on these results, limited to a small myocardial area, we found that in patients with HCM an abnormal MVG is present in both hypertrophied and nonhypertrophied areas. In the future, the development of angle-independent, two-dimensional DMI should allow interrogation of all segments of the LV wall. In this regard, Uematsu et al. (20) have already described a new method of angle correction of MVG measurements obtained from the two-dimensional short-axis view. However, their method offers lower temporal resolution than that with the M-mode technique and is still limited only to a section of the myocardial wall.

Conclusions. Based on our results, it appears that diastolic MVG $\leq 7\ s^{-1}$ measured in early diastole, during rapid ventricular filling, in a "young" group of patients (age 18 to 45 years), taken as a single indicator, is a very sensitive and specific variable to differentiate patients with HCM from athletes or age-matched normal subjects. This new variable may be used to differentiate between HCM hearts and athletes' hearts, when the thickness of the analyzed myocardial region is within borderline limits. It is precisely in this group of patients who have marginal or an uncharacteristic pattern of LV hypertrophy, or both, that this new diagnostic variable should have its greatest impact. In the future, the role of MVG measurements as a screening tool for identification of patients with preclinical HCM should be established.

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