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Global and Regional Myocardial Function Quantification by Two-Dimensional Strain

Application in Hypertrophic Cardiomyopathy

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OBJECTIVES Recently, a novel method to measure strain from standard two-dimensional images has been developed. Our goal was to characterize global and regional systolic function abnormalities using this technique in patients with hypertrophic cardiomyopathy (HCM).

BACKGROUND Strain has been proposed as a sensitive tool to detect early systolic function abnormalities in HCM. However, the clinical application of conventional Doppler-derived strain has been limited by poor reproducibility and angle dependency.

METHODS Echocardiographic examinations were performed in 26 patients with nonobstructive HCM and 45 healthy subjects. Using a dedicated software package, bidimensional acquisitions were analyzed to measure longitudinal and transverse strain in apical views and circumferential and radial strain in parasternal short-axis view.

RESULTS Despite apparently normal left ventricular systolic function, all components of strain were significantly reduced in HCM. Average longitudinal, transverse, circumferential, and radial strain in patients with HCM and controls were $-15.1 \pm 6.2\%$ versus $-20.3 \pm 5.6\%$, $23.3 \pm 17.0\%$ versus $27.2 \pm 14.9\%$, $-16.8 \pm 7.1\%$ versus $19.6 \pm 5.2\%$, and $25.2 \pm 13.9\%$ versus $36.8 \pm 17.2\%$, respectively (all $p < 0.001$). In patients with asymmetrical HCM, longitudinal septal strain was significantly lower than for other left ventricular segments combined: $-9.2 \pm 4.7\%$ versus $-12.7 \pm 7.1\%$ ($p = 0.001$). Average interobserver and intraobserver variabilities were 11% and 11.3%, respectively.

CONCLUSIONS Two-dimensional strain is a new simple, rapid, and reproducible method to measure different components of systolic strain. This technique identified early abnormalities in patients with HCM that have apparently normal left ventricular systolic function. (J Am Coll Cardiol 2006;47:1175–81) © 2006 by the American College of Cardiology Foundation

Hypertrophic cardiomyopathy (HCM) is a genetic disorder characterized by left-ventricular (LV) hypertrophy and myocardial disarray. Abnormalities in diastolic function and mitral valve dynamics have been well characterized; however, abnormal systolic function in the early stages has not been clearly demonstrated. Noninvasive evaluation of regional function can be performed by measuring myocardial strain or deformation (1–3). Initially obtained from Doppler-derived velocity measurements, strain has been proposed as a sensitive tool to detect early systolic function abnormalities in patients with HCM (4). However, clinical application has been limited by complexity of data postprocessing and limited reproducibility.

Recently, a novel method to measure strain from standard bidimensional images has been developed (5,6). The objective of this study was to characterize global and regional systolic function abnormalities using two-dimensional (2D) strain in patients with HCM.

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METHODS

Forty-five healthy subjects and 26 patients with familial nonobstructive HCM were included in the study. In the presence of a positive family history, asymmetrical HCM was diagnosed with a septal thickness >15 mm and septal-to-posterior wall thickness ratio >1.3 (7) and concentric HCM with septal and posterior wall thickness >13 mm. In both groups, diagnosis required the absence of an underlying etiology, cardiac or systemic, that might lead to LV hypertrophy. Patients with abnormal regional or global systolic function and with obstructive HCM were excluded.

Echocardiographic measurements. Standard echocardiographic examinations were performed in all patients using a Vivid Seven digital ultrasound system (GE Medical Systems, Horten, Norway). Three cardiac cycles were stored in cineloop format for offline analysis. Left ventricular and left atrial dimensions were measured according to the recommendations of the American Society for Echocardiography. Left ventricular mass was calculated using Devereux's formula and indexed for body-surface area and for height. Left ventricular ejection fraction was measured using Simpson's method. Diastolic function was evaluated by analysis of mitral Doppler inflow and tissue Doppler imaging (TDI) at

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Abbreviations and Acronyms

2D = two-dimensional
HCM = hypertrophic cardiomyopathy
LV = left ventricular
MR = mitral regurgitation
MRI = magnetic resonance imaging
TDI = tissue Doppler imaging

the lateral mitral annulus. The presence of an intraventricular or subaortic gradient at rest was sought. Mitral regurgitation (MR) was evaluated according to the recommendations of the American Society for Echocardiography.

Strain measurements. The LV was divided into 17 segments and each segment individually analyzed. Using a dedicated software package (EchoPac PC; GE Healthcare, Waukesha, Wisconsin), 2D strain was measured as previously described (6). Two-dimensional strain is a novel non–Doppler-based method to evaluate systolic strain from standard bidimensional acquisitions. By tracing the endocardial contour on an end-diastolic frame, the software will automatically track the contour on subsequent frames. Adequate tracking can be verified in real-time and corrected by adjusting the region of interest or manually correcting the contour to ensure optimal tracking.

Two-dimensional longitudinal and transverse strain were assessed in apical views and circumferential and radial strain in parasternal short-axis (Figs. 1 to 3). Transverse and radial strain both represent radial deformation during systole; however, because they were obtained from different echocardiographic views, they were analyzed separately. Average longitudinal and transverse strains were calculated for the 17 segments and average circumferential and radial strains for the six mid-LV segments.

For longitudinal and transverse strain, analysis also was performed according to LV segments (six basal, six mid-LV, and five apical). For HCM, the basal ventricular septum was analyzed separately and compared to other basal LV segments.

Tissue Doppler imaging longitudinal strain was measured in 10 patients on three consecutive cycles and compared with 2D strain. Color TDI loops were obtained for three consecutive cycles and analyzed off-line. Strain on TDI was measured by placing regions of interest on six segments in the apical four-chamber view (basal and mid-inferoseptal and anterolateral, septal and lateral apical segments). Two-dimensional longitudinal strain was measured on the same three consecutive cycles by analyzing bidimensional acquisitions. Average values and standard deviations using each method were calculated to assess potential beat-to-beat variations in strain measurement.

Reproducibility. The studies were analyzed offline by a second blinded observer for 10 patients, corresponding to 170 (longitudinal and transverse strain) and 60 segments analyzed (radial and circumferential strain). Intraobserver variability was calculated by the average difference between the 10 measurements realized. Interobserver variability was calculated as the absolute difference divided by the average of the two observations for all parameters.

Statistical analysis. All values were expressed as mean ± standard deviation. Comparisons between subject data were performed with a paired Student *t* test, and comparisons with healthy volunteers with an independent-samples *t* test. A p value of <0.05 was considered significant.

RESULTS

Baseline characteristics. Baseline characteristics of the study population are shown in Table 1. Fifteen patients (57.7%) had asymmetrical HCM and 11 (42.3%) concentric HCM. All had normal LV systolic function (mean LV ejection fraction, 69.3 ± 6.4%). Mean LV mass was 237.5 g/m^2 indexed for body-surface area or 100.9 $g/m^{2.3}$ indexed for height. Three patients had moderate MR and one had severe MR.

2D strain analysis. AVERAGE STRAIN. The 2D-strain software adequately tracked 94.4% myocardial segments in normal subjects and 94.8% in HCM, which could be analyzed. Average analysis time per patient for the parasternal short-axis, apical four-, three-, and two-chamber views was 15 min. When analysis was limited to the apical four-chamber view, average analysis time was between 2 and 3 min. Average strain values are shown in Table 2. All components of strain were significantly reduced in patients with HCM compared with control patients.

SEGMENTAL ANALYSIS. Longitudinal and transverse strain for basal, mid-LV, and apical segments are shown in Table 3. In controls, longitudinal strain increased significantly from base to apex, whereas transverse strain decreased significantly from base to apex. In patients with HCM, basal longitudinal strain was significantly lower than apical

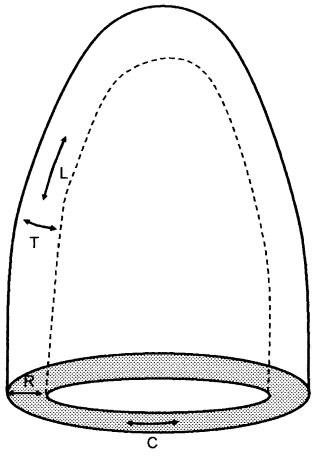

Figure 1. Illustration of the different components of systolic strain measured by two-dimensional strain analysis. C = circumferential; L = longitudinal; R = radial; T = transverse.

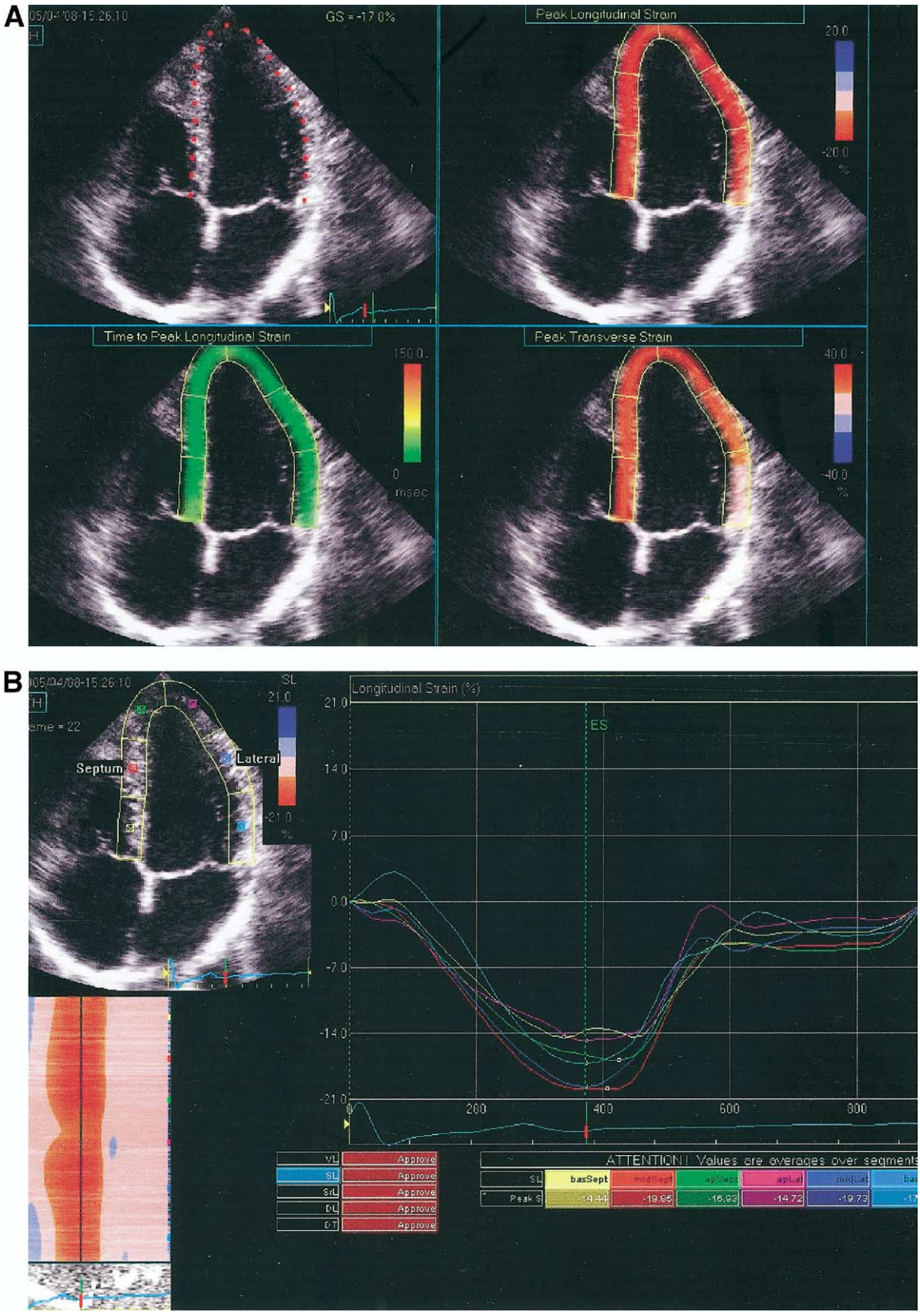

Figure 2. **(A)** Apical four-chamber view showing endocardial contour **(upper left)**, peak longitudinal strain **(upper right)**, peak transverse strain **(lower right)**, and time-to-peak longitudinal strain **(lower left)**. **(B)** Longitudinal systolic strain curves in apical four-chamber view with different colors depicting the different myocardial segments. Strain values are shown in the table **(lower right)**.

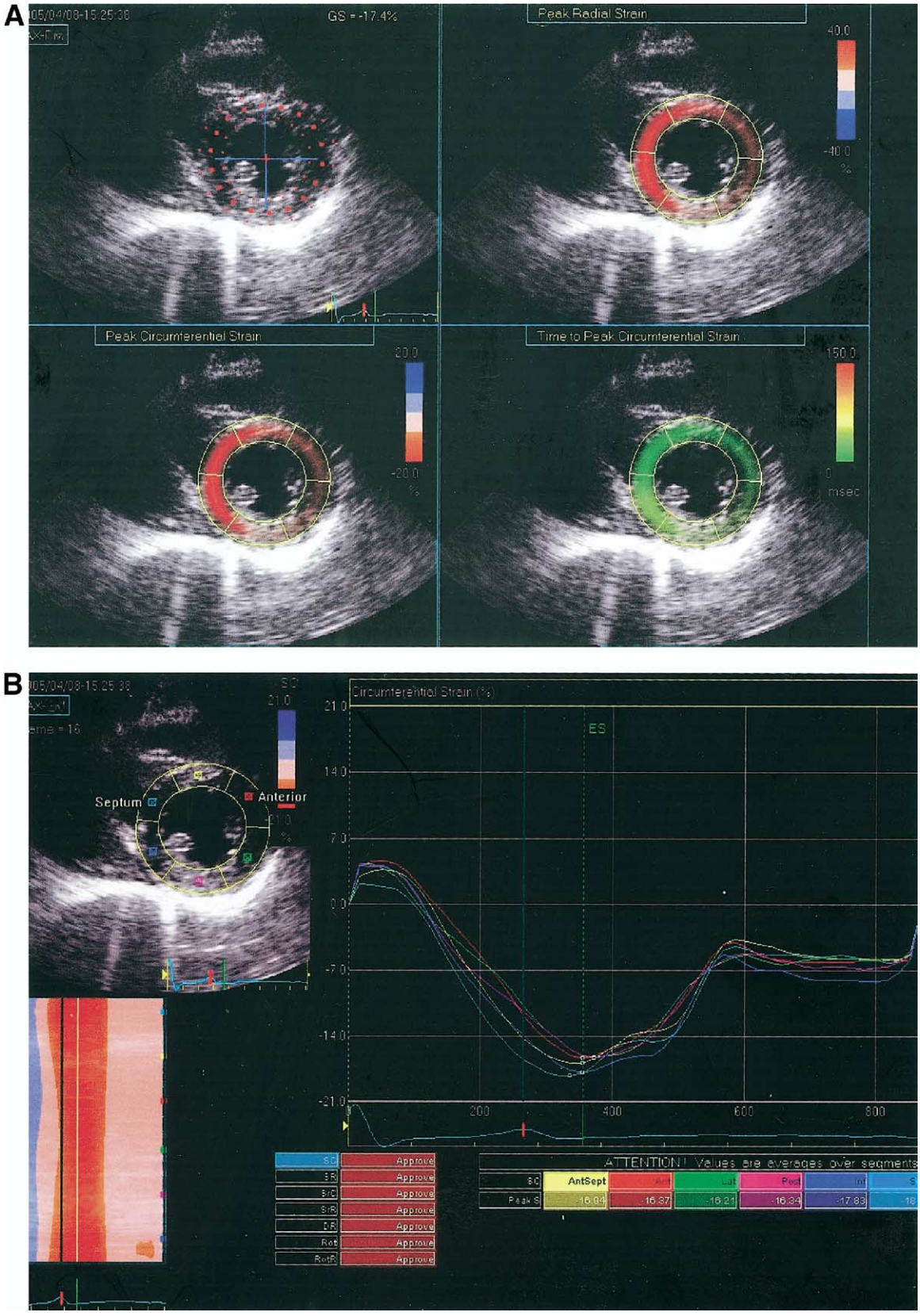

Figure 3. **(A)** Parasternal short-axis view showing endocardial contour **(upper left)**, peak radial strain **(upper right)**, peak circumferential strain **(lower left)**, and time-to-peak circumferential strain **(lower right)**. **(B)** Circumferential systolic strain curves in parasternal short-axis view with different colors depicting the different myocardial segments. Strain values are shown in the table **(lower right)**.

Table 1. Patient Characteristics

	Controls	HCM
Age, yrs	41.6 ± 14.1	47 ± 18.1
Gender (M/F)	25/21	18/7
Systolic blood pressure, mm Hg	119.7 ± 11.1	121.3 ± 12.2
Diastolic blood pressure, mm Hg	78.2 ± 9.7	81.1 ± 9.9
LVEF, %	67.1 ± 7.5	69.3 ± 6.4
LV mass, g	163.9 ± 53.2	425.2 ± 144.2
LV mass (indexed for BSA), g/m^2	91.0 ± 22.1	237.5 ± 77.9
LV mass (indexed for height), g/m$^{2.3}$	38.2 ± 8.4	100.9 ± 35.1
LVEDD, mm	47.0 ± 6.4	45.1 ± 4.9
LVESD, mm	29.7 ± 5.4	26.7 ± 4.0
Septum/posterior wall ratio	1.0 ± 0.1	1.4 ± 0.5
LAD, mm	33.6 ± 3.7	41.3 ± 11.3
LA area, cm^2	13.0 ± 2.8	19.9 ± 8.6
Diastolic function		
Normal	78%	58%
Abnormal relaxation	22%	37%
Pseudonormal	0%	2.5%
Restrictive	0%	2.5%

BSA = body surface area; HCM = hypertrophic cardiomyopathy; LA = left atrium; LAD = left atrial diameter; LV = left ventricular; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter.

strain. No significant variations were observed for transverse strain.

COMPARISON OF BASAL SEPTUM VERSUS OTHER SEGMENTS. In HCM, comparison between basal septal strain and other basal LV segments combined revealed significantly reduced longitudinal septal strain: −9.2 ± 4.7% versus −12.7 ± 7.1% ($p = 0.001$). In subgroup analysis, this difference remained significant only in patients with asymmetrical HCM, with a longitudinal septal strain value of −9.3 ± 5.2% versus −13.6 ± 5.9% for other LV walls ($p = 0.002$). Transverse septal strain was not significantly different from other segments ($p = 0.06$).

COMPARISON BETWEEN TDI AND 2D STRAIN. Longitudinal strain values obtained by TDI and 2D strain are shown in Table 4. Mean values measured on three consecutive cycles were comparable. However, greater beat-to-beat variations were observed for TDI strain, as illustrated by significantly greater standard deviations.

Reproducibility. Interobserver and intraobserver variabilities for the different strain parameters and comparison between TDI and 2D strain are shown in Tables 5 and 6, respectively.

Table 3. Longitudinal and Transverse Segmental Strain Values

	Controls	HCM
Longitudinal		
Base, %	−18.0 ± 5.5	−11.5 ± 5.7
Mid-LV, %	−19.9 ± 5.3*	−13.5 ± 5.1†
Apex, %	−23.8 ± 7.6*	−21.5 ± 8.1*
Transverse		
Base, %	29.9 ± 18.4	24.7 ± 19.4
Mid-LV, %	26.3 ± 14.1†	21.8 ± 15.9‡
Apex, %	25.2 ± 13.1†	23.5 ± 15.5‡

*$p < 0.001$ vs. basal segments. †$p < 0.05$ vs. basal segments. ‡p = NS vs. basal segments.
HCM = hypertropic cardiomyopathy; LV = left ventricular.

DISCUSSION

This study assesses the role of 2D strain, a new method to measure systolic strain from bidimensional acquisitions, in evaluating global and regional function in HCM. Our results show that: 1) the different components of strain (longitudinal, radial, and circumferential) can be measured with good reproducibility in normal subjects and in those with HCM; 2) global strain is significantly reduced in patients with HCM; and 3) basal longitudinal septal strain is significantly reduced compared to other segments in patients with asymmetrical HCM.

Comparison between TDI and 2D strain. Cardiac motion is a complex process involving rotation, contraction, and shortening. Currently, the term "strain" is used only as an index of longitudinal myocardial deformation. Two-dimensional strain analysis is unique as it allows one to study the different components of strain, namely longitudinal, circumferential, and radial deformation. The value of the method lies in its simple and rapid use as compared with traditional methods.

Clinical use of TDI strain has been limited by artifacts caused by myocardial translational motion, by the requirement for optimal Doppler alignment, by variable reproducibility, and by time-consuming off-line analysis. Furthermore, analysis generally is restricted to longitudinal strain or posterior wall assessment of radial strain.

We observed greater beat-to-beat variations for TDI longitudinal strain than for 2D strain, probably reflecting variations due to myocardial displacement. Measures of 2D longitudinal strain were highly reproducible when compared with the 10% to 15% interobserver and in-

Table 2. Average Longitudinal, Transverse, Circumferential, and Radial Strain Values

	Controls	HCM	Concentric	Asymmetrical
Apical				
Longitudinal, %	−20.3 ± 5.6	−15.1 ± 6.2*	−13.9 ± 5.8†	−16.2 ± 6.2
Transverse, %	27.2 ± 14.9	23.3 ± 17.0*	22.4 ± 17.2‡	23.8 ± 16.2
PSSAX				
Circumferential, %	−19.6 ± 5.2	−16.8 ± 7.1*	−18.9 ± 7.2†	−15.4 ± 6.6
Radial, %	36.8 ± 17.2	25.2 ± 13.9*	23.6 ± 14.1‡	26.2 ± 14.1

*$p < 0.001$ vs. control subjects. †$p < 0.05$ vs. patients with asymmetrical HCM. ‡p = NS vs. patients with asymmetrical HCM.
HCM = hypertrophic cardiomyopathy; PSSAX = parastental short axis.

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Table 4. Comparison Between Longitudinal TDI Strain and 2D Strain: Mean Values and Standard Deviations Measured on Three Consecutive Cycles by Each Method

	Basal IS	Mid IS	Sept Ap	Lat Ap	Mid AL	Basal AL	Averages
Mean							
TDI strain	−19.89	−18.30	−25.35	−16.14	−16.76	−18.27	−19.12
2D strain	−16.28	−19.40	−23.79	−18.18	−19.23	−16.69	−18.92
SD							
TDI strain	3.24	4.2	2.92	2.75	2.49	4.72	3.39
2D strain	1.44	1.45	2.07	2.91	2.51	2.75	2.19

2D = two-dimensional; AL = anterolateral; IS = inferoseptal; Lat Ap = lateral apex; Sept Ap = septal apex.

traobserver rates of variability generally reported for TDI strain (3,8,9).

Comparison with previous studies in normal subjects. LONGITUDINAL STRAIN. Our findings for longitudinal strain in normal subjects are in agreement with previously published studies. Values between −18% and −19% have been reported using either TDI or magnetic resonance imaging (MRI) (3,8) . Similar results were observed in a recent study using 2D strain (6).

BASE-APEX GRADIENT. Myocardial velocities are known to decrease from the mitral annulus toward the apex (3,8). However, the exact pattern of strain from base to apex has not been clearly established, with contradictory results reported in the literature. We observed an increase in longitudinal strain from base to apex, as did Leitman et al. (6). Results obtained by TDI have been variable, with certain authors describing decreasing strain toward the apex (8), whereas others found no variation (10). Using MRI, Bogaert and Rademakers (11) found increasing strain from base to apex in 87 healthy subjects. The impact of age also has to be considered, as the age-associated strain reduction appears to be more important for apical than for basal segments (12).

CIRCUMFERENTIAL, TRANSVERSE, AND RADIAL STRAIN. Instead of focusing solely on longitudinal deformation, 2D strain allows one to study other components of myocardial contraction, namely radial and circumferential deformation. However, these parameters have been the subject of much less investigation than longitudinal strain, mainly because of their relative inaccessibility by TDI analysis, which usually is limited to posterior wall study. Therefore, reference values have not been as clearly established. Values between 35% and 48% have been reported using MRI and Doppler, respectively (10,11) . Similarly, results for circumferential strain have ranged between −19.5% and −31.9% according to different investigators (11,13). We observed lower values for radial and circumferential strain than those reported. However, the wide range of normal values renders interpretation of abnormalities difficult.

Comparison with previous studies in HCM. GLOBAL STRAIN. This echocardiographic study is the first to characterize all three normal components of strain in patients with HCM. These parameters were found to be significantly reduced despite normal LV function as assessed by standard criteria, suggesting the presence of a global subclinical systolic dysfunction. Previous studies have shown reduced longitudinal and circumferential strain using TDI (14) and MRI (13), respectively. Mishiro et al. (15) showed decreased strain in both hypertrophied and nonhypertrophied regions. Hence, strain analysis appears to be a more sensitive index of global myocardial function than standard LV function assessment, underlining the diffuse nature of the disease.

VENTRICULAR SEPTAL STRAIN. In a segmental analysis, longitudinal septal strain was significantly lower than other LV segments. This difference was significant only for the subgroup of patients with asymmetrical HCM. In an earlier study using TDI, Yang et al. (4) showed reduced septal longitudinal strain when compared with control subjects (−10.3% vs. −19.4%).

Study limitations. Changes in preload and afterload are important determinants of myocardial deformation. The possibility that reduction in strain could be due to an increased wall stress cannot be entirely excluded. However, early hemodynamic studies have shown afterload often to be reduced in patients with HCM. Left ventricular end-diastolic dimensions were comparable in both groups, suggesting comparable preload. Thus, although strain is load-dependent, abnormal loading conditions should not have had a major impact on our results.

Conclusions. Two-dimensional strain is a new simple, rapid, and reproducible method to measure systolic strain from standard bidimensional images. Limited reproducibil-

Table 5. Interobserver and Intraobserver Variabilities for the Different Components of Strain Assessed by 2D Strain

	Longitudinal	Transverse	Circumferential	Radial	Average
Interobserver, %	7.5	14.3	10.0	13.5	11.0
Intraobserver, %	7.9	12.7	10.9	12.5	11.3

2D = two-dimensional.

Table 6. Interobserver and Intraobserver Variabilities for Longitudinal Strain Assessed by 2D Strain and TDI Strain

	Longitudinal 2D Strain	Longitudinal TDI Strain
Interobserver, %	7.5	13.7
Intraobserver, %	7.9	14.5

2D = two-dimensional; TDI = tissue Doppler imaging.

ity and measurement complexity have prevented strain analysis from gaining widespread use. With a more clinically oriented method, strain could finally become a standard echocardiographic tool.

In patients with HCM, 2D strain identified a subclinical global systolic dysfunction. Potential applications include differentiation of HCM from hypertensive cardiomyopathy or from athlete's heart, treatment monitoring, and eventually identification of preclinical disease in carriers of HCM mutations.

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