Evaluation of Myocardial Systolic Global and Segmental Function by Strain and Strain Rate Imaging in Patients with Hypertrophic Cardiomyopathy

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Abstract

Background- Hypertrophic cardiomyopathy (HCM) is a genetic cardiovascular disease with tremendous heterogeneity in its phenotypic expression. Global systolic function measured by ejection fraction (EF) does not seem to be a reliable marker for myocardial contractility in these patients. Tissue Doppler Imaging (TDI) indices, strain, and strain rate (SR) may be helpful in discriminating HCM from other mimetics. We decided to measure the regional myocardial function by strain and SR imaging to determine whether the regional myocardial function is related to the global systolic function and whether systolic strain and SR are reduced in all types of HCM.

Methods- Forty-one consecutive patients (20 women, mean age ± SD = 41 ± 13.0 years) with HCM were included. All the patients underwent complete clinical and echocardiographic evaluations. The global systolic function was measured visually and by Simpson's method. The strain and strain rate of 6 different basal and 6 mid-myocardial segments were measured offline by TDI. The mean values of these parameters were compared with normal reference values using one sample T-test leading to a significant reduction (P<0.05).

Results- The most common symptom was dyspnea. Nineteen (46.3%) patients were in NYHA function class II and 10 (24.4%) patients had a history of syncope. Mean left ventricular ejection fraction was 55% ± 4.9%. Considering an LVOT gradient >30mmHg, HCM was found in 18 (43.9%) patients. The mean myocardial wall thickness was 2 ± 0.7 cm. Mean of strain and strain rate were significantly reduced compare with normal values (P < 0.001). In all of the 12 segments, mean ± SD of strain was -10.6 ± 3.8 and that of strain rate was -0.73 ± 0.73.

Conclusion- TDI, strain, and SR analysis have better diagnostic yield in HCM patients. They are significantly reduced in all HCM patients, even in patients with a normal global systolic function. ***(Iranian Heart Journal 2010; 11 (3):6-12).***

Key words: hypertrophic cardiomyopathy ■ echocardiography ■ tissue Doppler

Hypertrophic cardiomyopathy (HCM) is the most common type of the genetic cardiovascular diseases characterized by cardiac hypertrophy, myocyte disarray, interstitial fibrosis, and left ventricular (LV) dysfunction. These patients usually exhibit LV relaxation and filling abnormalities despite a normal LV ejection fraction.[1-3]

A few recent studies have shown that despite a preserved global systolic function, the regional systolic function might be impaired in HCM.[4]

Tissue Doppler Imaging (TDI) is a well-established method for the quantification of the regional myocardial function.

It has been suggested that TDI predicts the development of HCM in subjects with subclinical disease, [5] (before development of hypertrophy), but the major limitation of TDI recording is that the measured velocity of an individual myocardial segment may be influenced by the motion of the adjacent muscle (tethering) or the translational motion of the heart. Accordingly, velocities measured by TDI may overestimate or underestimate the active component or function of the tissue.[6,7]

Strain ($\acute{\epsilon}$) and strain rate (SR) imaging can overcome this limitation by measuring the actual extent of stretching or contraction. Strain is the percentage change in length during myocardial contraction and is expressed as "%" in negative values, and strain rate is the rate of deformation, a strong index of the left ventricular contractility.[8,9] In this study, we decided to measure the regional myocardial function by $\acute{\epsilon}$ and SR imaging to determine whether the regional myocardial function is related to the global systolic function and whether systolic strain and SR are reduced in all types of HCM.

Methods

Patient population
Forty-one consecutive patients at a mean age of 41 years old with a diagnosis of HCM were included. The diagnosis of HCM was based on the conventional echocardiographic demonstration of a non-dilated, non-obstructed hypertrophic left ventricle in the absence of other cardiac or systemic diseases that might result in LV hypertrophy with the detection of myocardial hypertrophy (defined as having at least 15 mm LV wall thickness) in anyone of the lateral, anterior, inferior, septal, or apical segments.[10-12] They were classified as follows: Type I: HCM patients with hypertrophy limited to the anterior segment of the ventricular septum; Type II: hypertrophy of both anterior and posterior segments of the ventricular septum; Type III: involvement of both septum and free wall of

the LV; Type IV: atypical form, and Type V: apical HCM.[13]

Baseline data were age, sex, NYHA FC, familial history of syncope or arrhythmia, presence or absence of syncope or ventricular arrhythmia, LVH in ECG, ICD, or PPM history. Doppler echocardiograms were performed without changes in medications.

Echocardiography 2D and Doppler evaluation
The ultrasound device was a Vivid 7 Digital Ultrasound System (GE Vingmed, Horten, Norway) with a 2.5-MHz transducer. The studies were performed in the left lateral decubitus position in the apical four-chamber and the long- and short-axis parasternal views.

All the patients had complete M-mode, 2-D, and pulsed-wave Doppler studies from the standard approaches. The LV volume and EF were evaluated by visual assessment and Simpson's method and graded according to the American Society of Echocardiography guidelines.The presence of the systolic anterior motion of the mitral valve apparatus was noted if present in any 2-D or M-mode view. The severity of the mitral systolic anterior motion was assessed by the measurement of the septal-mitral valve distance at the onset of systole. The Doppler left ventricular outflow waveform was assessed for its contour and peak velocity. The presence of mitral valve regurgitation and its severity was noted if present in 2-D and color Doppler view according to the recommendations of the American Society of Echocardiography.

Tissue Doppler imaging
Upon completion of the standard echocardiographic measurements, TDI was performed. Digital data were transferred for offline analyses with the software incorporated in the Vivid 7 system to assess the regional systolic contraction in the 12 segments (base and mid-septal, lateral, inferior, anterior, and anteroseptal). Images

were acquired with a sweep speed of 100 cm/s, with gains and filters optimized. TDI-derived strain and SR measurements were sampled from 3 cardiac cycles at each location and the results were averaged (Figs. 1, 2). All the data were obtained by a cardiologist with a subspecialty in echocardiography.
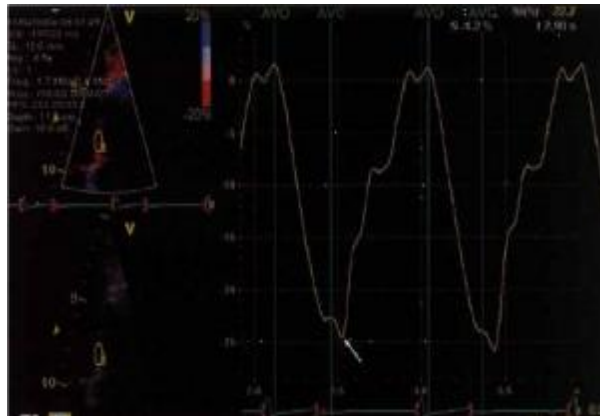

A

B

Fig. 1. A, View showing how to measure peak strain in the base of the anteroseptal segment. **B,** reduced peak systolic strain in an HCM patient
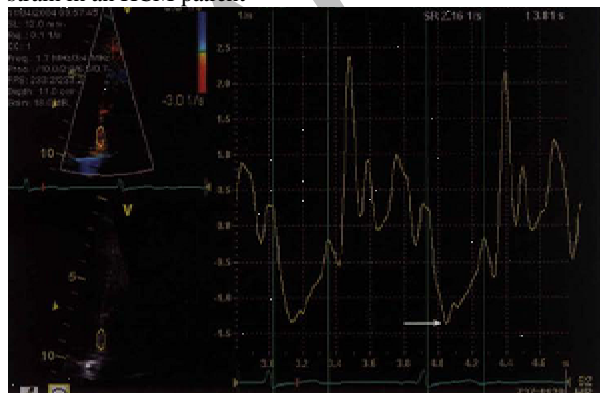

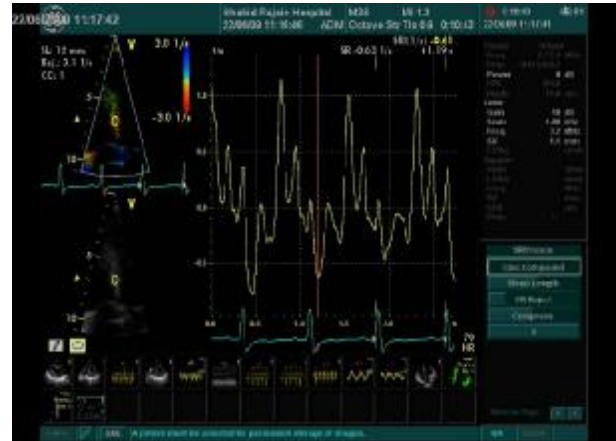**Fig. 2. A,** View showing how to measure peak strain rate at the base of the anteroseptal segment

Fig. 2. B, Reduced peak systolic strain rate in an HCM patient

Results

Statistical Analysis

We present the study findings as mean ± standard deviation for the interval and frequency (percentage) for the categorical data. One sample t-test was used for comparison between the strain and strain rate measures and their normal values. The strain and strain rate measures were compared by the Student t-test or Mann-Whitney U test between the subgroups. A P value < 0.05 was considered statistically significant. We used SPSS 15 for Windows (SPSS Corp., Chicago, Illinois) for the statistical analyses.

Background data

Forty-one patients (F/M = 20/21; mean age ± SD= 41 ± 15 years, range= 12 to 66 years) participated in the study. Nineteen (46.3%) patients were in NYHA function class II, four (9.8%) in function class III, and two (4.8%) in function class IV. The patients' most important signs/symptoms were syncope in 10 (24.4%), chest pain in four (9.8%), and dysrhythmia in 7 (17.1%) cases. Seven (17.1%) patients had a previously implanted ICD.

The mean myocardial wall thickness was 2 ± 0.7 cm, and mean LVEF was 55 ± 4.8%. Eighteen (45%) patients had an LVOT

gradient > 30 mmHg, categorized as hypertrophic obstructive cardiomyopathy (HOCM). Twenty-five (61%) patients had type III and six (14.6%) type IV HCM. Mean Em velocity was 5.44 ± 1.65 cm/sec, and Sm velocity was 5.70 ± 1.49 cm/sec (Table I). S-TDI values were reduced in all 12 segments. Table I presents the general echocardiographic findings in the study participants.

Table I. General echocardiographic findings of the patients

	Mean ± SD	Normal Value	P value
Strain base-septal	-9.4 ± 7.5	-22.85	< 0.001
Strain mid-septal	-9.9 ± 9.4	-24.54	< 0.001
Strain base-anteroseptal	-10 ± 6.9	-19.59	< 0.001
Strain rate base-septal	-0.70 ± 0.55	-1.88	< 0.001
Strain rate mid-septal	-0.76 ± 0.65	-1.73	< 0.001
Strain rate base-anteroseptal	-0.79 ± 0.68	-1.43	< 0.001

*Data are presented as mean ± standard deviation for interval and count (%) for nominal variables.

Table II. Echocardiographic strain and strain rate in cardiac basal segments of septal wall in cardiomyopathy patients, compared to normal values

Left ventricular ejection fraction (%)	55 ± 4.8
Left atrium area (cm²)	22 ± 8.6
Maximum septal thickness (cm)	2 ± 0.7
Asymmetric septal hypertrophy	27 (67%)
Left Ventricular outflow tract gradient (mmhg)	31.6 ± 34.4
Left Ventricular outflow tract gradient > 30 mmhg	18 (45%)
Systolic anterior motion of mitral valve	25 (64.1%)
Mitral regurgitation	34 (92.5%)
Right ventricular involvement	11 (28.2%)
E' velocity (cm/sec)	5.44± 1.65
S velocity (cm/sec)	5.70± 1.49

Echocardiographic strain and strain rate

We determined the strain and strain rates of 12 basal and middle segments. These parameters were compared with their normal values[14] (Figs. 1-4), and we found significantly smaller values compared with normal values (P < 0.001). In all the 12

segments, the mean ± SD of strain was -10.6 ± 3.8 and that of the strain rate was -0.73 ± 0.73. The mean of strain in our patients with HCM at the base and mid-septum was -9 .4% and -9.9 % (Fig. 5).
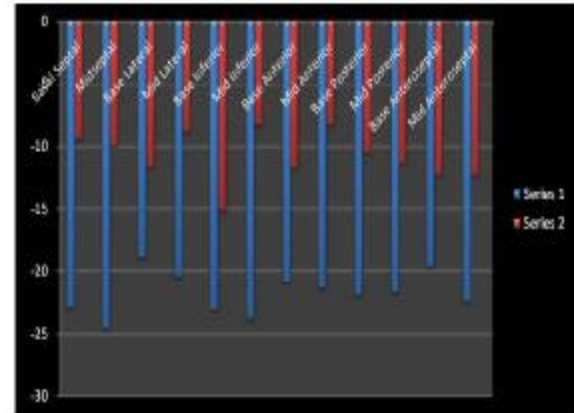

Fig. 3. Normal value (1) and calculated strain (%) in 12 LV segments in HCM cases (2) (all P-values <0.001)
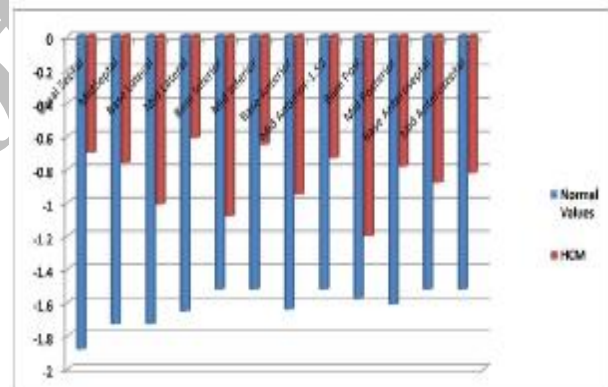

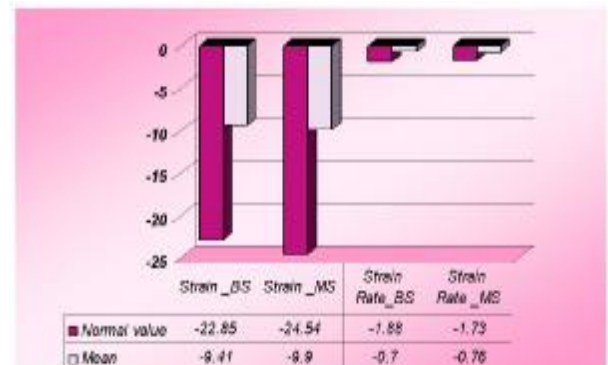**Fig. 4.** Strain rate (1/s) in 12 LV segments in HCM cases (all P-values <0.001).

Fig. 5. Normal values and calculated mean for strain and strain rate (1/s) in base and mid-septal segments in hypertrophic cardiomyopathy patients (all P-values < 0.001).

In addition, associations between these findings and the patients' clinical and

echocardiographic characteristics were investigated. There was an association between the strain rate of the base-septal segment and chest pain. The mean of the strain rate in patients with chest pain was -0.42±0.13 and in patients without chest pain it was -0.71±0.55 (P=0.02). Also, the mean strain of the 12 segments had an association with chest pain. The mean strain of the 12 segments was -10.8 ± 3.8 in patients without and -8.0 ± 1.4 in patients with chest pain (P=0.015). The regional myocardial systolic strain of the mid anterior and anteroseptal segments were lower in HCM patients with atrial fibrillation compared to sinus rhythm (Fig. 6), and patients with syncope or ICD insertion had significantly lower mid-lateral strain compared with HCM patients without ICD or syncope (Fig. 7).

Fig. 6. Comparison between mean value of significant results considering history of atrial fibrillation (AF) in hypertrophic cardiomyopathy strain values (%) (all P-values < 0.05).
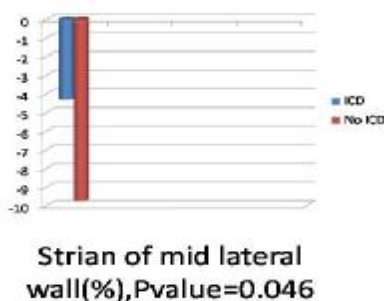

Strian of mid lateral wall(%),Pvalue=0.046

Fig. 7. Comparison of significant results regarding history of ICD in HCM patients (P value<0.05)

Discussion

Our study showed that despite a preserved global LV systolic function measured by EF (55.85 ± 4.86 %), the S-TDI, strain and SR values were significantly reduced in all the 12 myocardial segments. The mean of strain was -10.6 ± 3.8 and that of the strain rate was -0.73 ± 0.73 in our patients with HCM, which was independent from the type of HCM. Our results are consistent with the Yang et al. study,[16] which suggested that despite a normal global LV systolic function, the regional contractile dysfunction often existed in most patients with HCM. That study only evaluated the septal and lateral walls and found markedly decreased mid-septal longitudinal strain compared to the other segments of the septal and lateral walls and correlated it with the degree of septal hypertrophy. Other studies have found significantly decreased systolic wall thickening (strain) in patients with HCM compared to healthy patients, with the greatest impairment of segment function in the regions of the highest end-diastolic wall thickness.[17-19] TDI, in addition to its role in establishing the diagnosis of HCM in patients with left ventricular hypertrophy (LVH), can identify abnormalities in myocardial contraction and relaxation velocities before hypertrophy is manifest. In a TDI study, myocardial contraction and relaxation velocities were significantly reduced compared to controls in both patients with overt HCM and those with HCM mutations without LVH.[5,20] TDI is also useful in distinguishing HCM from athlete's heart or HCM from hypertrophy caused by hypertension.[21,22] We found even significantly lower strain values in the cases with chest pain, atrial fibrillation, and history of syncope or ICD insertion. These values were reduced in some segments, not all of which can be due to the anisotropic distribution of conventional risk factors. The mean strain in our patients with HCM at the base and mid-septum was -9.4 and -9.9%, which was consistent with the cutoff value of -10.6 % suggested for discriminating between HCM and hypertensive heart disease.[23]

The main limitation of our study was that we did not have a control group, so we could not determine cut points for the diagnosis of HCM. Instead, we used normal values from other references. Strain and strain rates in our study mostly reflected the longitudinal myocardial motion without considering the influence of the motion of the entire heart; and like other echocardiographic methods, its value was influenced by the alignment with the Doppler beam incident angle. However, in our study, attention was paid to make segments measured as parallel to the echocardiography beam as best possible.

Conclusion

It seems that the global systolic function as measured by EF is not a reliable marker for myocardial contractility in patients with HCM. TDI-derived parameters, i.e. S velocity, strain, and SR, have a better diagnostic yield. They are significantly reduced in HCM patients, even in patients with subtle myocardial contractility dysfunction.

Conflict of Interest
No conflicts of interest have been claimed by the authors.

References

1. Wigle ED, Rakowski H, Kimball BP, Williams WG. Hypertrophic cardiomyopathy: clinical spectrum and treatment. Circulation 1995; 92: 1680–1692.

2. Hanrath P, Mathey DG, Siegert R, Bleifeld W. Left ventricular relaxation and filling pattern in different forms of left ventricular hypertrophy: an echocardiographic study. Am J Cardiol 1980; 45: 15-23.

3. Spirito P, Maron BJ, Chiarella F, Bellotti P, Tramarin R, Pozzoli M, et al. Diastolic abnormalities in patients with hypertrophic cardiomyopathy: relation to magnitude of left ventricular hypertrophy. Circulation 1985; 72: 310-316.

4. Hayashida W, Kumada T, Kohno F, Noda M. Use of strain imaging in detecting segmental dysfunction in patients with hypertrophic cardiomyopathy. Am Soc Echocardiogr 2003;16: 233-9.

5. Nagueh SF, McFalls M, Meyer D, Zoghbi W, Tam JW, Quiñones MA, Roberts R, Marian AJ. Tissue Doppler imaging predicts the development of hypertrophic cardiomyopathy in subjects with subclinical disease. Circulation 2003; 108: 395.

6. Price DJA, Wallbridge DR, Stewart MJ. Tissue Doppler imaging: current and potential clinical applications. Heart 2000; 84 (Supplement 2):11.

7. Chitman D, Barattamtsac S, Fernandez H, Marani A, Ferroni F, Bilbao J, Kotliar C, Utrimtsac D, Hita A: Clinical value of tissue Doppler analysis of systolic phase contraction in the discrimination of physiological and pathological ventricular hypertrophy. Rev Argent Cardiol 2006; 74: 129-135.

8. Sutherland GR, Di Salvo G, Claus P, et al: Strain and strain rate imaging: a new clinical approach to quantifying regional myocardial function. J Am Soc Echocardiogr 2004; 17: 788.

9. Yip G, Abraham T, Belohlavek M, Khandheria BK: Clinical applications of strain rate imaging. J Am Soc Echocardiogr 2003; 16:1334.

10. Maron BJ. Hypertrophic cardiomyopathy: a systematic review. JAMA 2002; 287: 1308-1320.

11. Elliot AP, McKenna WJ. Hypertrophic cardiomyopathy: seminar. Lancet 2004; 363: 1881-1891.

12. Maron BJ, McKenna WJ, Danielson GK, Kappenberger LJ, Kuhn HJ, Seidman CE, et al. American College of Cardiology/European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy; a report of American College of Cardiology foundation task force on clinical expert consensus documents and the European Society of Cardiology committee for practice guidelines. Eur Heart J 2003; 24: 1965-1991.

13. Maron BJ, Gottdiener JS, Epstein SE: Patterns and significance of distribution of left ventricular hypertrophy in hypertrophic

cardiomyopathy. Am J Cardiol 48: 418-428, 1981.

14. Normal values according to Kowalski & Andersen studies that were reported in text book of echocardiography (Sautherland.

15. Yang H, Sun JP, Lever HM, Popovic ZB, Drinko JK, Greenberg NL, et al. Use of strain imaging in detecting segmental dysfunction in patients with hypertrophic cardiomyopathy. J Am Soc Echocardiogr 2003;16: 233-9.

16. Usyk TP, Omens JH, McCulloch AD. Regional septal dysfunction in a three-dimensional computational model of focal myofiber disarray. Am J Physiol Heart Circ Physiol 2001; 281: 506-514.

17. Dong SJ, MacGregor JH, Crawley AP, McVeigh E, Belenkie I, Smith ER, et al. Left ventricular wall thickness and regional systolic function in patients with hypertrophic cardiomyopathy: a three-dimensional tagged magnetic resonance imaging study. Circulation 1994; 90: 1200-209.

18. Bergey PD, Axel L. Focal hypertrophic cardiomyopathy simulating a mass-MR tagging for correct diagnosis. Am J Roentgenol 2000; 174: 242-244.

19. Nagueh SF, Bachinski LL, Meyer D, Hill R, Zoghbi A, Tam JW, et al. Tissue Doppler imaging consistently detects myocardial abnormalities in patients with HCM and provides a novel means for an early diagnosis before and independently of hypertrophy. Circulation 2001; 104: 128-130.

20. Pelliccia A, Maron BJ, De Luca R. Remodeling of left ventricular hypertrophy in elite athletes after long-term deconditioning. Circulation 2002; 105: 944-949.

21. Nunez I. Zamorano JL, Perez De Isla L. Differences in regional systolic and diastolic function by Doppler tissue imaging in patients with hypertrophic cardiomyopathy and hypertrophy caused by hypertension. J Am Soc Echocardiogr 2004; 17: 717 -722.

22. Kato TS, Noda A, Lzawa H. Discrimination of nonobstructive hypertrophic cardiomyopathy from hypertensive left ventricular hypertrophy on the basis of strain rate imaging by tissue Doppler ultrasonography. Circulation 10: 3808. 7.