Two Dimensional Strain Profiles in Patients with Physiologic and Pathologic Hypertrophy and Preserved Left Ventricular Systolic Function: A Comparative Analysis

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Article summary

Focus:

- Differentiating variant forms of left ventricular hypertrophy using conventional 2D echocardiography can be challenging
- Data on the usefulness of 2D strain echocardiography to differentiate hypertrophic cardiomyopathy from hypertensive left ventricular hypertrophy (LVH) are sparse

Key message

- Longitudinal strain is significantly attenuated in patients with HCM compared to other variant forms of LVH
- 2D longitudinal strain mapping (Automated Function Imaging) allows rapid characterization of regional and global systolic function and has the potential to differentiate HCM from variant forms of LVH
- Left ventricular morphological and tissue Doppler parameters are better suited to differentiate the athlete heart from pathologic LVH

Strengths and Limitations

- Largest head-to-head comparative 2D strain analyses of variant forms of LVH
- Findings only applicable individuals with preserved left ventricular ejection fraction

Two Dimensional Strain Profiles in Patients with Physiologic and Pathologic Hypertrophy and Preserved Left Ventricular Systolic Function: A Comparative Analyses

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Abstract

Objective: This study was designed to examine the utility of 2-dimensional strain or speckle tracking imaging (2DS) to typify functional adaptations of the left ventricle in variant forms of left ventricular hypertrophy (LVH).

Design: Cross-sectional study.

Setting: Urban tertiary care academic medical centers

Participants: A total of 129 subjects, 56 with hypertrophic cardiomyopathy (HCM), 34 with hypertensive left ventricular hypertrophy (H-LVH), 27 professional athletes with LVH (AT-LVH) and 12 healthy controls in sinus rhythm with preserved left ventricular systolic function

Methods: Conventional echocardiographic and Tissue Doppler examinations were performed in all study subjects. Bi-dimensional acquisitions were analyzed to map longitudinal systolic strain (Automated Function Imaging, AFI, GE Healthcare) from apical views.

Results: Subjects with HCM had significantly lower regional and average global peak longitudinal systolic strain (GLS-avg) compared to controls and other forms of LVH. Strain dispersion index (SDI), a measure of regional contractile heterogeneity was higher in HCM compared to the rest of the groups. On receiver operator characteristics analysis, GLS-avg had excellent discriminatory ability to distinguish HCM from H-LVH (AUC 0.893, $p<0.001$) or AT-LVH AUC (0.920, $p<0.001$). Tissue Doppler and LV morphologic parameters were better suited to differentiate the athlete heart from HCM.

Conclusions: 2D strain (AFI) allows rapid characterization of regional and global systolic function and may have the potential to differentiate HCM from variant forms of LVH.

Key Words: 2 D strain, hypertrophic cardiomyopathy, left ventricular hypertrophy

Introduction

Differentiating variant forms of left ventricular hypertrophy using conventional echocardiography can be clinically challenging and in the case of hypertrophic cardiomyopathy (HCM) carries serious clinical implications[1].

HCM is characterized by myofibrillar disarray, disruption of structural myocardial architecture, chaotic myofiber alignment, patchy replacement fibrosis and intercellular matrix deposition[2, 3, 4] in contradistinction to the parallel disposition of myocytes and limited extent of fibrosis observed in hypertensive left ventricular hypertrophy (LVH)[5]. Considerable phenotypic heterogeneity in the distribution and magnitude of LVH is characteristically observed in HCM patients [6, 7], leading to regional perturbations of contractile function.

2D myocardial strain imaging is a relatively new tool that has the potential to characterize regional contractile function and has been used to typify the intramural deformation in HCM [8, 9, 10], however, its utility in discriminating HCM from other forms of LVH has not been adequately studied.

In the present study, we sought to characterize and compare functional adaptations of the left ventricle in various forms of left ventricular hypertrophy by mapping global and regional longitudinal 2D strain (2D strain), in subjects with preserved systolic function.

Methods

One hundred twenty nine patients (mean age 45.1±16.2, 66% males), 56 consecutive patients with HCM, 34 patients with hypertensive left ventricular hypertrophy (H-LVH), 27 professional athletes with LVH (AT-LVH) and 12 healthy controls, exhibiting sinus rhythm and preserved regional and global (left ventricular systolic ejection fraction, EF>55%) systolic function were prospectively studied.

Inclusion criteria for pathologic LVH were as follows: A) HCM: consecutive patients with known familial HCM and/or unexplained LVH in the absence of identifiable cardiac or systemic cause, exhibiting a septal wall thickness >15 mm and septal–posterior wall thickness ratio >1.3 [7] and B) Hypertensive LVH (H-LVH): consecutive, asymptomatic, known hypertensive patients (diastolic blood pressure> 90 mm Hg before treatment) exhibiting at least moderate left ventricular hypertrophy (septal or posterior wall thickness>13.0 mm) were selected in an attempt to closely approximate magnitude of LVH observed in the HCM subgroup. All included athletes were highly trained elite basketball players, participating at the National Basketball Association league level and engaged in high intensity endurance as well as isometric exercise training. Patients with abnormal regional or global systolic function (LVEF <55%), significant valvular heart disease, prior infarction or known obstructive coronary artery disease, were excluded. The Institutional Review Board of the University approved the protocol in compliance with the Health Insurance Portability and Accountability Act (HIPAA) prior to data utilization.

All subjects underwent standard echocardiographic exams. Two dimensional echocardiographic (2D) measurements which included septal and posterior wall thickness, left ventricular end-diastolic and systolic dimensions and left atrial dimensions were obtained in the left lateral position. All conventional and strain data was acquired using a standard commercial ultrasound machine (Vivid 7, GE Vingmed, Horten, Norway) with a 2.5- or 3.5-MHz.multiphased array probe and the images digitally stored for offline analysis.

Left ventricular outflow tract (LVOT) obstruction was defined as the presence of a resting late peaking LVOT gradient ≥ 30 mm Hg (spectral Doppler). Relative wall thickness (RWT) was calculated from linear dimensions in standard manner and left ventricular ejection

fraction was calculated using the Simpsons biplane method[11]. Color-coded TDI from the apical four chamber view was used to determine the septal annular velocities, including systolic (S') and early (E') and late (A') diastolic velocities, in accordance with American Society of Echocardiography (ASE) guidelines [11].

Strain Analysis

2D strain using ultrasound speckle tracking was utilized to characterize longitudinal systolic strain. Images were acquired at 70-100 frames per second at end-expiration in the apical long (LAX), two (2C) and four (4C) chamber views and analyzed in blinded fashion, offline using a dedicated software package (Automatic Function Imaging, EchoPac.PC; GE Healthcare, Waukesha, Wisconsin).

2D-strain is a novel non-Doppler based imaging technology that can estimate longitudinal systolic strain from standard bidimensional grayscale acquisitions (Fig 1). Using the AFI program [(Automated Function Imaging software (AFI), EchoPAC, GE-Vingmed)], a point-and-click approach was utilized to identify 3 anchor points (2 basal and 1apical), following which, the software tracked the endocardial contour automatically. For each of the individual apical views, tracking was visually inspected throughout systole to ensure adequate border tracking and the endocardial contours adjusted manually if necessary, to facilitate tracking. The LV was divided into 17 segments and automated measurements of segmental systolic longitudinal strain values in the apical long, two and four chamber views were then used to generate a 17- segment polar map (Figure 2). Patients with suboptimal 2D image quality and/or poor speckle tracking, defined as inadequate tracking of >1/17 ventricular segments (7 patients) were excluded from the analysis.

For descriptive purposes, the following nomenclature was utilized:

- Global LV longitudinal strain (GLS): auto-computed, partitioned according to echo-views (GLS- LAX, GLS-4C, GLS-2C, Figure 1).
- Average Global LV longitudinal strain (GLS-avg): auto-computed, average of GLS-LAX, GLS-4C and GLS-2C. A measure of **overall** systolic longitudinal strain.
- Global longitudinal strain dispersion index (SDI): calculated as the average of the standard deviation values of mean segmental longitudinal strain in the basal, mid and apical segments

In summary, broadly two characteristics of LV strain were studied;

1. Indices of magnitude of longitudinal LV strain: e.g. GLS-avg, global LV strains in different echo views. Higher negative values corresponded to higher strain (contractility).
2. Indices of homogeneity of longitudinal LV strain: Strain dispersion index (SDI). Higher values corresponded to heterogeneous strain patterns.

Finally, left ventricular wall thickness corresponding to the mid portions of the 17 constitutive polar map segments was measured perpendicular to the long axis of each segment, from the apical views. Thickness dispersion index (ThDI) was then computed as the average of the SDs of segmental thickness values at the basal, mid and apical layers.

Statistical Analysis

Mean and standard deviation were used as appropriate for continuous variables Differences of means or proportion (%) among study subgroups were assessed through Mann-Whitney test or Chi-square test for continuous and categorical variables respectively. To assess the discriminatory ability of various echo parameters, Receiver-operator characteristic (ROC) curve analysis was performed where variables with higher area under curve (AUC) values would indicate a superior ability to distinguish HCM from other variants of LVH. A two sided p value of ≤ 0.05 was considered statistically significant.

To assess reproducibility, strain parameters were independently measured by two blinded observers on 15 randomly selected patients. Interobserver correlation coefficients (ICC) were calculated using the Spearman correlation analysis. All statistical analyses were performed using the SPSS 13.0 software package (SPSS, Inc., Chicago, Illinois).

Results

Baseline characteristics and conventional echo parameters are depicted in Tables 1. Patients with HCM were older and had higher interventricular septal thickness and IVS/PW ratio compared to other groups. Most frequently involved territories exhibiting prominent LVH in HCM patients were septal (78.6%), followed by apical (16%) and concentric LVH (5.4%).

E' was significantly lower in patients with HCM compared to hypertensives or athletes, suggesting abnormal longitudinal diastolic function. Despite preserved systolic function across groups, S' in the HCM cohort was significantly lower than patients with H-LVH or athletes. H-LVH and HCM subsets had lower E' velocity compared to athletes and controls with the lowest diastolic velocities observed in the HCM cohort (Table 1).

Table 1. Baseline characteristics of the study population

	Control (Healthy adults) N=12	HCM N=56	AT-LVH* N=34	H-LVH ** N=27	p value†
Demographics					
Age (years)					
Mean ± SD	29.3 ±6.3	54.9±14.9	28.8 ±7.2	47.6 ±10.6	a,c,d,e,f
Range (minimum-maximum)	20 □ 45	25 □ 89	20 □ 49	25 □ 68	
Gender (male) %	11 (91.7%)	29 (49.2%)	27 (100%)	20 (58.8%)	a,c,d,e,f
Height (m)	1.73 ±0.04	1.7±0.11	1.99 ±0.12	1.74 ±0.12	b,d,e
Weight (kg)	76.2 ±4.5	80.9±23.9	103 ±11.7	82.8 ±25	b,d,e
Body surface area (m^2)	1.9 ±0.11	1.98±0.32	2.4 ±0.22	1.9 ±0.29	b,d,e
Blood pressure (mmHg)					
Systolic	119 ±5	133 ±19	133±19	149 ±16	a,c,d.f
Diastolic	75 ±4	76 ±10	76±10	84 ±12	c,f
Heart rate (bpm)	71 ±10	73±13	64 ±10	75 ±9	d
QRS duration (ms)	101 ±4	105±15	96 ±8	97 ±14	b,d,f
Corrected QT interval (QTc) ms	384 ±31	460±22	404 ±18	445 ±32	a,c,d,e
2-D Echocardiography parameters					
LA dimension					
diameter, cm	3.2 ±0.4	4.2±0.6	3.6 ±0.4	3.8 ±0.5	a,c,e
indexed for BSA, cm/m2	1.7 ±0.2	2.2±0.5	1.5 ±0.2	2 ±0.4	a,c,d,e
LV dimensions					
end-diastolic diameter, cm	4.7 ±0.5	4±0.8	5.3 ±0.5	4.1 ±0.7	a,c,d,e,f
end-systolic diameter, cm	3.1 ±0.5	2±0.6	3.2 ±0.9	2.1 ±0.7	a,b,c,d,e
LV Fractional shortening (%)	34.1 ±10.4	50.3±12.5	39.6 ±15	48.4 ±11.9	a,c,e
LV Ejection fraction (%)	63 ± 2	65 ± 5	61 ± 4	64 ± 5	e
Septal wall thickness (mm)	8.8 ± 1.4	23.3 ± 4.9	11.5 ± 1.1	16.3 ± 2.3	a,b,c,d,e,f
LV posterior wall thickness (mm)	8.6 ± 1.4	15.6 ± 4	10.5 ± 1.2	15.2 ± 2.5	a,b,c,d,e
Septum-posterior wall ratio	1 ± 0.3	1.5 ± 0.4	1.1 ± 0.2	1.1 ± 0.1	a,e,f
Relative wall thickness (RWT)	0.4 ± 0.1	0.9 ± 0.4	0.4 ± 0.1	0.8 ± 0.3	a,c,d,e
Tissue Doppler imaging:					
S' wave (cm/s)	6.6 ±0.8	4.7±1.2	6.9 ± 1.3	5.9 ±1.3	a,e,f
E′ wave (cm/s)	9.8 ±1.5	3.1±1.7	10.0 ± 1.7	5.3 ±1.7	a,c,d,e,f
A′ wave (cm/s)	6.6 ±1.1	4.9±1.8	5.9 ± 1.8	6.4 ±2.1	f
Global thickness dispersion index (ThDI)	1.22 ±0.32	2.35±0.84	1.12 ±0.31	1.52 ± 0.48	a,d,e,f

Data are presented as Mean ± SD. *=professional athletes with physiological left ventricular hypertrophy. **=hypertensive left ventricular hypertrophy †=p values were obtained through Mann-Whitney test or chi-square as appropriate. a=statistically significant ($p<0.05$) difference between controls vs. HCM; b= statistically significant ($p<0.05$) difference between controls vs. AT-LVH; c= statistically significant ($p<0.05$) difference between controls vs. H-LVH;d= statistically significant ($p<0.05$) difference between AT-

LVH vs. H-LVH; e= statistically significant ($p<0.05$) difference between AT-LVH vs. HCM; f= statistically significant ($p<0.05$) difference between H-LVH vs. HCM;ns=no significant difference upon subgroup comparison; Abbreviations: HCM=hypertrophic cardiomyopathy; LV=left ventricle; LA=left atrium; BSA=body surface area.

Patients with HCM had the highest segmental LV thickness dispersion and thickness dispersion index (Table 1).

Longitudinal strain profiles

A total of 2,193 segments were analyzed and adequate tracking was achievable in 2185 (99 %) segments. The magnitude and homogeneity of longitudinal strain among groups is depicted in Figures 2 & 3. As shown in the box-plots (Fig 3A), subjects with HCM had lower median and quartile global longitudinal strain but higher dispersion when compared to hypertensive and athletic LVH. On the other hand, subjects with H-LVH had similar GLS-avg but higher strain dispersion values in comparison to AT-LVH. In addition, a scatter plot of strain magnitude vs. dispersion (Fig 3B) showed clustering of HCM subjects in the higher SDI -lower GLS-avg corner. AT-LVH cases were superimposed on control subjects suggesting similarities in strain profiles in these groups. In contrast, H-LVH cases were spread out horizontally suggesting similar GLS-avg but higher SDI.

While an increasing basal to apex strain gradient in patients with hypertension and athletes was observed, no such gradient was noted in patients with HCM (Table 2).

Table 2. Comparison of longitudinal strain and strain dispersion in the overall study population

Variable	Controls N=12	HCM N=56	AT-LVH* N=27	H-LVH** N=34	p value†

Segmental average longitudinal strain (%)					
Basal	-18.4 ±2.4	-8.2±5	-16.3 ±2.4	-15.3 ±2.2	a,c,e,f
Mid-LV	-19 ±2	-9.2±4.8	-17.8 ±1.9	-17.1 ±3	a,e,f
Apical	-19.2 ±3.3	-12.3±9	-21.1 ±3.5	-22.1 ±4.9	a,e,f
Global LV longitudinal strain (%)					
LAX	-17.6 ±2.6	-11.2±5	-17.1 ±2.9	-17.7 ±3.2	a,e,f
4C	-18.4 ±1.6	-11.2±4.2	-17.3 ±2.5	-17.3 ±3.8	a,e,f
2C	-19.9 ±2.7	-11.1±4.2	-19 ±2.3	-18.5 ±4.2	a,e,f
Global LV longitudinal strain average (GLS avg,%)	-18.7 ±1.8	-11.2±4.2	-17.8 ±2.2	-17.8 ±3.1	a,e,f
Global longitudinal strain dispersion index (SDI)	2.9 ±0.8	4.6±1.7	2.6 ±0.5	3.5 ±1	a,c,d,e,f

Data are presented as Mean ± SD. *=professional athletes with left ventricular hypertrophy; * *=hypertensive left ventricular hypertrophy; †=p values were obtained through Mann-Whitney test or chi-square as appropriate.

a=statistically significant ($p<0.05$) difference between controls vs. HCM; b=statistically significant ($p<0.05$) difference between control vs AT-LVH; c=statistically significant ($p<0.05$) difference between control vs H-LVH

d=statistically significant ($p<0.05$) difference between AT-LVH vs. H-LVH; e=statistically significant ($p<0.05$) difference between AT-LVH vs HCM ;f=statistically significant ($p<0.05$) difference between H-LVH vs HCM

ns=no significant difference upon subgroup comparison; Abbreviations: HCM=hypertrophic cardiomyopathy; LV=left ventricle

Significantly lower GLS-avg was observed in patients with HCM (-11.2 ±4.2%) compared to H-LVH (-17.8 ±3.1%) and professional athletes (-17.8 ±2.2%) respectively. No significant differences were noted in GLS-avg between AT-LVH, H-LVH and controls. SDI was significantly higher in patients with HCM compared to the other groups (Table 2).

To summarize (Figure 3, Table 2 and Table 3), while no particular LV segment or wall was consistently involved among the HCM patients, high variability (i.e. higher SDI) and attenuated longitudinal strain (i.e. lower GLS-avg) was the hallmark in individual patients.

Discriminating HCM from variant forms of LVH

To assess the discriminatory ability of various echo parameters to distinguish HCM from other variants of LVH, receiver-operator characteristic (ROC) curve analysis was performed in separate study subgroups (Table 3). In the model with HCM & AT-LVH study subjects, as might be expected, GLSs avg had comparable discriminatory ability with other conventional echo parameters namely septal wall thickness, posterior wall thickness, indexed LA size, S' and E′. In the model with HCM & H-LVH study subjects, however, GLS-avg performed better than conventional echo parameters, suggesting that GLSavg may have clinical applicability to distinguish HCM from hypertensive LVH.

For differentiating HCM from other forms of LVH, the highest accuracy was achieved with a GLS avg cut off value of -14.3 % (sensitivity: 77 % and specificity: 97 %, predictive accuracy: 87%). At this cut off value, a high diagnostic accuracy was achievable even when GLS was obtained from limited echo views (detailed data not shown). Further, at a cut off value

of -11.5%, a specificity of >99% was achievable in all views (i.e. LAX, 2C, 4C and GLS-avg) with sensitivities in the range of 50-57%.

Table 3. Receiver operator characteristics analysis for various echocardiography parameters to distinguish HCM from other left ventricular hypertrophy variants

	Between HCM and AT-LVH*		Between HCM and H-LVH**	
	Area (95% Confidence Interval)	*p value*	*Area (95% Confidence Interval)*	*p value*
Septal wall thickness, mm	1.000 (0.998 — 1.001)	<0.001†	0.869 (0.788 — 0.949)	<0.001†
LV posterior wall thickness, mm	0.908 (0.843 — 0.972)	<0.001†	0.479 (0.354 — 0.605)	0.76
Indexed LA dimension, cm/m^2	0.921 (0.861 — 0.981)	<0.001†	0.591 (0.459 — 0.722)	0.18
LV Fractional shortening (%)	0.714 (0.580 — 0.848)	0.003†	0.511 (0.381 — 0.641)	0.87
ThDI	0.952 (0.909 — 0.995)	<0.001†	0.827 (0.734 — 0.920)	<0.001†
Tissue Doppler imaging:				
S' wave (cm/s)	0.912 (0.987 — 0.837)	<0.001†	0.709 (0.824 — 0.594)	0.002†
E′ wave (cm/s)	0.995 (1.005 — 0.984)	<0.001†	0.818 (0.906 — 0.731)	<0.001†
A′ wave (cm/s)	0.666 (0.796 — 0.535)	0.02†	0.719 (0.833 — 0.606)	0.001†
GLS-avg,%	0.920 (0.862 — 0.978)	<0.001†	0.893 (0.827 — 0.960)	<0.001†
SDI	0.890 (0.818 — 0.961)	<0.001†	0.671 (0.552 — 0.789)	0.01†

*=Professional athletes with physiological left ventricular hypertrophy; **=Hypertensive left ventricular hypertrophy; †=statistically significant ($p<0.05$) .Abbreviations: HCM=hypertrophic cardiomyopathy; LV=left ventricle; LA=left atrium; BSA=body surface area, ThDI= Globalthickness dispersion index, GLS-avg=Global longitudinal strain average, SDI= Global longitudinal strain dispersion index

In all, LVOT obstruction was observed in 15 out of 56 (26.7%) patients with HCM (defined as a resting late peaking LVOT gradient ≥ 30 mm Hg); this subgroup displayed higher GLSavg compared to non-obstructive HCM cases (mean ± SD, 12.9 ± 3.9 vs. 9.2 ± 3.2

respectively, p 0.001). In a separate ROC curve analysis; when only obstructive HCM cases were analyzed, AUC for GLSavg remained excellent (AUC= 0.872, 95% CI 0.796 − 0.948, p<0.001). None of the other groups exhibited LVOT obstruction.

Inter-examiner agreement for strain parameter measurements were excellent for both GLPS-avg (Mean ±SD -12.5±8.2, -14.5±3.3 for observer 1 and 2 respectively; ICC: 0.879, P<0.001; 0.982, P<0.001) and SDI (mean ± SD: 4.1±1.9 and 3.7±1.8) , for observer 1 and 2 respectively, ICC: 0.982, P<0.001).

Discussion

This study assessed the role of 2D strain in the characterization of global and regional function and its potential for differentiating HCM from other variants of LVH, using a semiautomated strain mapping software program (AFI). Unlike prior reports[8, 12], this study is the first and largest of its kind to provide a comprehensive, head-to-head, comparative 2D strain analyses (using a 17-segment model) in variant forms of LVH. Our findings indicate that in addition to markedly attenuated global and regional longitudinal strain, patients with HCM characteristically exhibit significant heterogeneity or non-uniformity of regional function and form (as evident from the strain and thickness dispersion indices respectively) and can be differentiated from hypertensive LVH that is typified by relatively preserved global systolic strain.

We observed a statistically significant lower average global and segmental longitudinal strain in patients with HCM compared to hypertensive LVH. Similarly, we found that strain and thickness dispersion indices (surrogate markers of functional and morphologic heterogeneity

respectively) tracked in parallel, being most pronounced in HCM and least deranged in athletes and controls.

Collectively, these findings likely represent regional myocardial disarray and replacement fibrosis, characteristic of HCM that lead to nonuniformity of morphology, contractile function and altered intramural deformational mechanics. Our observations complement results from a prior quantitative study of autopsy hearts that reported a 72% higher level of stainable collagen in HCM hearts compared to hypertrophied control hearts and also corroborate previously reported associations between fibrosis and regional contractile dysfunction using gadolinium enhanced cMRI and MRI myocardial tagging techniques [13, 14]. Interestingly, altered ultrasonic longitudinal systolic strain rate patterns were recently shown to accurately identify areas of regional fibrosis mapped by cMRI in a variety of conditions including HCM [15].

Comparison with previous studies of Tissue Doppler strain vs. 2D strain in HCM.

Although HCM is associated with depressed longitudinal or axial ventricular function, global systolic function (assessed by radial parameters such as ejection fraction or fractional shortening) is typically normal or hyperdynamic in the large majority[16]. Tissue Doppler Imaging (TDI) permits appraisal of axial ventricular function and has been proposed for the preclinical diagnosis of HCM[17] as well as the differentiation of physiologic from pathologic LVH[18]. However, TDI is vulnerable to translation and tethering [19, 20] and may not reliably discriminate between variants of pathologic LVH. TDI-strain (derived from TDI velocity data) is superior to TDI for regional function analysis, but suffers from inherent limitations of the

Doppler technique (angle dependency), requires image acquisition at high frame-rates(>100 fps) and is exquisitely sensitive to noise artifact[21].

Weidemann et al first described focally attenuated longitudinal" tissue Doppler"-derived strain and strain rate in the midseptum of a patient with nonobstructive HCM [22]. Yang et al extended these findings comparing healthy controls with HCM and reported a significant reduction in mid septal strain (ε) compared to adjacent myocardial segments. Over half of the HCM cohort demonstrated paradoxical strain or systolic expansion and the extent of strain attenuation correlated with the magnitude of LVH in affected segments[9]. A later tissue Doppler-derived strain study by Kato et al, correlated strain data with endomyocardial biopsy and suggested that an epsilon (sys) strain cutoff value of -10.6% discriminated between HCM and H-LVH with a sensitivity of 85.0%, and specificity of 100.0% [10]. While, tissue Doppler-based strain imaging suffers from several disadvantages alluded to earlier [8, 21], tissue Doppler mitral annular E' velocity along with other left ventricular morphologic parameters (in accord with prior literature), were noted to be superior to GLS for differentiating athlete LVH from HCM (Tables 2 and 3)

In comparison, 2D strain imaging or speckle tracking imaging is a novel imaging modality that circumvents some of the above limitations and provides strain data rapidly and reproducibly. Unlike TDI, speckle 2D strain imaging is angle-independent and so permits strain measurements in the longitudinal and circumferential planes. Of note, the ability of 2DS to assess myocardial shortening in the apical segments (particularly relevant in apical HCM variants) represents yet another advantage of 2DS over TDI[23]. 2D strain has been extensively validated against sonomicrometry and tagged-magnetic resonance imaging (MRI)[24]

Only a handful of studies to date have profiled intramural deformational patterns or evaluated the potential usefulness of 2 D strain imaging to differentiate variant forms of LVH. Serri et al first reported an attenuation of longitudinal, transverse, radial and circumferential strain in a cohort of patients with HCM, compared to reference normals, despite preserved systolic function. Excellent correlation between tissue Doppler and 2D strain techniques was reported for longitudinal strain measurements along with superior reproducibility for the latter technique[8]. Similarly, reductions in "radial and circumferential "strain, along with significant LV dyssynchrony were reported in another descriptive study comparing HCM to hypertensive heart disease[25]. More recently, Richand et al concluded that reductions in strain parameters differentiated HCM from physiologic LVH in professional soccer players[12]. These authors suggested that a longitudinal basal inferoseptal (**a single segment**) strain value of -11% identified HCM from physiologic LVH with a sensitivity of 60% and specificity of 96%, predictive accuracy 78 %. In contradistinction, our data are more robust, obtained from a much larger series of subjects (n=129) and based on average longitudinal strain derived from 17 segments. Our findings may have wider applicability, as we included hypertensive LVH in addition to athlete LVH cohorts in a head-to-head comparative analysis. Of note, our observations are in close agreement with the Kato study that reported similar cutoff values (albeit using tissue Doppler) in a unique study that used endomyocardial biopsy as the gold standard[10].

Paradoxical strain (PS) or systolic lengthening is a more frequent occurrence in TDI-derived strain mapping of HCM (80% of patients)[26], in comparison to 2D strain mapping as noted in our study (30 out of 59, 51% of HCM cases). This disparity stems largely from differences in the two techniques (i.e. 2D strain represents average segmental strain as opposed

to TDI-derived strain that can provide focal or sub-segmental deformational information[26]). None of the other comparator groups exhibited PS.

From a clinical application standpoint, compared to indices of dispersion that have to be manually computed, GLSavg can be rapidly and reproducibly obtained using AFI in less than 60 seconds[27] . GLS from any apical view (2C, 4C or LAX) or GLS-avg may be used interchangeably with comparable predictive accuracy (utilizing a common cutoff value of -11.5 %). Further validation of these data in a larger series will be required before these results can be applied to routine practice.

The disparities in gender and age between groups in our study should not be perceived as a limitation; a prior strain study comprehensively showed that unlike myocardial tissue velocities and strain rate, systolic strain values are not influenced by age or gender [28]. Despite careful attention to tracking and frame rates, poor acoustic windows prevented adequate tracking in a minority (8/2193 segments). In spite of our best attempts to match groups for degrees of LVH, a methodological limitation of this work is the disparity in wall thickness in the cohort of athletes. Finally, our findings should not be extrapolated to patients with reduced ejection fraction.

Conclusions

In the setting of preserved LV systolic function, automated 2D strain (AFI) mapping of regional and global longitudinal strain reveals distinct subclinical functional differences in axial left ventricular function in variant forms of LVH. Although AFI appears to show promise as a discriminating tool, further validation will be required before adopting it into routine clinical practice.

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Figure legends

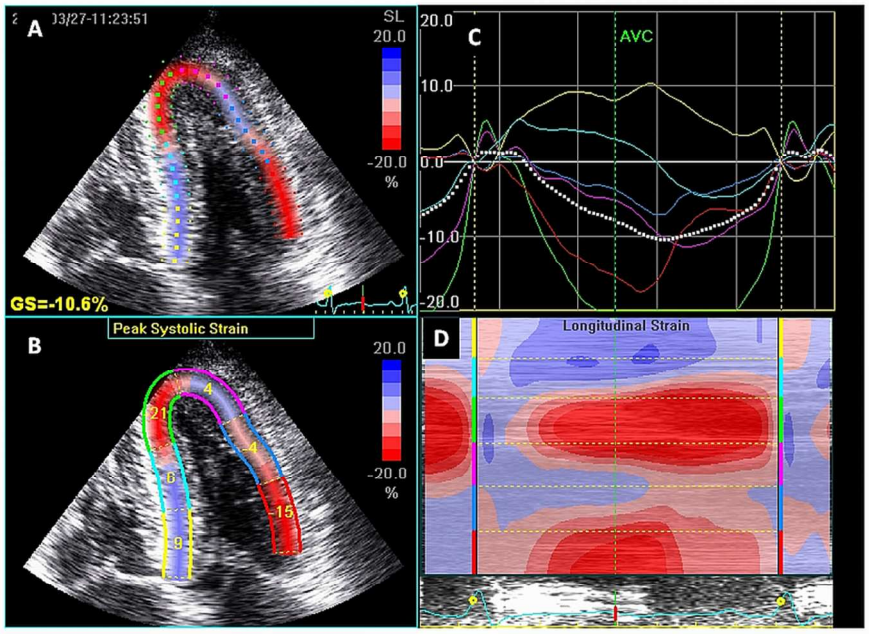
Fig 1. Representative 2D strain analysis (4-chamber view) in a patient with HCM. Panels A and B depict qualitative strain and peak longitudinal systolic strain measurements respectively, note paradoxical strain in septal and lateral segments (shades in blue) in parametric images and corresponding color coded strain curves (Panel C), including global strain for this view (white tracing). Panel D displays curved anatomic M-mode parametric data.

Fig 2. Representative polar maps (Automatic Function Imaging) displaying peak longitudinal strain in an athlete (panel A), hypertensive LVH (panel B), HCM (panel C) and apical HCM (panel D)

Figure 3A. Box plot diagrams of GLS-avg and SDI showing the median, interquartile range and 95% confidence intervals of study subgroups.

3B. Scatter plot showing relationship between left ventricular longitudinal strain magnitude (GLS-avg) and SDI (strain homogeneity) in study subgroups. Each dot represents an individual subject's strain parameter.

Abbreviations: HCM= Hypertrophic cardiomyopathy, AT-LVH=LVH in professional athletes, H-LVH= left ventricular hypertrophy secondary to hypertension



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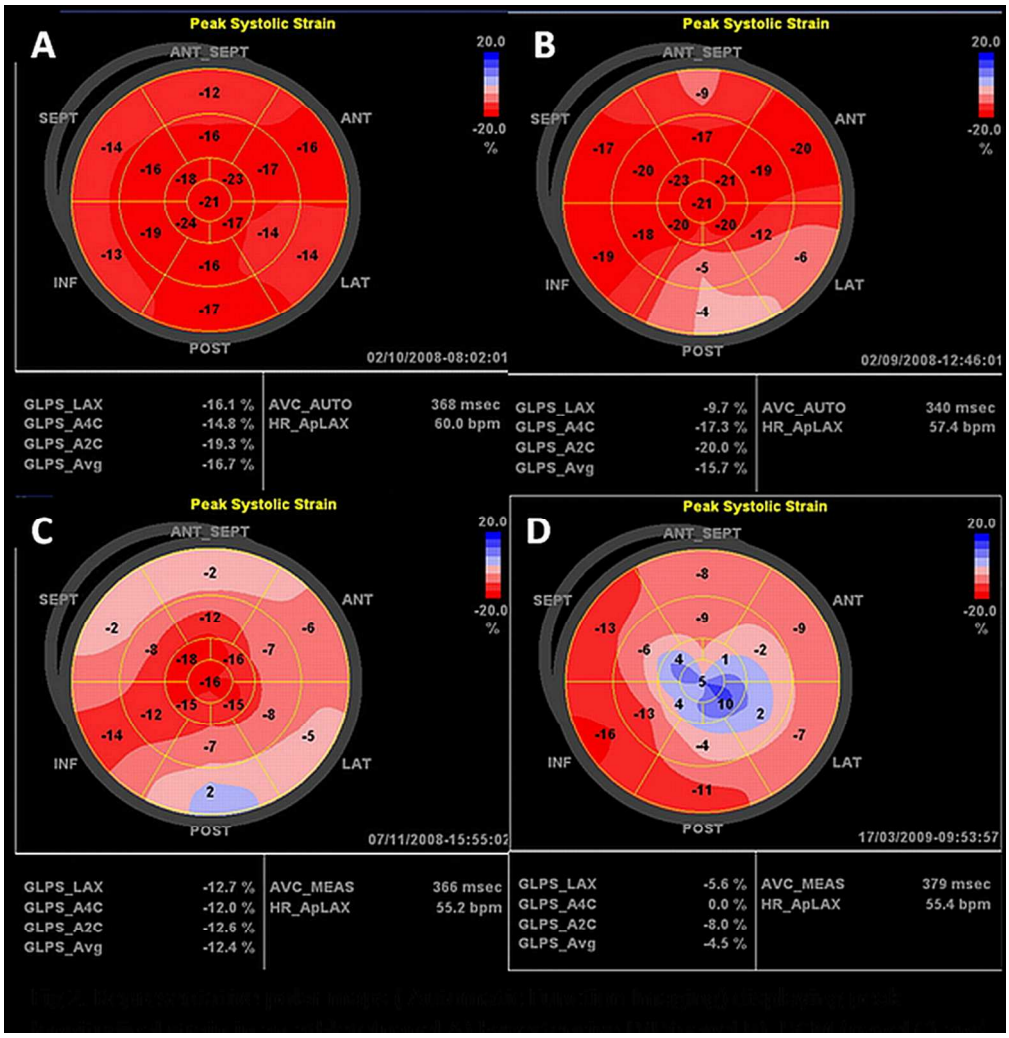
90x67mm (300 x 300 DPI)



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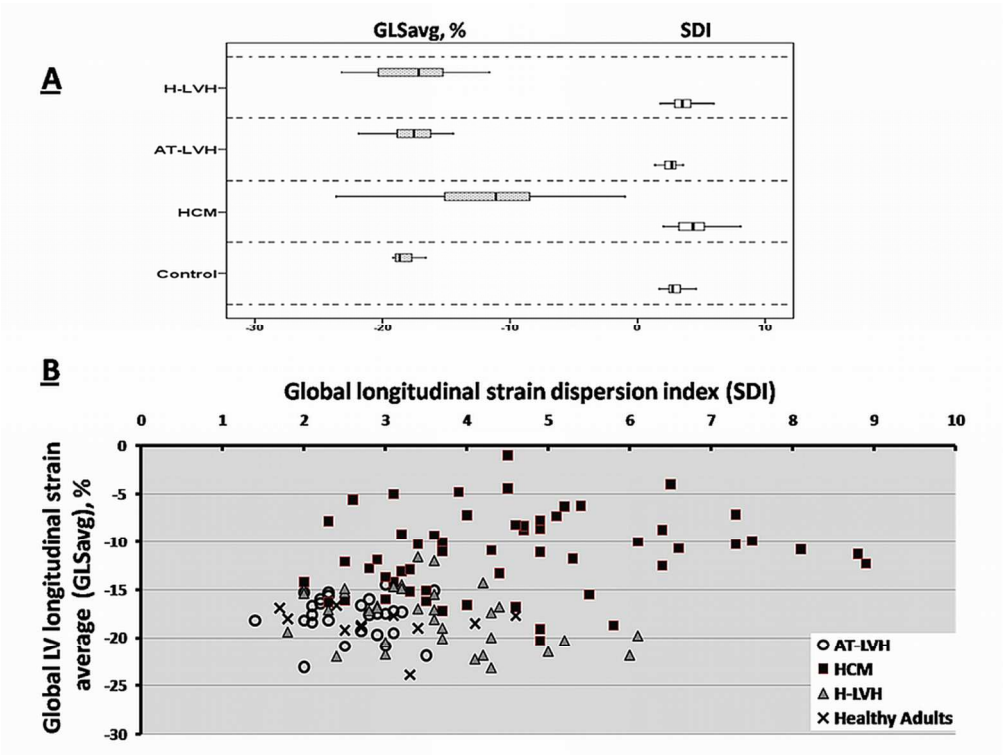

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