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Original Article

3D speckle tracking echocardiographic strain pattern in Hypertrophic Cardiomyopathy and its relation with Sudden Cardiac Death risk markers

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ABSTRACT

Context: Sudden cardiac death (SCD) predictability for assessing the need for primary insertion of Implantable Cardioverter Defibrillator (ICD) in patients with Hypertrophic cardiomyopathy (HCM) is difficult though there are several conventional risk markers. The role of deformation indices in predicting SCD in HCM is less addressed.

Objectives: To analyse the 3D speckle tracking echocardiographic strain parameters of HCM patients and its relation with SCD risk markers.

Design and study methodology: It was a cross-sectional observation study done over a period of one year with a follow up period of one year. Fifty HCM patients were included after screening eighty-two patients. Their global LV strain parameters, Global Longitudinal Strain (GLS), Global Circumferential Strain (GCS), Global Radial Strain (GRS) and Global area strain (GAS) were analysed with respect to their age and gender-matched controls. The various strain parameters were correlated with the conventional SCD risk markers and the ESC SCD risk score among these HCM patients.

Results: All the global strain parameters were significantly low in HCM patients compared to their controls {GLS -7.30 ± 3.424 vs −18.78 ± 2.342, $p < 001$; GCS -11.26 ± 2.754 vs −25.08 ± 3.542, $p < 001$; GRS 20.56 ± 8.929 vs 39.70 ± 7.546, $p < 001$}. On subgroup analysis of HCM patients with LV thickness >30 mm, abnormal exercise test, family history of SCD, LVOT gradients >30mmHgand more than one SCD risk marker had significantly low values for all global deformation parameters, when compared with their control HCM cohort. The ESC risk score also had significant inverse correlation with all deformation parameters (GLS 0.496, $p < 0.001$; GCS 0.491, $p < 0.001$; GRS -0.529, $p < 0.001$; GAS 0.519, $p < 0.001$). On follow up, only one event was recorded in this cohort.

Conclusion: There exists a possible linear correlation between conventional SCD risk markers and 3D deformation parameters, which may be utilized for risk stratification and SCD predictability in HCM patients after confirmation with further large prospective studies.

1. Background

Hypertrophic Cardiomyopathy (HCM) is one of the most common genetic cardiovascular diseases. Several epidemiological studies reported the prevalence of HCM in the general population as 1:500, and more recent studies claim that the prevalence is, even more reaching up to 1:200[1].Clinically HCM may have protean presentations; Sudden Cardiac Death (SCD) in young "healthy" individual is the most devastating among this. Its incidence is 0.7-1% per annum. Insertion of Implantable Cardioverter Defibrillator (ICD) has been the treatment of choice for HCM patients, who had documented VT/VF or resuscitated cardiac arrest in the past. ICD insertion as a primary prophylaxis intervention is also advised for high-risk HCM patients. This risk stratification is based on various clinical risk markers and imaging parameters, but they still lack accuracy[2]

Two major society guidelines to identify high risk HCM patients are AHA ACC 2011 and ESC 2014 guidelines. The former identifies six established risk markers and three potential risk modifiers for SCD in HCM patients[3] that includes 1) Prior cardiac arrest or

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sustained VT, 2) Family history of HCM related sudden death in first-degree relatives, 3) Unexplained syncope, 4) Maximum LV wall thickness more than 30 mm, 5) Non sustained VT (NSVT) on Holter, 6) Abnormal exercise BP response. Late Gadolinium Enhancement (LGE) more than 15% of left ventricular mass, left ventricular apical aneurysm, and left ventricular outflow tract (LVOT) obstruction are the potential risk modifiers. ESC-2014 guidelines instead have devised an SCD risk formula for primary prevention.[1] The HCM -SCD risk formula gives the probability of SCD risk over the next 5 years. This composite risk score takes into consideration of patient's age, left atrial diameter (mm), maximal wall thickness (mm), maximum LVOT gradient, family history SCD, NSVT, and unexplained syncope. ESC-2014 guidelines recommended primary ICD insertion based on the risk score.[3]

The evolution of new technologies like 3D echocardiography and 3D speckle tracking echocardiography (3D STE) strain has revolutionized the assessment of cardiac performance from a mere assessment of 2D imaging and ejection fraction to a more sophisticated appraisal of regional cardiac mechanics. These advances have facilitated preclinical diagnosis, refined risk stratification, and furthered our understanding of existing therapies for HCM. Among the various deformation parameters, the longitudinal strain is the most studied and has shown consistent results. For example, the Lower Global longitudinal strain (GLS) and segmental longitudinal strain dispersion time have shown a positive correlation with the incidence of ventricular arrhythmias in HCM patients.[5] In this study, we have analysed the various 3D STE Strain parameters of HCM patients and compared their relations with the conventional SCD risk markers among them.

2. Materials and methodology

2.1. Study population

The study was conducted at a tertiary care hospital in Kerala, India. The study was approved by the institutional ethics committee, and each participant had given a written informed consent. Patient recruitment was completed over a period of one year from December 2016 to December 2017. All patients between 18 and 60 years of age attending and diagnosed to have HCM according to AHA 2011 criteria[3] having normal 2D echocardiography ejection fraction (EF) values were included in the study. Exclusion criteria include: (1) end-stage HCM (ejection fraction, <50%); (2) evidence of obstructive coronary artery disease (lesions, >50% on angiography); (3) prior history of myocardial infarction or myocarditis (4) patients with irregular heart rhythms or AF (5) patients with poor echo window or suboptimal offline 3D STE analysis interpretation. A control group of age and gender-matched healthy volunteers (with no known cardiovascular disease, symptoms or complaints and having a normal 2D echocardiography report) underwent 3D-STE and was used for comparison of myocardial mechanics. The sample size was calculated based on previous studies.[6,7,8,9]

2.2. Study methodology

After enrolment into the study cohort, past medical history was taken to know the presence of conventional SCD risk factors like un-explained syncope, resuscitated cardiac arrest and family history of SCD in first degree relatives. 24 h Holter monitoring was carried out to assess the occurrence of NSVT in all patients. The hypotensive BP response during exercise (>20 mm Hg drop from peak exercise pressure or >20 mm Hg pressure drop during exercise from baseline[10,11,12]) was recorded in 48 patients excluding those having a history of cardiac arrest. Maximal symptom-limited exercise testing and blood pressure recording were done using a Modified Bruce protocol. In patients who were unable to proceed to stage II in Modified Brue protocol, the 6-min walk test was done. After history taking and 2D echo the ESC SCD risk score was calculated for each HCM patient utilizing the online formula. All patients were followed up for a period of one year. The maximum follow period was 18 months. Over the telephone enquiry for syncope, resuscitated cardiac arrest and SCD was done six monthly and patients were also encouraged to report any significant events voluntarily.

2.3. Two -dimensional echocardiography

The detailed baseline 2D echocardiography was performed in both patients and their age and gender matched controls. The pattern of myocardial hypertrophy, 2D ejection fraction (EF), Left ventricular outflow tract obstruction (LVOTO), Systolic anterior motion (SAM) of the mitral valve, Mitral regurgitation, Left atrial size, and ventricular aneurysm was recorded. Modified Simpson method was used to calculate the EF in both HCM patients and healthy controls. The apical four-chamber views were used to know the LV apical aneurysm, the wall thinning and paradoxical ballooning of thinned out the area during systole was assessed. The 2D echocardiography was performed in this cohort as per ACC/AHA 2011 and 2014 ESC guidelines for HCM using the Vivid E9 system.[3,4]

2.4. 3D speckled tracking echocardiography

It was recorded using the same Vivid E9 system (GE Healthcare, Horten, Norway) in HCM patients and their controls. GE's EchoPAC version 113 software and 4D imaging protocol were used to record the Global LV strain parameters.[13] 4D Strain integrates speckle-tracking with three-dimensional echocardiography, enabling the computation of all LV Strain components from a single apical LV 4D data set. In comparison with two-dimensional (2D) speckle-tracking, 4D Strain seems potentially more apt to capture the complex LV deformation with no issues related to the “out-of-plane” motion of speckles or the need to interpolate the whole LV myocardium from the partial information contained in three thin slices of the LV. ECG gating and frame rate of at least >25 were set as standard. A good four-chamber view was taken and recorded with maximum breath holding capacity possible for the patient. Finally, the data acquired was processed offline and global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS), global area strain (GAS) and segmental strains were calculated. The detailed 4D imaging protocol is provided in Annexure-1.

2.5. Reproducibility

To know the intra-operator variability, two sets of strain values were calculated for each patient and their control from two different 3D echo images recorded within a 24 h time period. Another experienced independent operator who had been blinded for the details of cases and controls repeated the 3D echo and off-line deformation analysis in all HCM patients and their healthy controls. This was done to assess the inter-operator variability of strain values.

3. Statistical analysis

Continuous and qualitative variables were expressed as mean with standard deviation (SD), and discrete variables were expressed as absolute numbers and percentages. Paired Student's *t*-test was used for comparisons of independent samples and was used for comparison of means. Independent sample *t*-tests were used for subgroup analysis. Linear correlations were evaluated

Table 1
The baseline characteristics of HCM patients and healthy age and gender-matched controls.

Parameters	HCM patients (50)	Controls (50)
Age	46.16	46.87
Gender(M:F)	38:12	38:12
EF	69.12	71
Heart rate	60	69
Systolic blood pressure	126	118
Diastolic blood pressure	84	76
Pattern of hypertrophy		
Ash	35	-
Apical	9	-
Global	5	-
Lateral wall nyha class	1	-
I/II	44	-
III/IV	6	-
Unexplained syncope	2	-
Prior resuscitated cardiac arrest	2	-
NSVT in holter	3	-
Positive family history of SCD	10	-
LV wall thickness > 30 mm	7	-
LV aneurysm	1	-
LA size	35.94	29
Presence of LVOT gradient	25	-
Presence of significant Mitral regurgitation	12	-
Presence of SAM	26	-
LVIDD	39	32
ESC SCD risk score		
>6%	2	-
4–6%	5	-
<4%	41	-
Medications		
Beta blockers	50	-
CCB	5	-
Aspirin	3	-

between LV strains and ESC SCD risk score and other continuous variables using the Pearson test. Interobserver and intraobserver variability were assessed by the intraclass correlation coefficient. All statistical tests were 2-tailed; p-value < 0.05 was considered significant. All statistical tests were carried out in the IBM-SPSS 22 (SPSS Institute, Chicago, IL, USA).

4. Results

Out of the 82 patients screened for selection into the study, eight patients were excluded as they had evidence of CAD (Three patients had AWMI, three had critical lesions in CAG and two had IWMI). Six patients had atrial fibrillation (AF) and one had frequent VPCs. Ten patients had been excluded due to poor quality echo window and seven patients had a poor 3D image. Finally, after excluding 32 patients altogether 50 patients were enrolled for the analysis.

4.1. Baseline characters

The baseline characteristic of HCM patients and controls were comparable except for EF and heart rate (Refer Table 1). The predominant pattern of involvement of hypertrophy was asymmetrical septal hypertrophy. Most of the patients were in NYHA class I/II. Most prevalent risk markers were LVOT obstruction followed by family history of SCD and presence of maximum LV wall thickness of more than 30 mm. NSVT and abnormal blood pressure response were seen in three patients each. There were eight patients having more than one conventional risk markers in the study cohort and three patients had three risk markers clustered in them. Twenty-six patients had systolic anterior motion (SAM) of the anterior mitral leaflet (AML) and twelve patients had more than mild mitral regurgitation.

The ESC SCD risk score was calculated for forty-eight patients as two patients already had a history of resuscitated cardiac arrest. It is a risk scoring system which takes into consideration of the patient's age, maximal left atrial size, maximum LV thickness, the maximum LVOT gradient, the presence of family history of SCD in first degree relatives, the presence of NSVT in Holter and presence of unexplained syncope in the past. The ESC risk score is supposed to give the probability of SCD over the next five years. In the study cohort, two patients had a score of more than six which warrant the insertion of ICD for primary prophylaxis. Five patients had a score of more than four and less than six. Majority of the patients (Forty-one out of forty-eight) had a low score.

4.2. Deformation parameters of HCM patients

All the deformation parameters of HCM patients were significantly lower compared to age and gender-matched healthy controls. The detailed observations are depicted in Table 2.

4.3. SCD risk markers and 3D STE deformation

To study the relationship between various risk markers and 3D STE strain parameters two groups were created within the study cohort of HCM patients and compared using appropriate statistical tests depending on the nature of variable (Refer Table 3).

There were ten patients with a family history of SCD in the patient cohort. When on comparing the various strain parameters between patients with and without a family history of SCD, it was found that GLS, GRS, and GAS were significantly low in patients with a family history of SCD. GCS even though found to be low in those with a family history of SCD was not significant statistically. There were seven patients with a maximum LV wall thickness of more than 30 mm in the patient cohort. All the strain parameters (GLS, GCS, GRS, and GAS) were significantly low in patients with LV wall thickness of more than 30 mm. The absolute value of the maximum LV wall thickness was then compared with the various strain parameters using the Pearson correlation coefficient. There was a significant inverse correlation with the absolute value of all strain parameters (Table 4). Three patients had NSVT in Holter test and these patients had a low value for all strain parameters but not significant statistically. The exercise test was done in forty-eight patients and three had an abnormal response as defined in the methodology. These three patients had all the strain parameters detected low and were statistically significant when compared to

Table 2
Comparing various deformation parameters between HCM patients and healthy age and gender-matched volunteers.

Parameters	HCM patients		Healthy controls		p value
	Mean	Std deviation	Mean	Std deviation	
GLS	−7.30	3.424	−18.78	2.342	<0.001
GCS	−11.26	2.754	−25.08	3.542	<0.001
GRS	20.56	8.929	39.70	7.546	<0.001
GAS	−14.80	5.869	−29.34	4.976	<0.001

Table 3
Association between various SCD risk markers and deformation parameters compared with the independent sample *t*-test.

Variable	Group	GLS	Sig	GCS	Sig	GRS	Sig	GAS	Sig
Family history of SCD	Yes-10	−4.10		−9.90		12.50		−9.40	0.01
	No-40	−8.10	0.01	−11.60	0.08	22.58	0.01	−16.15	
LV wall thickness >30 mm	Yes-7	−4.00		−9.14		11.00		−5.42	
	No-43	−7.84	0.01	−11.60	0.02	22.12	0.01	−8.86	0.01
Abnormal exercise test	Yes-3	−3.00		−7.67		8.33		−7.00	
	No-45	−7.56	0.03	−11.44	0.02	21.31	0.01	−15.22	0.02
NSVT	Yes-3	−5.67		−8.33		15.00		−12.00	
	No-47	−7.40	0.40	−11.45	0.05	20.91	0.27	−14.98	0.40
LVOT gradient at rest	Yes-25	−5.60		−10.44		16.60		−11.96	
	No-25	−9.00	0.01	−12.08	0.03	24.52	0.01	−17.64	0.01
SAM	Yes-26	−6.04		−10.58		17.73		−12.69	
	N0-24	−8.67	0.01	−12.00	0.06	24.63	0.01	−17.08	0.01
Significant MR	Yes-12	−5.58		−9.92		17.08		−12.25	
	No-38	−7.84	0.04	−11.68	0.05	21.66	0.12	−15.61	0.08
Unexplained syncope	Yes-2	−5.50		−9.50	0.39	16.50	0.52	−10.50	0.29
	No-48	−7.38	0.45	−11.33		20.73		−14.98	
Resuscitated cardiac arrest	Yes-2	−8.00	0.77	−12.50		22.00	0.82	−17.00	0.59
	No-48	−7.27		−11.21	0.52	20.50		−14.71	
LV aneurysm	Yes-1	−4.00	0.34	−10.00	0.65	20.00	0.95	−12.00	0.64
	No-49	−7.37		−11.29		20.57		−14.86	
Pattern of hypertrophy	Apical-9	−9.33	0.04	−12.33	0.20	24.78	0.12	−18.22	0.52
	Nonapical-41	−6.85		−11.02		19.63		−14.05	
More than one SCD risk marker	Yes-8	−3.88	0.01	−9.13	0.02	10.75	0.01	−8.75	0.01
	No-42	−7.95		−11.67		22.43		−15.95	

those of patients with a normal response to exercise. There were twenty-five patients with significant LVOT gradient and all the strain parameters were significantly lower in these patients. There were twenty-six patients with SAM of AML in this group and all the strain parameters were low in those having SAM with a statistically significant difference with respect to GLS, GRS, and GAS. Twelve patients had significant MR out of the twenty-six and all of them had lower strain parameters compared to those without MR. This difference was significant only for GLS. Patients with unexplained syncope, resuscitated cardiac arrest and LV aneurysm were found to have low deformation parameters, but as patients with these risk markers were less, no meaningful statistical conclusions could be made. Nine patients had a pure apical type of HCM and they had better GLS values compared to the non-apical variety of HCM. There were eight patients having more than one conventional risk markers. These patients had lower values of all strain parameters and that was also statistically significant.

Age and left atrial size had no significant correlation with any of the deformation parameters in this study (Table 4).

4.4. 3D STE deformation and ESC SCD risk score

The relations between ESC SCD risk score and various strain parameters were assessed. There was a strong positive correlation with GLS, GCS and GAS and a negative correlation with GRS. As fractional lengthening occurs in radial strain compared to longitudinal and circumferential strain by default, it was concluded that ECS SCD risk score and all strain parameters had an inverse correlation (Table 4).

4.5. Reproducibility

The reproducibility of the 3D strain parameters was assessed using the ICC (Intra-class Correlation Coefficient). The ICC test was done in all HCM patients and in their healthy controls. In HCM patients and in their healthy controls all the strain values showed excellent intra and inter-operator reproducibility (Table 5).

4.6. Follow up

Five patients lost follow and in all others at least one year follow up was done, maximum follow up period was 18months and minimum one year. There were two deaths due to non-cardiovascular causes (One due to sepsis and the other due to malignancy). Only one significant event recorded. It was syncope in a patient who has the following strain values and ESC-SCD risk score (GLS -5; GCS -7; GRS 14 and risk score of 4.77).

5. Discussion

Strain studies are crucial in studying the segmental and global myocardial mechanics in patients with HCM, as most of them would have normal or falsely increased 2D ejection fraction (EF). Strain abnormalities tend to precede the EF change. EF is not considered to be a robust predictor the risk in HCM patients.[14] In this study cohort, six patients had NYHA class III/IV symptoms, and the rest were in NYHA class I/II. The mean age of this cohort was 46.16. All patients in this cohort had a normal 2D EF. These baseline characters were almost similar to previous studies.

Table 4
Correlation with continuous variables and strain parameters.

Variables	GLS	*p* value	GCS	*p* value	GRS	*p* value	AS	*p* value
ECS SCD risk score	0.496	<0.001	0.491	<0.001	−0.529	<0.001	0.519	<0.001
Absolute maximum LV wall thickness	0.576	<0.001	0.595	<0.001	−0.680	<0.001	0.672	<0.001
LA size	0.223	0.119	0.114	0.431	−0.207	0.149	0.188	0.191
Age	−0.005	0.973	−0.012	0.934	0.001	0.995	−0.018	0.901

Table 5
Intra-class Correlation Coefficient (ICC) for various deformation parameters.

Strain parameter	Intra-operator Variability	*p*-value	Inter-operator Variability	*p*-value
GLS	0.914(0.85–0.951)	<0.001	0.758(0.610–0.855)	<0.001
GCS	0.763(0.617–0.858)	<0.001	0.401(-0.140–0.609)	0.002
GRS	0.670(0.48–0.798)	<0.001	0.670 (0.483–0.798)	<0.001
AS	0.928(0.87–0.958)	<0.001	0.742 (0.586–0.845)	<0.001

It was observed in previous studies that all the strain parameters were significantly reduced in HCM patients,[6,15] Later studies showed that there was a compensatory increase in global circumferential strain compared to reduced global longitudinal strain in early stages of HCM. Once the disease progresses, this compensation seems to get exhausted and all strain parameters tend to fall.[14]

The EACVI NORRE study had given the normal reference range of the 3D strain parameters. It was found that all strain components were higher in women than in men. The lower range was −18.6% in men and −19.5% in women for 3D GLS, −27.0% and −27.6% for 3D GCS and 38.8% and 40.7% for 3D GRS, respectively.[16]

In our study, all the global strain parameters were significantly low in HCM patients compared to normal healthy controls. This finding had excellent intra and inter-operator reproducibility also. The compensatory increase in GCS was not observed in the study. The role of medication in this finding was not assessed as all these patients were on beta blockers.

Research utilizing deformation characteristics with emphasis on SCD predictability in HCM patient is very few. Urbano-Moral et al had studied the relation of GLS, GCS, and GRS with that of LV wall thickness and compared the same with LGE at the hypertrophied segments. In that study it was found that these global strain parameters were found to be low in areas where LV thickness was more than 15 mm or more and in these areas, the LGE percentage was also found to have high concentration.[15] Another study by Debonnaire et al demonstrated that GLS less than −14% and a left atrial indexed volume more than or equal to 34 mL/m2 were independent predictors of appropriate ICD therapy during follow-up.[17]Later Haland et al demonstrated that HCM patients with ventricular arrhythmia had worse GLS than the control HCM patients.[5] While Marie-Philippe Vergé et al showed that in line with GLS, basal longitudinal strain, and longitudinal strain in the hypertrophic area are valuable parameters for evaluating risk stratification in HCM. Mean longitudinal strain in the hypertrophic area, in particular, appears more predictive of SCD occurrence and appropriate ICD shocks than GLS.[18]

In this study, the conventional risk markers were related to the global strain parameters. The two most common conventional risk markers in this cohort were a family history of SCD in first-degree relatives and LV wall thickness of more than 30 mm. The global strain parameters were significantly low in patients with these risk markers (Except for GCS vs family history of SCD). Patients with LV thickness more than 30 mm had significantly low values for all global strain parameters. Additionally, the absolute value of the LV thickness also had a significant inverse correlation with all strain parameters. This finding goes with the already published data. It should be noted that in the present study the segmental strain analysis was not carried out.

Abozguia et al had demonstrated that there was a significant exercise limitation in non-obstructive HCM patients compared to healthy controls even though both cases and controls had similar EF. It was also shown that longitudinal systolic and diastolic strain rate correlated significantly with exercise capacity measured by peak VO2 ($r = -0.34$, $p = 0.01$ and $r = 0.36$, $p = 0.006$, respectively).[19] D. Saura et al had demonstrated the significant inverse correlation between left atrial volume index and exercise capacity measured in METs (r:-0.39; $p < 0.01$) in HCM patients.[20] In our cohort, the abnormal exercise blood pressure response was seen in three patients, and these three patients had significantly lower strain parameters. Over the known fact that strain rate and exercise capacity had an inverse correlation, our study had revealed that this relation holds good in those with abnormal blood pressure response also.

Di Salvo et al demonstrated that the presence of more than 3 LV segments with a longitudinal 2D strain less than −10 was an independent predictor of NSVT (sensitivity, 81%; specificity, 97.1%; $p < 0.0001$).[21] In our study even though patients with NSVT had low strain parameters, it was not statistically significant. This may be due to the relatively low incidence of NSVT in this cohort and needs further studies with a large number of patients. It was noticed that patients with LVOT obstruction had a significant reduction in all strain parameters. A previous study by Wu Hao et al showed that GLS, GCS, and GRS were significantly reduced in patients with non-obstructive HCM patients than with Obstructive HCM.[22] Our study, however, had shown contradictory observation. The role of significantly low GLS, GRS and Area strain in those with SAM and low GLS in those with SAM and significant MR needs to be validated in further studies as no similar studies were identified. The relation with the presence of unexplained syncope, prior resuscitated cardiac arrest and LV aneurysm with that to the strain parameters showed no significant association. The very low incidence of these risk markers had to be taken as a limitation in this study. During the short follow up period, the event rate was very low. The recorded one syncope event had no statistically significant correlation with strain parameters and ESC −SCD risk score. This emphasizes the need for including more number of subjects or long follow up period in future studies.

Whenever multiple conventional risk markers were seen in a given HCM patient there was a significant reduction in all strain parameters. This observation was strengthened by the strong inverse correlation shown between ESC SCD risk score and various strain parameters. The ECS SCD risk score being a composite risk score, this strong inverse correlation clearly denotes the ability of strain parameters for accurate risk stratification in HCM patients. To the best of our knowledge, no similar studies had directly compared the various conventional risk markers and ESC SCD risk scoring to the various strain parameters. These findings emphasize the possibility of a linear association between conventional SCD risk markers and deformation parameters in HCM, which warrant further research.

In this study the left atrial size and age of the patients were found to have no significant correlation with all global strain parameters, the LA volume index (LAVI) was not assessed in this study and the authors suggest LAVI would be a better parameter compared to 2D parasternal long axis left atrial size. The relatively better global strain values in Apical HCM compared to those of non-apical HCM also warrant further studies. Some case reports had identified paradoxical strain (means systolic lengthening of apical

hypertrophied segments instead of shortening) in apical HCM segments and relatively normal strain parameters in mid and basal LV segments.[23]

6. Limitations

This is basically an observational cross-section study and has its own limitations in concluding about the quantum of linear correlation observed between conventional risk markers/score and 3D deformation parameters. The author admits that the study was underpowered for subgroup analysis and the event rate during the relatively short follow up period was also very low to comment on an arbitrary cutoff for strain rate to predict SCD risk. The overall outcome from the study warrants future large prospective studies especially for risk stratification. The effects of medications were not taken into consideration. As all the patients in this cohort were on a beta blocker subgroup analysis was not possible. Sub optimal echo window was still a matter of concern in a few cases even though most of such cases were excluded from the study prior to enrolment. The technical feasibility of 3D STE study was 67% only. 24 out of 74 patients were excluded from the study due to technical difficulty in 3D STE strain analysis. The main reason for exclusion was inadequate echo window, arrhythmia (AF) and inability to maintain breath holding. This study did not compare the strain parameters to the quantum of scar on LGE by cardiac MRI.

7. Conclusions

All 3D deformation parameters are found to be low in HCM patients compared to controls. There exist a possible linear correlation between conventional SCD risk markers and 3D deformation parameters, which may be utilized for risk stratification and SCD predictability in HCM patients after confirmation with larger prospective studies.

What IS already KNOWN about this research

SCD risk estimation in HCM patients still lacks an accurate predictor. The role of novel 3D deformation technique in this regard is still evolving. It has been shown that Longitudinal strain is consistently reduced in HCM patients. The perceived change in deformation parameters has never been taken as a tool for SCD predictability.

What this study adds

Most of the 3D deformation parameters have a more or less linear association with other known SCD predictors. In SCD predictability the role of 3D deformation parameters has to be subjected to more prospective studies.

Declaration of competing interest

Nil.

Acknowledgement

Nil.

Appendix –1

4D imaging protocol for GE's EchoPAC version 113 software.

- 3D image acquisition
  - Select 4Vprobe
  - ECG GATING IS A MUST FOR 4D IMAGING
  - Select the volume size LARGE for a FULL VOLUME acquisition
  - Acquire a 4D LARGE VOLUME image with MULTI-BEAT until the frame rate is higher than 25 or at least 40% of patient heart rate.
  - Store this image by pressing IMAGE STORE twice.
- 3D STE offline analysis
  - Press MEASURE on the control panel, select VOLUME, and then 4D AUTO LVQ.
  - Press EDV, mark two points– base of MV and the apex.
  - Press ESV, mark the same two points again.
  - Press Volume Waveform. The machine will generate the LV 4D Shell model.
  - Then click on LV MASS, the machine will trace the outer myocardial border, and compute the 4D LV MASS.
  - Select 4D Strain ROI, and select 4D STRAIN RESULTS.
  - The machine will take 20–30 s, and shall display the 4D strain curves as well as the Bulls–eye plot for 4D strain.
  - By default, LONGITUDINAL 4D STRAIN shall be displayed first.
  - By clicking on the LONGITUDINAL STRAIN button on the touch-screen, the CIRCUMFERENTIAL, AREA and RADIAL Strain shall also be displayed with the respective curves and the Bulls–eye plot.
  - By pressing the ES (end systoli) point on strain curve, the averaged respective Strain values for all the segments and global strain valves can be obtained.
  - Select APPROVE & EXIT to approve the results and exit the application.

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