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ORIGINAL ARTICLE

Clinico-morphological Evaluation of Hypertrophic Cardiomyopathy Patients in Cardiac MRI with an Evaluation of Prognostic Parameters in Tertiary Cardiac Centre

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Abstract

Background: Cardiac Magnetic Resonance Imaging (MRI) has several advantages over 2D Echocardiography (Echo) for the diagnosis, management, and prognostication of Hypertrophic cardiomyopathy (HCM). The efficacy of which is less studied in our part of the world. Thus, this study aims to evaluate, clinical and morphological characteristics involving Echo and cardiac MRI along with the comparison of morphological features and determination of morphological prognostic factors of HCM from MRI.

Methods: This is a prospective, cross-sectional study conducted in SGNHC and Bir Hospital Kathmandu, Nepal. This Study included 73 patients fulfilling inclusion criteria from 20th May 2023 to 19th May 2024.

Results: Out of 73 patients, with a clinical diagnosis of the HCM, 59 (80.8%) were males and 14 (19.2%) were females. Statistically significant differences (P <0.001) in findings were seen in Mean LVEF (6.60%) and LVH thickness (4.34 mm) between MRI and Echo respectively. Additional detailed HCM phenotypes and prognostic parameters including mean fibrotic burden, and diastolic cavity obliteration in 5(6.8%) patients were also obtained from MRI.

Conclusion: Cardiac MRI appears to be highly relevant in the clinical, morphological, and prognostic evaluation of HCM patients if financially and practically feasible.

Keywords: Hypertrophic Cardiomyopathy (HCM), Magnetic Resonance Imaging (MRI), Prognosis, Nepal

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Introduction:

Hypertrophic cardiomyopathy (HCM) is a relatively common myocardial genetic disease, affecting approximately 0.2"0.5% of the general population. The estimated prevalence rate is 1 out of 500 young adults (<35 years of age).[1-2] which translates to approximately 700000 affected Americans and up to 2 million people in India or China.[3] Indeed, the clinical HCM patient population actively under surveillance represents only the 'tip of the iceberg relative to the overall disease population.[4]

The disease exhibits extreme variation, in terms of age of onset, disease progression, the occurrence of sudden cardiac death (SCD), spectrum and extent of symptoms, and most importantly, the degree, and location of hypertrophy.[5] Disease heterogeneity can range from clinically and morphologically unaffected with an asymptomatic course and normal longevity, to severe dysfunction, including heart failure (HF), or SCD with the latter often being the first manifestation of the disease.[6,7]

Hypertrophic cardiomyopathy is caused by the mutations of autosomal dominant transmitted genes, while the identification and diagnosis of this disease are largely based on clinical imaging findings, including asymmetrical Left Ventricular Hypertrophy (LVH) without any underlying diseases leading to LVH.[8,9] Echocardiography is used to observe HCM because of its easy accessibility, capacity to measure the gradient across the left ventricular outflow tract

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(LVOT) at rest and under provocative maneuvers, capability to assess valvular dysfunction, and because there are no contraindications for any patient. Nonetheless, the use of cardiac Magnetic Resonance Imaging (MRI) is strongly recommended when making a diagnosis and evaluating the severity of HCM because it has several advantages over echocardiography: accurate measurement of wall thickness and myocardial mass using cine steady-state free precession (SSFP) MR imaging, detailed observation of cardiac structures without the limited view, and the unique and important capability of late gadolinium enhancement (LGE) MR imaging to identify myocardial fibrosis related to the prognosis of HCM.[10] In addition, T2- weighted imaging shows myocardial edema or inflammation related to chest pain or syncope associated with HCM.[11,12] Cardiac MR imaging is also valuable for differentiating between HCM and other myocardial diseases showing LVH.[13]

Technical advantages of MRI in the evaluation of patients with HCM over Echo can be enlisted as below.[14]

1. Possibility of obtaining infinite imaging planes
2. Better estimation of ventricular volumes and function
3. Assessment of co-existing valvulopathies
4. Better estimation of the magnitude of hypertrophy as compared to echocardiography
5. Better identification of focal forms
6. Visualize and quantification of fibrosis and risk stratification
7. Offers differential diagnosis

Clinico-morphological studies in our part of the world are scarce, especially with the aid of cardiac MRI. So, this study aims to report clinical, and morphological characteristics involving echocardiography and cardiac MRI along with the comparison of morphological features and determination of morphological prognostic factors of HCM from MRI in the tertiary cardiac center.

Methods:

This is a hospital-based, cross-sectional study conducted at Shahid Gangalal National Heart Centre (SGNHC), and Bir Hospital, Kathmandu, Nepal from 20th May 2023 to 19th May 2024(12 months). Informed consent was taken before enrolment in the study. After approval from the Institutional Review Board (IRB) of the National Academy of Medical Sciences (NAMS), Bir Hospital, and administrative approval taken from the study sites, 73 patients who fulfilled inclusion criteria were enrolled. Clinically Diagnosed HCM patients with the aid of 2D- echocardiography as per task force guidelines.15 who attend OPD, IPD, and Emergency in Bir hospital and SGNHC and screening health camp along with First-degree family members of a diagnosed case of HCM were included in the study. Patients and family members not willing to undergo MRI and contraindications to MRI were excluded. An echocardiography test followed by MRI after counseling regarding the advantages of MRI was done. HCM phenotypes have been classified as per Baxi et al16 study. Recent documents were reviewed and data were collected and recorded as per proforma by the principal investigator.

Data Analysis

All data were entered into Microsoft Excel and the statistical analysis was done using the SPSS version 23 software (SPSS INC, Chicago, III). Categorical variables were analyzed as numbers and percentages, and continuous variables with normal distribution were presented as mean ± SD. After processing all available information, a statistical analysis of their significance was done.

All categorical variables were expressed in frequency and percentage. Mean LVEF and LVH thickness were compared between different groups by performing a paired t-test for normalized data. For this study, a 95% confidence interval was accepted.

Results

Baseline characteristics of the patients

Seventy-three patients were included in the study. Out of 73 patients, with a clinical diagnosis of the HCM, 59 (80.8%) were males and 14 (19.2%) were females. The demographic details are described in Figures 1 and 2. The majority of the participants 18 (24.7%) were from the 50- 59 age- group.

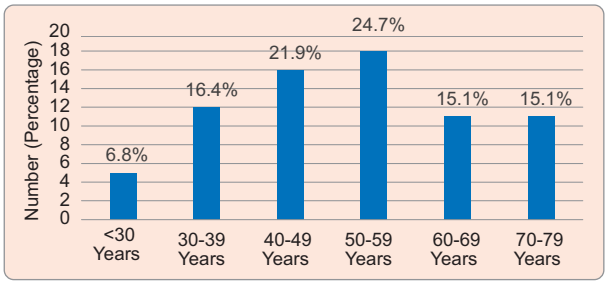

Figure 1: *Age-wise distribution of patients*

Clinical characteristics

The most common form of the symptoms in HCM patients was shortness of breath which was seen in 47 (64.4%) patients followed by chest pain in 46 (63.0 %) patients, and palpitation in 32 (43.8%) patients

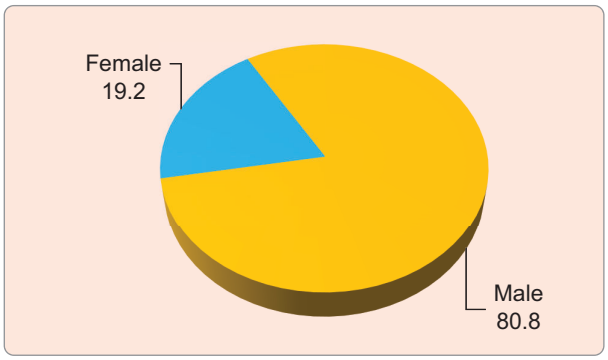

Figure 2: *Gender-wise distribution of patients*

respectively. Twenty-two (30.1%) patients reported having syncopal episodes and other characteristics are detailed in Table 1. Out of 73 patients, none died due to sudden cardiac death. Out of 73 patients, 10 (13.7%) patients were incidentally diagnosed as asymptomatic cases from cardiac echo screening as a part of the pre-operative evaluation and health camp.

Table-I

Baseline Characteristics of Patients

Characteristics	Number of Patients	Percentage (%)
Shortness of Breath	47	64.4
Chest Pain	46	63.0
Palpitation	32	43.8
Syncope	22	30.1
SCD in Family Members	12	16.4
HCM diagnosed during Screening	10	13.7

2D-Echo findings

Out of 73 participants, 36 (49.3%) patients had Focal Basal Septum (asymmetrical septal) HCM followed by Concentric and diffuse type in 22 (30.1%) patients. SAM was present in 24 (32.9%) participants with a mean LVEF of 61.0 ± 4.44%. The mean LV wall thickness was 17.13 ± 3.52 mm with the maximum wall thickness being found to be 32 mm.

Table-II

Types of HCM on Echocardiogram

Types	Cases	Percentage (%)
Focal Basal Septum	36	49.3
Concentric and diffuse	22	30.1
Diffuse septum	10	13.7
Apical	3	4.1
Free wall (Lateral)	1	1.4
Mid-Ventricular	1	1.4
Total	73	100.0

Cardiac MRI Findings

Out of several types, Concentric and diffuse phenotype HCM was seen in 25 (34.2%) participants which was a common finding among the study population. The mean LV wall thickness was 21.46 ± 4.95mm with the maximum LV wall thickness found to be 33.5 mm. The LVEF was found to be 67.6 ± 8.56%. The mean difference in LVEF and LVH thickness between MRI and echo was statistically significant (P<0.001) as shown in Table 4. The mean fibrotic burden was 3.87 ± 5.57 % with a maximum burden of 36%. Five (6.8%) patients in the study group had RV involvement.

Table-III

Types of HCM in cardiac MRI

Types of HCM	Cases	Percentage (%)		
Concentric and Diffuse	Cases	Percentage(%)	25	34.2
Concentric with predominant diffuse septum	7	9.6		
Concentric with predominant InferoSeptum	6	8.2		
Concentric with predominant Apical	4	5.5		
Concentric with predominant MidVentricular	2	2.7		
Concentric with predominant Anteroseptum	6	8.2		
Diffuse septum		21	28.8	
Focal Basal Septum		18	24.7	
Apical		6	8.2	
Mid-Ventricular		2	2.7	
Free-wall (Lateral)		1	1.4	
Total	73	100.0		

Table-IV

Comparison between Echo and MRI for Mean LVEF and LVH thickness

Indicators	MRI	Echo	Mean Difference (MRI-Echo)	Paired t-test	P-Value
Mean LVEF (%)	67.6±8.56	61.0±4.44	6.60	6.391	<0.001
Mean LVHThickness(mm)	21.46±4.95	17.13±3.52	4.34	9.368	<0.001

Table-V

Findings in cardiac MRI

Findings in MRI		Cases (Percentage)
RV involvement		5(6.8%)
LV Diastolic cavity obliteration		5(6.8%)
Mean Fibrotic burden	Mean ±sd (min, max)	3.87 ± 5.57 % (0,36)

Twenty-five (34.24%) patients showed dynamic obstruction in the form of the presence of SAM. Diastolic cavity obliteration was seen in 6.8% of participants. None of them had apical aneurysm

Discussion:

The use of cardiac MRI is strongly recommended when making a diagnosis and evaluating the severity of HCM because it has the advantage over echocardiography.[10] We studied 73 patients, of which there was male preponderance. Men are more often affected than women in HCM.15 This study showed a preponderance of HCM in males (80.8%) with a sex ratio of 4.2:1 similar to another study (3.7:1) by Tanjore RR et al.17 The majority of the participants, 24.7% followed by 21.9% were from the 50- 59 and 40-49 age- group respectively at the onset of the disease. It has been shown that the early age of onset of disease, is associated with a higher burden of adverse events.[18] So, early diagnosis is pertinent to prevent and minimize adverse events shortly.

Palpitation is an important clinical manifestation, which affects the quality of life of HCM patients and predicts poor prognosis.[19] Thirty-two (43.8%) patients had a history of palpitation in this study. AF is common and has a major clinical impact on HCM patients.[20] Every HCM patient needs proper evaluation of arrhythmia as a systematic analysis of stored ECG shows that the majority of ventricular arrhythmias occur while in normal sinus rhythm and are precipitated by premature ventricular complexes.[21] Palpitations can be the harbinger of SCD, so symptoms of palpitations need proper attention and meticulous evaluation.

Family history in all HCM patients in this study showed that 12 (16.4%) family members of diagnosed HCM patients, died of Sudden Cardiac Death (SCD). SCD is the most common cause of death in HCM and often affects young and frequently asymptomatic patients.[22] So, proper history and evaluation are of paramount importance.

In this study, patients with shortness of breath in 47(64.4%) followed by chest pain in 46 (63.0 %) patients and palpitation in 32 (43.8%) patients respectively, and a history of syncope in 22 (30.1%) patients which is similar to other studies.23 this finding justifies that cases of HCM are clinically unrecognized, representing the “tip-of-the-iceberg” of the disease spectrum suggested by Maron and colleagues.[24] This may be related to the lack of HCM-specific symptoms. So, more frequent screening with echocardiography and MRI is very important in suspected patients as early as possible.

There has been a greatly increased use of MRI for the diagnosis of HCM because of its precise determination of myocardial anatomy and the depiction of myocardial fibrosis.[25] The clinical and prognostic weight depends on the type of the disease-causing LVH and the extent and severity of myocardial damage.[26] This highlights the need to characterize as best as possible LVH in terms of diagnosis and severity. MRI has a higher potential to define wall thickness and the extent of LVH in comparison to TTE due to higher spatial resolution and multiplanar approach that makes it a three-dimensional imaging technique.[27]

In this study, 36(49.3%) of the patients had a Focal Basal Septum (asymmetrical septal type) HCM from

2D-Echo, whereas, 18 (24.7%) patients were only detected as Focal Basal Septum (asymmetrical septal) in cardiac MRI. Whereas 25(34.2%) patients had Concentric and Diffuse types with further subdivision as shown in Table 3. These findings are similar to the studies done by Aquaro, G.D et al.[26] and Bois, J.P. et al.[28] Apical HCM was seen more in MRI, 6 (8.2%) patients than in echocardiography 3(4.1%). The anatomic findings between echo and MRI showed disparity owing to the higher diagnostic yield of MRI. These findings highlight the advantage of MRI over echo in the precise determination of myocardial anatomy and LV involvement.[24]

In addition, in this study, left ventricular thickness measurements and LVEF via Echo and MRI were statistically significant (p-value: <0.001). These findings are similar to the findings of many correlative studies, as proper LVH thickness patterns and LVEF are better defined in cardiac MRI than in 2D-echo.24 In this study, mean LV thickness was 21.46 ± 4.95 mm from MRI with a maximum thickness of 33.5 mm whereas, 17.13 ± 3.52 mm with a maximum thickness of 32 mm was from echocardiography. Non-invasive imaging of LV wall thickness has proven to have a role in risk stratification: LV hypertrophy of ≥30 mm identifies HCM patients at high risk of arrhythmia who could benefit from ICD therapy for SCD prevention.[29] Therefore, an accurate assessment of maximal wall thickness is an essential part of the initial evaluation of all HCM patients. Previous observations have demonstrated that CMR can identify massive LV wall thickening (≥30 mm) that was underestimated in TTE.[27] So, cardiac MRI appears superior for LVH pattern assessment than 2D-echo.

Myocardial fibrosis or scarring detected by CMR occurs in up to 33-86% of patients with HCM. Cardiac MRI can evaluate the Extent of myocardial fibrosis with the help of Late Gadolinium Enhancement (LGE).[24] LGE-CMR characteristics are not specific for HCM, but the regional location of diffuse LGE within the septum is very suggestive of HCM.[30] The mean Fibrotic burden in this study was 3.87 ± 5.57 % with a maximum of 36%. High Fibrotic burden indicates poor prognosis in HCM. Different studies have published an increase in the risk of ventricular arrhythmias in patients with HCM related to the presence of fibrosis evaluated by LGE in comparison with individuals without LGE.[14,31] An LGE amount of >5% (of LV mass) portends a higher risk for SCD, increasing the risk from 5.5% at 5 years to 13.0% at 10 years and 33.3% at 15 years. Conversely, patients with no or ≤5% LGE amount seem to have a favorable prognosis.[32] These findings aid the important role of cardiac MRI in HCM and the need for MRI to assess prognosis in HCM.

Systolic anterior motion (SAM) of the mitral valve, in this study from echo, was present in 24(32.9%) patients whereas 25(34.2%) had SAM in cardiac MRI. This finding in our study is per the similar findings from many studies which estimate the prevalence of SAM in HCM based on small numbers of patients, and range from 31–61%.[33] Of the HCM patients with SAM, between 25–50% have evidence of resting LVOT obstruction and associated asymmetric septal hypertrophy and Mitral regurgitation. Based upon SAM, new methods to relieve obstruction have been developed: revised surgical techniques, dual chamber pacing, and percutaneous transluminal septal myocardial ablation.[34] So, accurate SAM detection is an important parameter not only for diagnosis but also for therapeutic purposes as well.

Among 73 patients with HCM, 5 (6.8%) patients with RV involvement and Diastolic LV cavity obliteration were identified by cardiac MRI. 2D- TTE is unable to delineate RV anatomy correctly owing to its complex geometry. Patients with RV involvement showed more severe myocardial dysfunction of the LV and RV, suggesting that it can be considered an indicator of severe HCM. RV wall thickness is best assessed by MRI in comparison to Echo.[35] As RV involvement and diastolic LV cavity obliteration are also important prognostic parameters in HCM, cardiac MRI needs to be considered as an important investigation tool.

Conclusion

HCM is a genetic disorder that is more prevalent in males. Patients are often diagnosed in the age group of 40-59 years where people are more physically active. Shortness of breath and chest pain are common clinical presentations. Echocardiography is the most common diagnostic test used for long for hypertrophic cardiomyopathy, however, the use of cardiac MRI has various advantages over echocardiography. As suggested by this study, cardiac MRI appears to be highly relevant in the clinical as well as research evaluation of patients with overt as well as pre-clinical HCM. Late enhancement after gadolinium administration allows tissue

characterization of myocardial fibrosis. The method may potentially identify HCM patients at greatest risk for adverse cardiac events. CMR can identify the presence and spatial extent of LV hypertrophy, with better visualization of some segments in comparison to echocardiography. Also, its good spatial resolution allows for accurate thickness measurements. The different phenotypic expressions of HCM can be adequately characterized with CMR. So, as far as possible cardiac MRI assessments are needed for the proper evaluation of HCM patients if financially and practically feasible.

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