SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY
TRIVANDRUM, KERALA

MORPHOLOGICAL ABNORMALITIES IN HYPERTROPHIC CARDIOMYOPATHY - A CARDIAC MRI BASED STUDY

THESIS

Submitted during the course of

DM Cardiology

Dr. VIJAYAN.G
DM Trainee

DEPARTMENT OF CARDIOLOGY

July 2019

DECLARATION

I, **Dr. Vijayan.G**, hereby declare that the project in this book titled "**Morphological abnormalities in Hypertrophic cardiomyopathy – A cardiac MRI based study**" was undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

Date**:**

Dr.Vijayan.G

DM cardiology

CERTIFICATE

I, **Dr. Vijayan.G**, hereby declare that the project in this book was undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

Thiruvananathapuram

Date:

Prof. Dr. Ajit Kumar.V.K

Head of Department of cardiology

CERTIFICATE

I hereby certify that the work in this project titled "**Morphological abnormalities in Hypertrophic cardiomyopathy – A cardiac MRI based study**" is a certified record of original research work undertaken by **Dr. Vijayan.G** in partial fulfillment of requirement for the purpose of award of DM cardiology degree under my guidance and supervision.

Guide:

Dr. Ajit Kumar.V.K

Professor and Head

Department of Cardiology

Sree Chitra Tirunal institute for Medical Sciences and Technology

Trivandrum – 695011

TITLE

MORPHOLOGICAL ABNORMALITIES IN HYPERTROPHIC CARDIOMYOPATHY - A CARDIAC MRI BASED STUDY

PRIMARY INVESTIGATOR

Dr. Vijayan.G
Senior Resident
Department of Cardiology,
Sree Chitra Tirunal Institute for Medical sciences and Technology
Thiruvananthapuram

GUIDE

Dr. Ajit Kumar.V.K
Professor and Head
Department of Cardiology,
Sree Chitra Tirunal Institute for Medical sciences and Technology
Thiruvananthapuram

CO-GUIDES

Dr. Sanjay.G
Additional Professor
Department of Cardiology,
Sree Chitra Tirunal Institute for Medical sciences and Technology
Thiruvananthapuram

Dr. Anoop.A
Assistant Professor
Department of Cardiology,
Sree Chitra Tirunal Institute for Medical sciences and Technology
Thiruvananthapuram

INDEX

ACKNOWLEDGEMENT

At the outset I would like to thank my mentor, guide **Dr. Ajit Kumar.V.K,** Professor and Head, Department of cardiology, to whom I am greatly indebted to, for his immense support, encouragement and inspiring attitude – not only for this project, throughout my DM period.

I deeply thank my co-guide Dr**. Sanjay.G**, Additional Professor, Department of cardiology, for his constant guidance, valuable inputs and motivation throughout this project.

Special thanks to my co-guide **Dr. Anoop.A**, Assistant Professor Department of imaging sciences & intervention radiology, for his valuable suggestions.

I deeply thank **Dr. Mukhund Prabhu,** Assistant Professor, Department of cardiology, for his valuable inputs in analysis of this project.

My sincere thanks to **Dr. Ajay Alex**, Senior resident, Department of cardio-vascular imaging sciences & intervention radiology, for helping me in interpreting MRI images.

Finally I express my gratitude to all my patients, and all those who directly and indirectly helped me do this study.

Vijayan.G

Acronyms and Abbreviations

ACRONYMS AND ABBREVIATIONS:

AML	–	Anterior mitral leaflet
ASA	–	Alcohol Septal Ablation
CMRI	–	Cardiac Magnetic Resonance Imaging
HCM	–	Hypertrophic cardiomyopathy
IVS	–	Inter ventricular Septum
LGE	–	Late gadolinium enhancement
LV	–	Left ventricle
LVOT	–	Left ventricular outflow tract
MR	–	Mitral regurgitation
MV	-	Mitral valve
PM	–	Papillary muscle
PML	–	Posterior mitral leaflet
PW	-	Posterior Wall
RV	–	Right ventricle
SAM	–	Systolic anterior motion of mitral valve

Introduction

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) has a varied clinical course due to its genotypic and phenotypic heterogeneity. Several autopsy studies have shown abnormalities of the mitral valve in some HCM patients. Cardiovascular magnetic resonance (CMR) has become the imaging modality of choice due to its high spatial resolution, well suited to define the diverse phenotypic expression of this complex disease.

HCM has been documented to have various mitral valve abnormalities like an increased length of the leaflets and area, leaflet thickening, impaired mitral leaflet coaptation, and left ventricular outflow tract obstruction (LVOT) due to the systolic anterior motion of the mitral leaflets. Cardiovascular magnetic resonance (CMR) provides an excellent opportunity to assess the papillary muscle (PM) abnormalities like an increased number and mass, bifidity, hypertrophy, antero-apical displacement and LGE of the papillary muscle.

Various guidelines recommend surgical myectomy as the preferred modality for patients with left ventricular outflow tract (LVOT) gradient ≥50 mm Hg who fail to respond to medications or who experience side effects. Alcohol septal ablation (ASA) in patients with mitral valve abnormalities results in persistent SAM, gradients, and mitral regurgitation (MR).

Hypothesis

HYPOTHESIS

HCM is characterized by abnormalities of mitral valvular apparatus and papillary muscles. The abnormal mitral valve and papillary muscle morphology are associated with increased LVOT obstruction.

Aims & Objectives

AIMS & OBJECTIVES

- To determine the pattern of hypertrophy of ventricles.
- To determine the mitral valve and the papillary muscle abnormalities in hypertrophic cardiomyopathy.
- To determine the relationship between the mitral valve and the papillary muscle abnormalities and obstruction in hypertrophic cardiomyopathy.

Review of Literature

REVIEW OF LITERATURE

LVOT obstruction in HCM was caused by systolic anterior motion (SAM) of the mitral valve and mitral-septal contact[1]. 2011 American guidelines state: "Mitral valve abnormalities plays an important role in the generation of left ventricular outflow tract obstruction, suggesting the potential value of additional surgical approaches (e.g., plication, valvuloplasty, and papillary muscle relocation) and making myectomy more appropriate than alcohol septal ablation in some patients"[2]. 2015 European guidelines state: "Septal myectomy, rather than alcohol septal ablation, is recommended in patients with an indication for septal reduction therapy and other lesions requiring surgical intervention (e.g., mitral valve repair/replacement, papillary muscle intervention) Class I, Level of Evidence: C"

Mitral regurgitation (MR) in obstructive HCM most commonly results from the poor coaptation, due to the inadequate length or mobility of PML to move along with the anterior mitral leaflet[3]. The SAM abolition either with optimal medical or surgical treatment results in the reduction of MR.

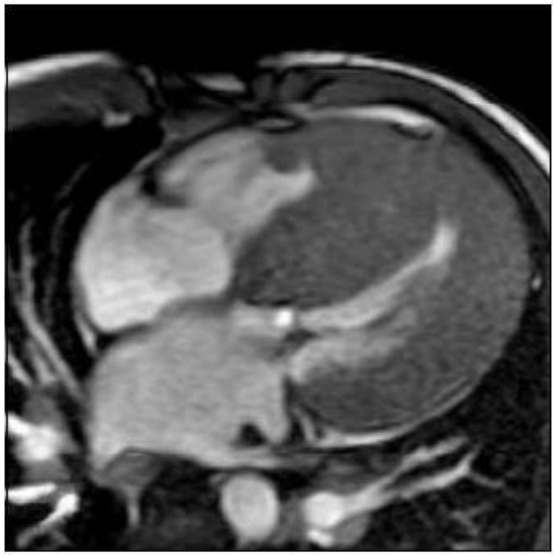
PATTERN OF VENTRICULAR HYPERTROPHY:

Asymmetric septal hypertrophy is the commonest morphologic pattern of HCM and the most commonly involved hypertrophied segment is the anteroseptal myocardium[18]. The prevalence of LVOT obstruction in asymmetric septal hypertrophy is 20–30%[19]. Symmetric HCM occurs in up to 42% of HCM and it has to be distinguished from other causes of concentric left ventricular hypertrophy. Apical HCM was initially reported in the Japanese population. Prevalence of apical HCM is variable in studies, ranging from 25% in Japanese patients to fewer than 2% of all HCM patients in Western countries[20].

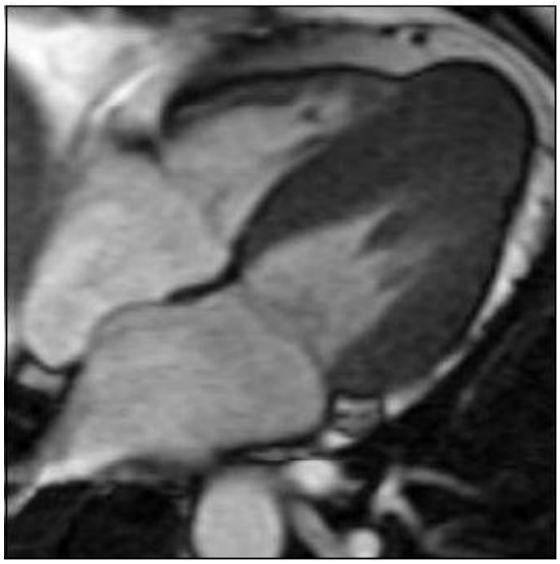
Midventricular obstruction in HCM predominantly involves the middle third of the left ventricle, which results in elevated systolic pressure in the apex and formation of an apical aneurysm. Mass-like thickening of the left ventricle may be a rare presentation of HCM. The burnt-out phase results from small vessel ischemia leads to loss of ventricular myocardium which is replaced by fibrosis. Around 60% of the symptomatic patients with apparently nonobstructive HCM show features of obstruction during exercise[21].

Figure 1: PATTERN OF LV HYPERTROPHY

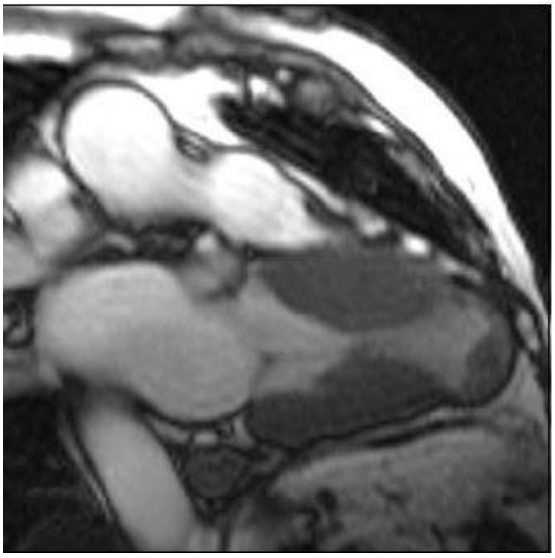
A - Asymmetric septal hypertrophy



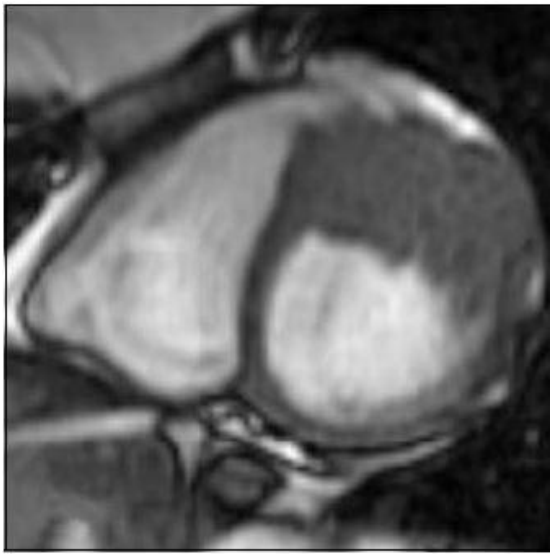
B – Apical HCM



C – Mid-ventricular



D – Mass Like



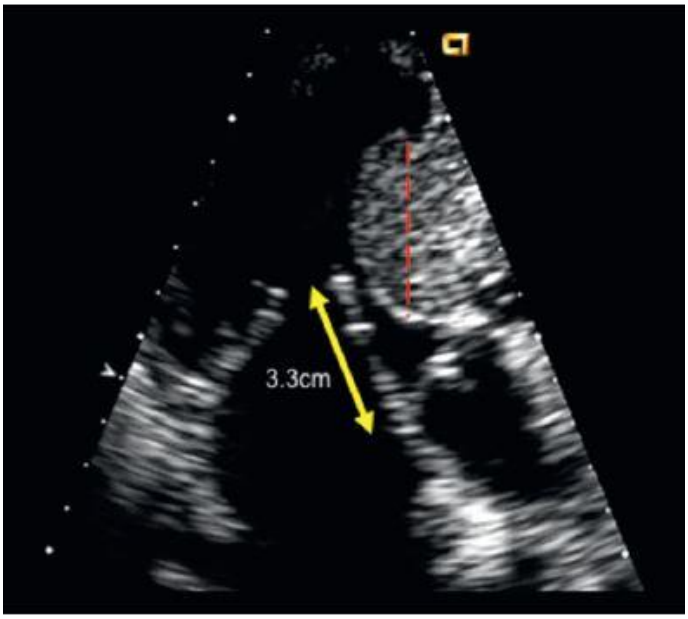
LATE GADOLINIUM ENHANCEMENT:

Late gadolinium enhancement of the left ventricular myocardium occurs in around 80% of HCM patients and is located commonly in the mid-wall with a patchy distribution. The most usual location of LGE is combined interventricular septum and the free wall location (~30% of patients) but the free wall, septum, apex, and the right ventricular insertion areas into the septum are the less commonly involved sites[23]. LGE commonly involves the anteroseptal area of the inter-ventricular septum from basal to mid segments. LGE in HCM may be attributed histologically to plexiform fibrosis (fibrosis seen in areas of myocyte disarray), expanded interstitial spaces, and replacement fibrosis due to microvascular ischemia[22].

ELONGATED ANTERIOR AND POSTERIOR MITRAL LEAFLETS:

The length of the anterior mitral leaflet in patients with obstructive HCM and normal hearts is 34 mm and 24 mm respectively. Elongated mitral leaflets protrude beyond the level of the mitral annulus into the LV cavity, with a mean of 26 mm compared with 13 mm in normal hearts[4]. Blood flow during late diastole and early systole strikes the posterior surfaces of the protruding leaflets and push them towards the inter-ventricular septum[5]. Increased ratio of anterior mitral leaflet length to LVOT diameter is associated with both provocable and resting gradients. Mitral valve abnormalities are treated with various surgical techniques like vertical plication (parallel to the long axis of the mitral valve) and horizontal placation (perpendicular to the long axis of the mitral valve).

Figure 2: Elongated AML and thickened inter-ventricular septum



Elongated mitral leaflets can displace the mitral-septal contact point (and site of subaortic obstruction) distally creating the need for an extended muscular resection[15]. The mitral-septal contact (and obstruction) can persist even after adequate septal muscular resection due to extremely elongated AML length. Various surgical reports of severely symptomatic obstructive HCM patients advocates the combined approach of septal myectomy and AML repair, with leaflet extension or shortening reconstruction or plication[16].

SYSTOLIC ANTERIOR MOTION OF MITRAL VALVE (SAM):

The following factors may contribute to SAM in HCM (1) increased length of the anterior or posterior leaflet; (2) aorto-mitral angle <120°; (3) elongation and buckling of the chordae; (4) anteromedial displacement of the papillary muscles; (6) minimum distance between the coaptation point to the septum (C-Sept, <2.5 cm) [14]. (7) Venturi effect, which is defined as "when fluid flows through a region of reduced cross-sectional

area, fluid pressure decreases, and velocity increases". Septal hypertrophy in HCM creates the venturi effect through the reduction in the LVOT diameter, which leads to increased velocity and reduced pressure of the ejected blood in the LVOT. The pressure difference between the left atrium and the outflow tract may lead to the movement of the mitral valve towards the septum. Other conditions causing SAM are hypertension, diabetes mellitus, acute myocardial infarction, post mitral valve repair, and even in asymptomatic patients during pharmacologic stress with dobutamine.

GRADING OF SAM:

Echo grading of systolic anterior motion of the mitral valve:

I: No mitral leaflet-septal contact, the minimum distance between the mitral valve and the ventricular septum during systole = 10 mm;

II: No mitral leaflet-septal contact, the minimum distance between the mitral valve and the ventricular septum during systole <10 mm;

III: Brief mitral leaflet-septal contact (<30% of systole time);

IV: Prolonged mitral leaflet-septal contact (>30% of systole time).

ELONGATED POSTERIOR LEAFLET WITH SAM:

SAM can be caused by isolated posterior leaflet elongation due to the protrusion of the residual leaflet through inter-chordal space to contact the inter-ventricular septum[11].

MITRAL VALVE ABNORMALITIES CAUSED BY MUTATIONS IN GENES CODING FOR SARCOMERIC PROTEINS:

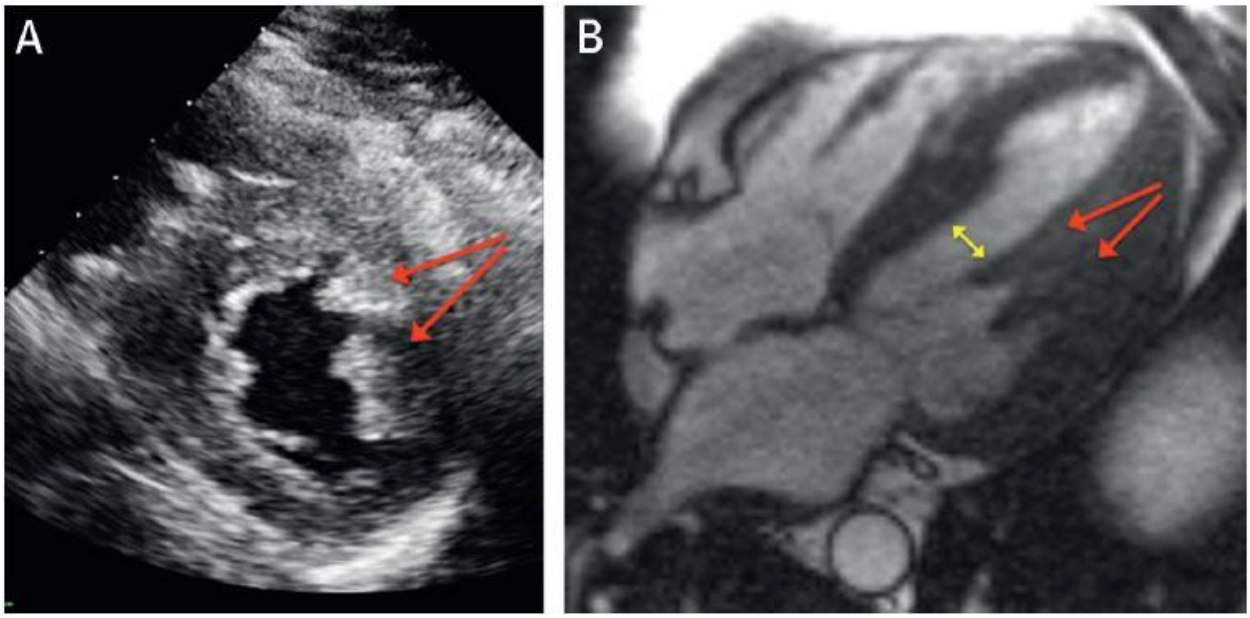
Elongation of mitral leaflets has been documented in subjects with HCM-associated mutations who have not yet developed thickening. Mitral leaflet elongation is considered to a major phenotypic expression of HCM and is not obtained due to stretch from SAM.

ANTERIOR AND BASILAR DISPLACEMENT OF THE ANTEROLATERAL PAPILLARY MUSCLE:

Anterior displacement of the papillary muscles results in the deviation of the coaptation plane of the mitral valve anteriorly in the LV cavity[6]. Two most common papillary muscles abnormalities in HCM are: 1) Antero-basilar displacement of the anterolateral papillary muscle. 2) Abnormal muscular connections between the papillary muscular head and the anterolateral wall, inserted into or near the A1 scallop[7]. CMR study by Kwon et al.[8] has shown a higher prevalence of bifid papillary muscles in HCM; Patients with LVOT obstruction due to SAM had closer proximity of papillary muscle to the septum.

Figure 3: A: ECHO - Bifid anteriorly displaced papillary muscle positions

B: MRI - Hypertrophied bifid antero-lateral papillary heads (red arrows), with the superior head in close proximity to the septum



The extended myectomy by Messmer et al[9] includes the extension of the resection laterally into the free wall above its base to release the anterolateral papillary muscle and thinning the hypertrophied heads. Papillary muscle release results in a more normal parallel orientation of the plane of the mitral annulus and aortic valve.

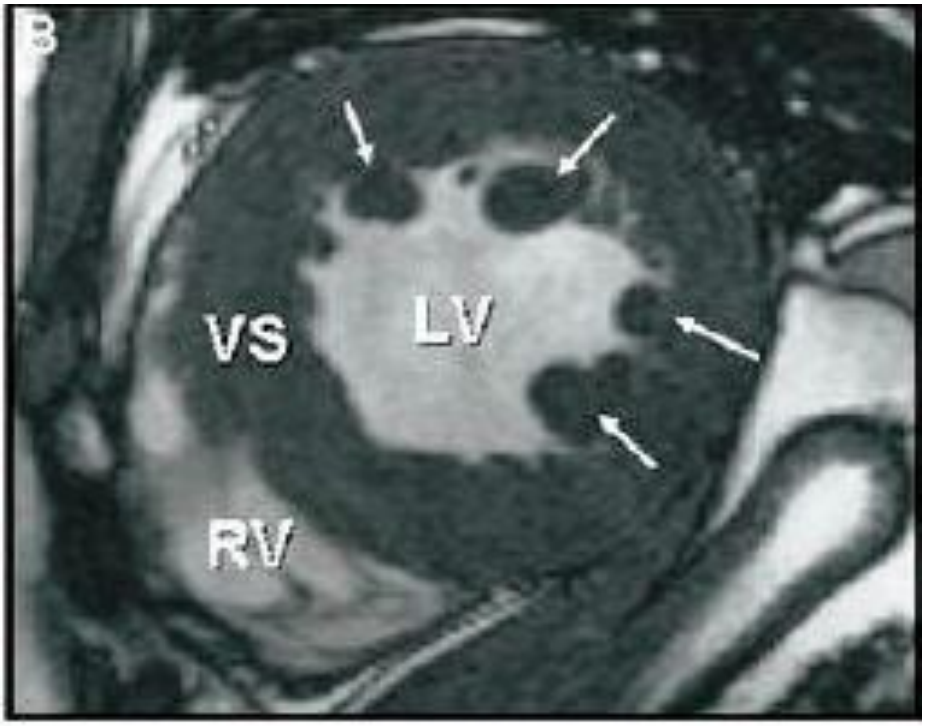
PAPILLARY MUSCLE HYPERTROPHY:

PM hypertrophy is seen in more than 50% of patients, with twice the muscle mass than controls and marked hypertrophy is present in 20%. A subgroup of patients with HCM with normal LV mass showed substantially hypertrophied PMs with increased mass. In those patients, the disproportionate papillary muscle involvement compared with the LV wall is seen. HCM patients with LV outflow obstruction is associated with higher PM mass index compared with those without obstruction. PM mass index was significantly higher in non-obstructive HCM patients compared with normal subjects[17].

INCREASED NUMBER, BIFIDITY AND LGE OF PAPILLARY MUSCLE:

The absolute number of PMs identified in patients with HC significantly exceeded that in normal subjects, ~50% have multiple PMs (i.e., 3 or 4). Around 5% of patients in HCM will have delayed LGE (i.e., indicative of myocardial fibrosis) of the PMs. Papillary muscle bifidity (involving one or more PM) is seen if there is more than one head seen on multiple cine images (apical 4-chamber and 3-chamber views).

Figure 4: Multiple accessory (four) papillary muscles

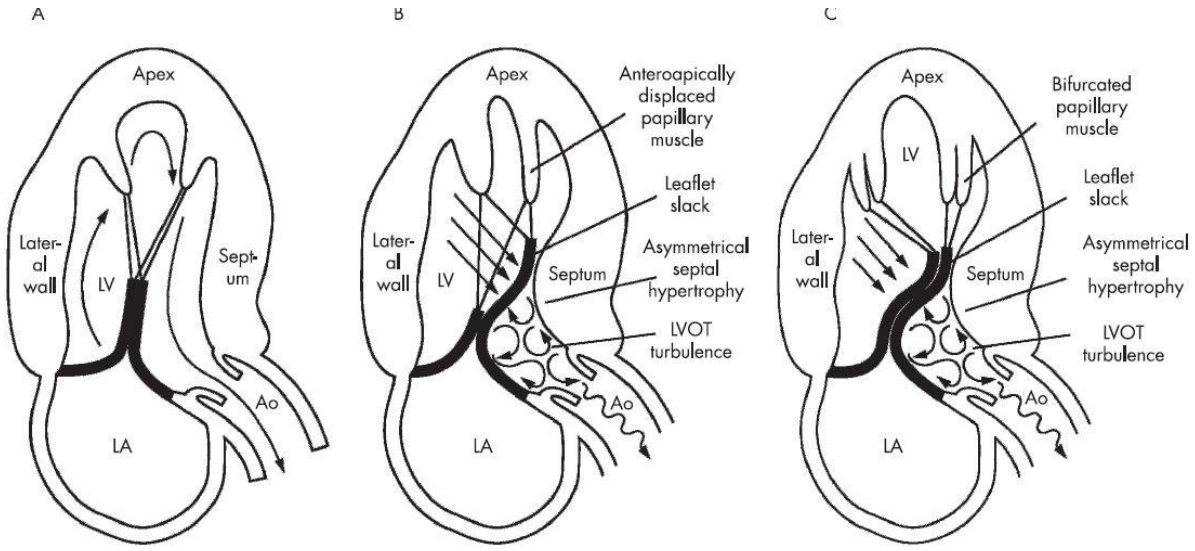


INSERTION OF ANTEROLATERAL PAPILLARY MUSCLE DIRECTLY INTO THE MIDANTERIOR MITRAL VALVE LEAFLET:

Anterolateral papillary muscle head may be directly inserted into the middle of the anterior mitral valve leaflet in the absence of intervening chordae is demonstrated in HCM. It may result in the apposition of the papillary muscles with the septum which leads to LVOT

obstruction[10]. If a large anomalous papillary muscle could not be excised, longitudinal resection to thin it, even to its base has been performed successfully.

Figure 5: A - Normal PM Morphology; B – Anteroapical displacement of PM; C – Double bifid PMs.



VARIOUS MORPHOLOGIC PATTERNS IN HCM

Figure 6: Normal LV morphology

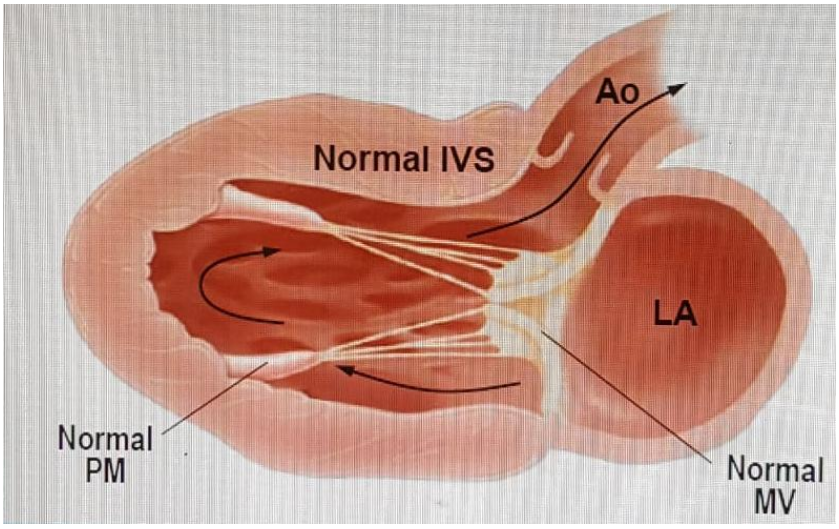


Figure 7: HCM - Thick septum with normal leaflets

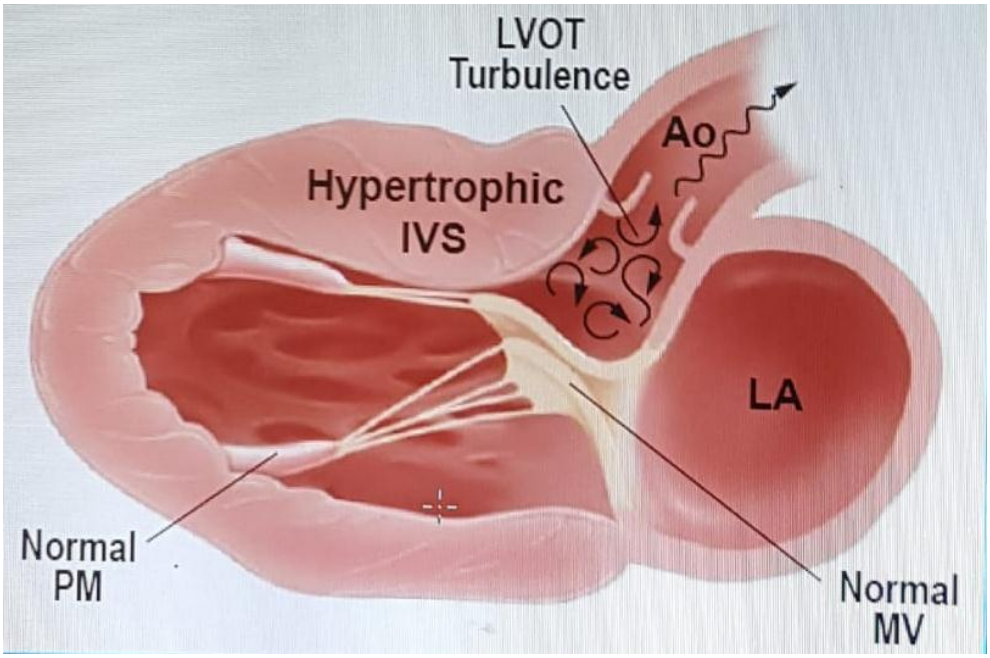


Figure 8: HCM - Thick septum and abnormal leaflets

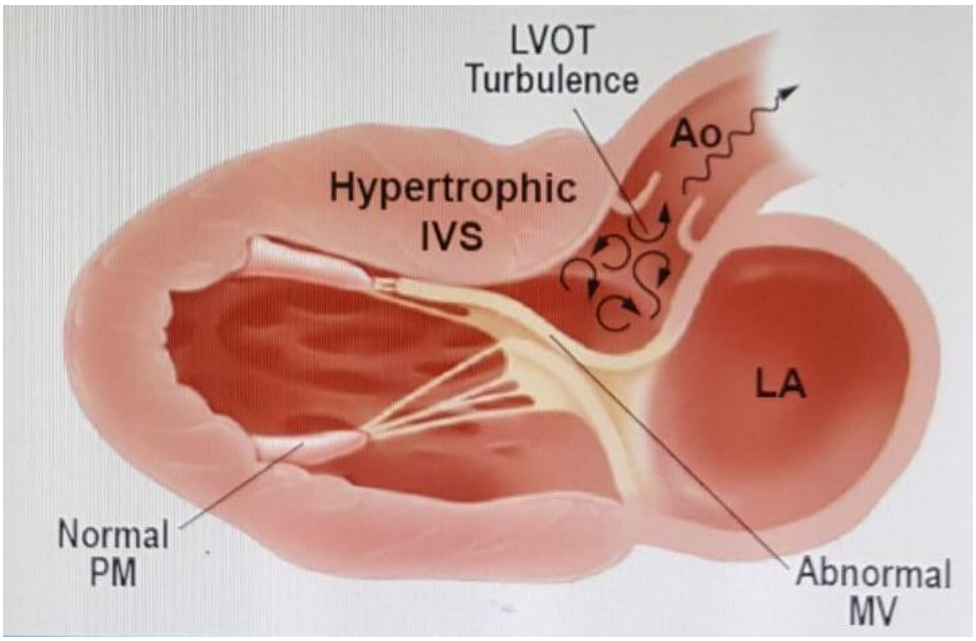


Figure 9: HCM - Thick septum, normal leaflets and apically displaced papillary muscle

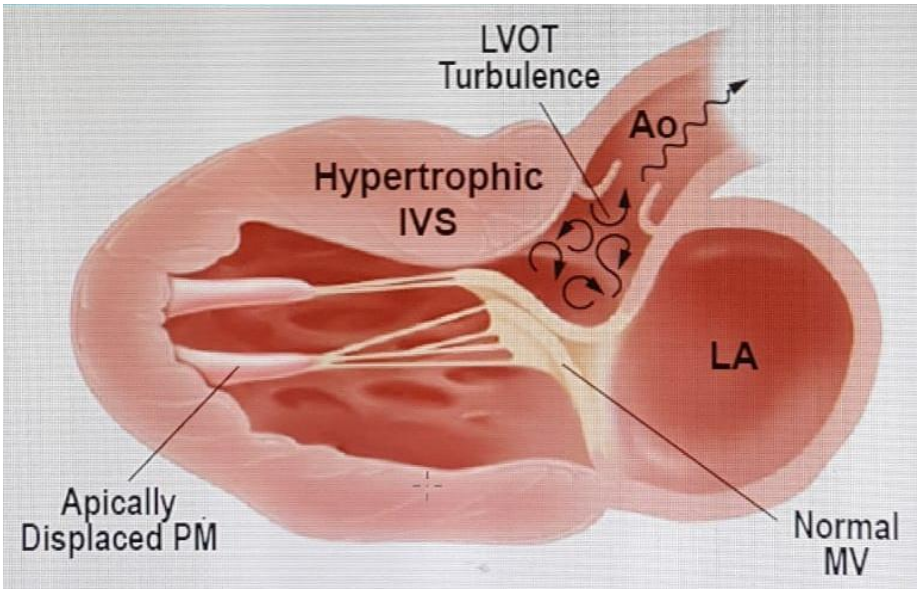


Figure 10: HCM - Thick septum and multiple accessory papillary muscles

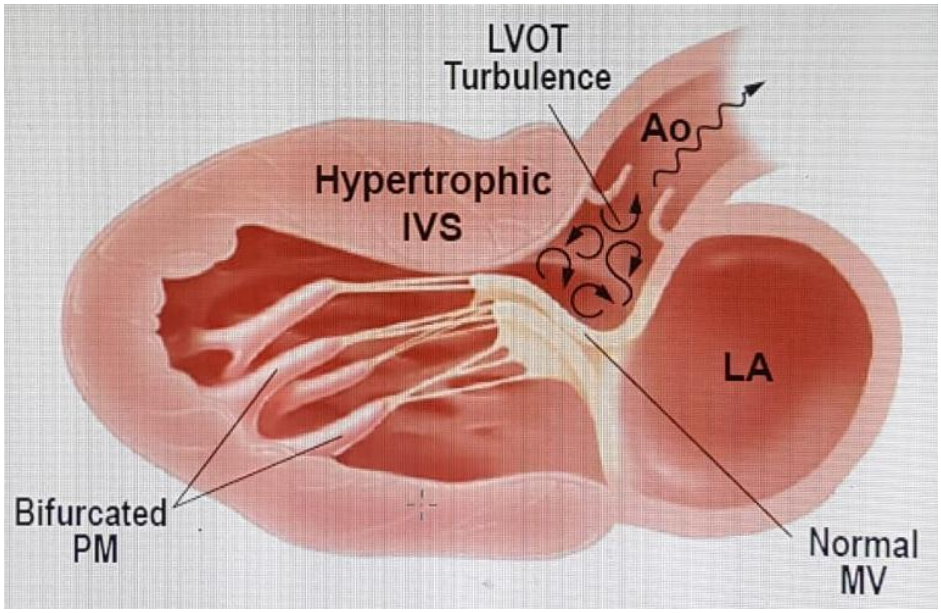
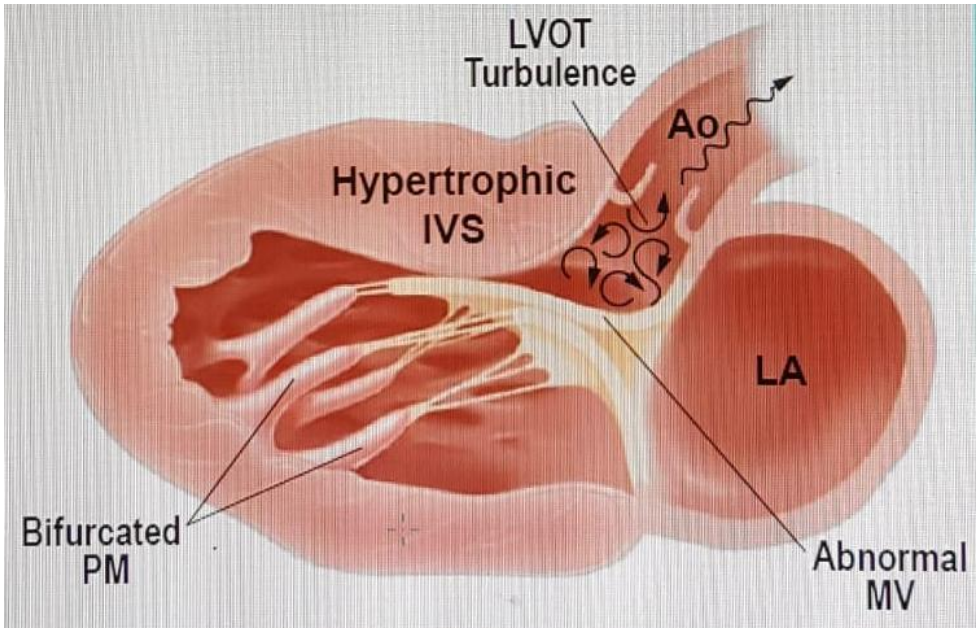


Figure 11: HCM - Thick septum, multiple accessory papillary muscles and abnormal mitral valve



Materials & Methods

MATERIALS AND METHODS

STUDY DESIGN:

The study was a retrospective observational study (approved by the Institutional Ethics Committee, No: - SCT/IEC/1176/APRIL-2018) was conducted between June 2017 to June 2019 at Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Trivandrum, a tertiary care hospital in India.

STUDY PATIENTS:

Medical records of 100 patients with HCM suspected of echocardiography, who underwent a cardiac MRI, during the period between June 2013 to June 2019 were reviewed.

INCLUSION CRITERIA:

In this study, 100 patients (>18 yrs of age) with HCM suspected of echocardiography, who underwent a cardiac MRI, were enrolled.

EXCLUSION CRITERIA

- Patients not willing to participate in the study
- Known case of amyloidosis/storage disorders
- Known case of coronary artery disease
- Contraindication to MRI
- Patients with LV systolic dysfunction (EF<50%)

METHODOLOGY:

Baseline demographic data of all enrolled patients were taken from medical records including full clinical history, symptomatic status, electrocardiogram, echocardiography details, catheterization study and CMR findings were also recorded.

TRANS-THORACIC ECHOCARDIOGRAPHY:

Detailed Echocardiography was done prior to CMR with emphasis on the following parameters:

- LV internal dimensions, septal and posterior wall thickness in end-diastole.
- Patterns of hypertrophy of the ventricles.
- LVOT and mid-cavity gradients.
- Systolic anterior motion of the mitral valve and mitral regurgitation severity.
- Maximum LV wall thickness in end-diastole.

CARDIAC MRI:

Cardiac MRI was done with SIEMENS 1.5 T somatom sensation, Seimens health care Germany and GE 3 Tesla system (Discovery 750w; General electric GE healthcare; USA). Following parameters were assessed:

- Ventricular hypertrophy distribution
- Assessment of the level of ventricular obstruction
- LV function
- Mitral valvular abnormalities
- Papillary muscle abnormalities

MITRAL VALVE ABNORMALITIES:

The following parameters of the mitral valve were assessed.

- AML and PML length
    - Measured at end-diastole in 3-chamber view, with the leaflets maximally extended parallel to the anterior septum and LV free wall.
    - AML - distal most extent to its insertion into posterior aortic wall
    - PML – distal most extent to its insertion into basal LV posterior free wall.
- SAM and MR severity
- LGE of the mitral valve
- Correlation of AML length with LV obstruction
- Correlation of PML length with LV obstruction
- Correlation of SAM with LV obstruction

PAPILLARY MUSCLE ABNORMALITIES:

The following parameters of the papillary muscle were assessed.

- Number of papillary muscles in short-axis cine images at 3 levels (basal, mid-ventricular and apical)
- Bifidity of the papillary muscles (in apical 4-chamber and 3-chamber view)
- Late gadolinium enhancement of the papillary muscles
- Correlation of the papillary muscle abnormalities with LV obstruction

STATISTICAL ANALYSIS:

The data were analyzed with commercially available statistical software (SPSS) to study the percentage of patients who had the mitral valve and papillary muscle abnormalities in hypertrophic cardiomyopathy. Continuous variables are expressed as mean with standard deviations and discrete variables as counts and percentages. For categorical variables, the chi-square test and Fisher exact t-test were used, and for continuous variables, Student t-test was used. HCM patients were divided into two groups such as HCM with obstruction and HCM without obstruction. Mitral valve and papillary muscle abnormalities in both the groups were noted and their correlation with left ventricular obstruction was assessed. A p-value less than or equal to 0.05 was considered statistically significant.

Results

RESULTS

Hundred patients of HCM who underwent cardiac MRI were included in the study. Males constituted 64% and females 36% of the study population. The mean age was 43.4 ± 14.33 years. Mean follow-up duration in months was 38.83 months (median 1-226 months). Family history of HCM was present in 13% of patients. H/o sudden cardiac arrest was present in 17% of patients. Dyspnea was the most common presenting symptom in 61% of patients, followed by chest pain in 41% of patients.

Figure 12: SYMPTOMATOLOGY

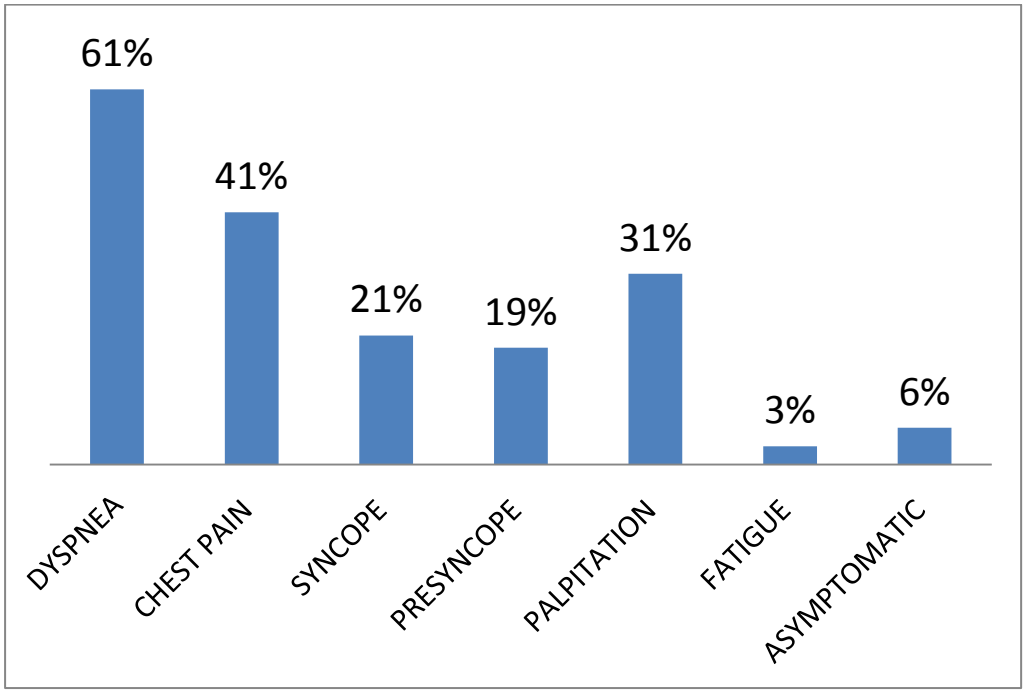


Table 1: BASELINE CHARACTERISTICS

	HCM (100 pts)	HCM WITH OBSTRUCTION (36 pts)	HCM WITHOUT OBSTRUCTION (64 pts)	CONTROLS (25 pts)
AGE IN YEARS (±SD)	43.4 (±14.3)	44.8 (±14.6)	48.5 (±14.0)	44.32 (±15.6)
GENDER MALE FEMALE	 64 36	 29 9	 37 27	 12 13
Family history Of HCM	13(13%)	3(8.3%)	10(15.6%)	2(8%)
Family history of SCD	17(17%)	5(13.9%)	12(18.7%)	4(16%)
NYHA FC (mean) FC 1 FC 2 FC 3 FC 4	2.06 14% 66% 20% nil	2.25 2.8% 69.4% 27.8% nil	1.95 20.3% 64.% 15.6% nil	1.72 28% 72% nil nil
CATH (mm Hg) PCWP LVed	 18.43(38 pts) 23.39(38 pts)	 20.7(17 pts) 26(17 pts)	 16.7(21 pts) 21.28(21 pts)	 not done not done

Catheterization study was performed in 38 HCM patients and mean pulmonary capillary wedge pressures (PCWP) and LV end-diastolic (LVed) pressures were 18.43 and 23.39 mm hg respectively. Mean PCWP and LVed in patients with obstructive HCM were 20.7 and 26 mm hg respectively. Mean PCWP and LVed in patients without obstructive HCM were 16.7 and 21.28 mm hg respectively.

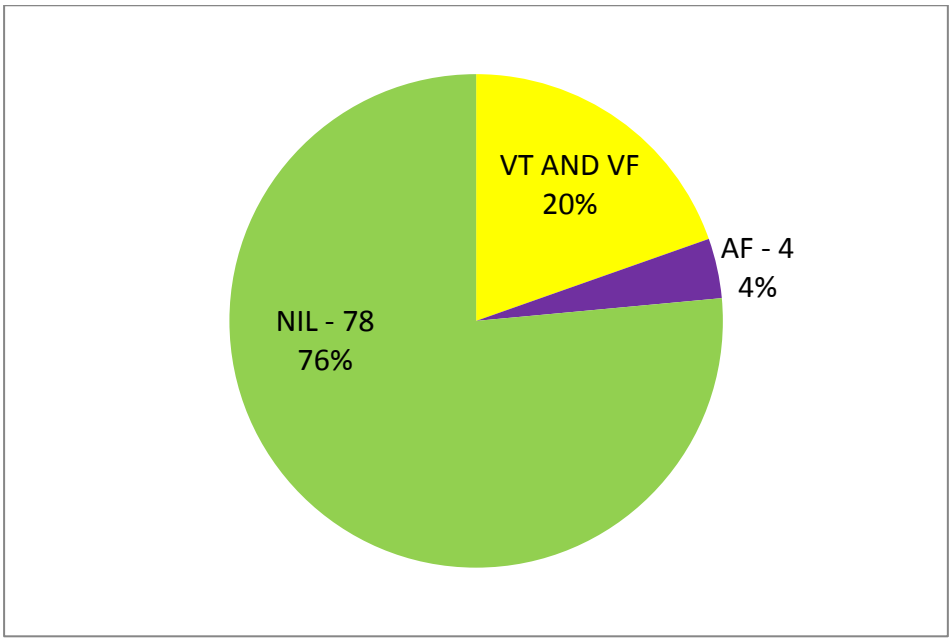
Table 2: INVASIVE PROCEDURES

PROCEDURE	No. of patients
Alcohol Septal Ablation (ASA)	10
Electrophysiology Study (EPS)	8
Permanent pacemaker implantation (PPI)	5
Implantable Cardioverter Defibrillator (ICD)	9 (1-primary,8-secondary prophylaxis)
Cardiac Resynchronization Therapy (CRT-D)	1

No events were noted in HCM patients with either ICD or CRT-D over 38.83 months of follow-up.

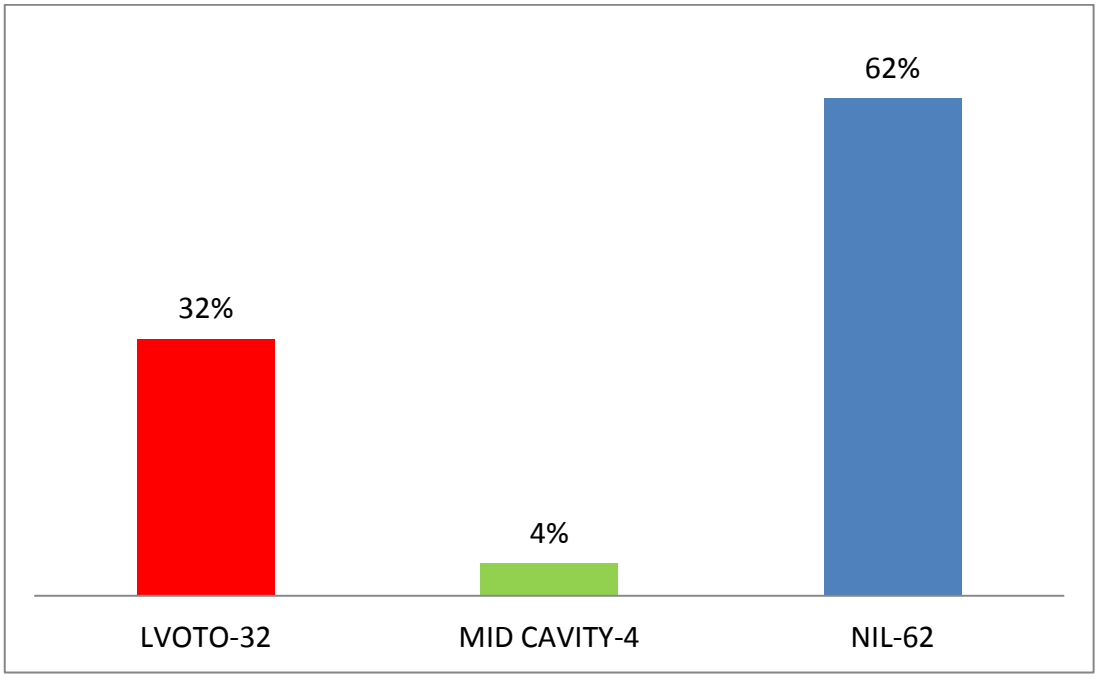
Arrythmia was documented in 24% of patients. VT/VF was the most common arrhythmia was seen in 20% of patients and atrial fibrillation was seen in 4% of patients.

Figure 13: ARRYTHMIA



Trans-thoracic echocardiography showed LV obstruction in 36% of patients (LVOT obstruction -32% and mid cavity obstruction – 4%).

Figure 14: LEVEL OF LV OBSTRUCTION – BY ECHO



MRI CHARACTERISTICS:

Mean LVEF was 70.1 ± 11%. Asymmetric septal hypertrophy was the most common pattern of LV involvement seen in 71% of patients. Maximum LV thickness in end-diastole is 22.88 ± 6.17 mm. Mean indexed myocardial mass is 99.5 ± 31.11 g/mm^2. LGE of the myocardium is seen in 67% of patients. Mid-myocardial LGE is seen in 88% and sub-endocardial LGE in 6% of patients. LGE of the inter-ventricular septum is the most common involved segment in 66% of patients.

Figure 15: PATTERN OF VENTRICULAR HYPERTROPHY - ALL HCM PATIENTS

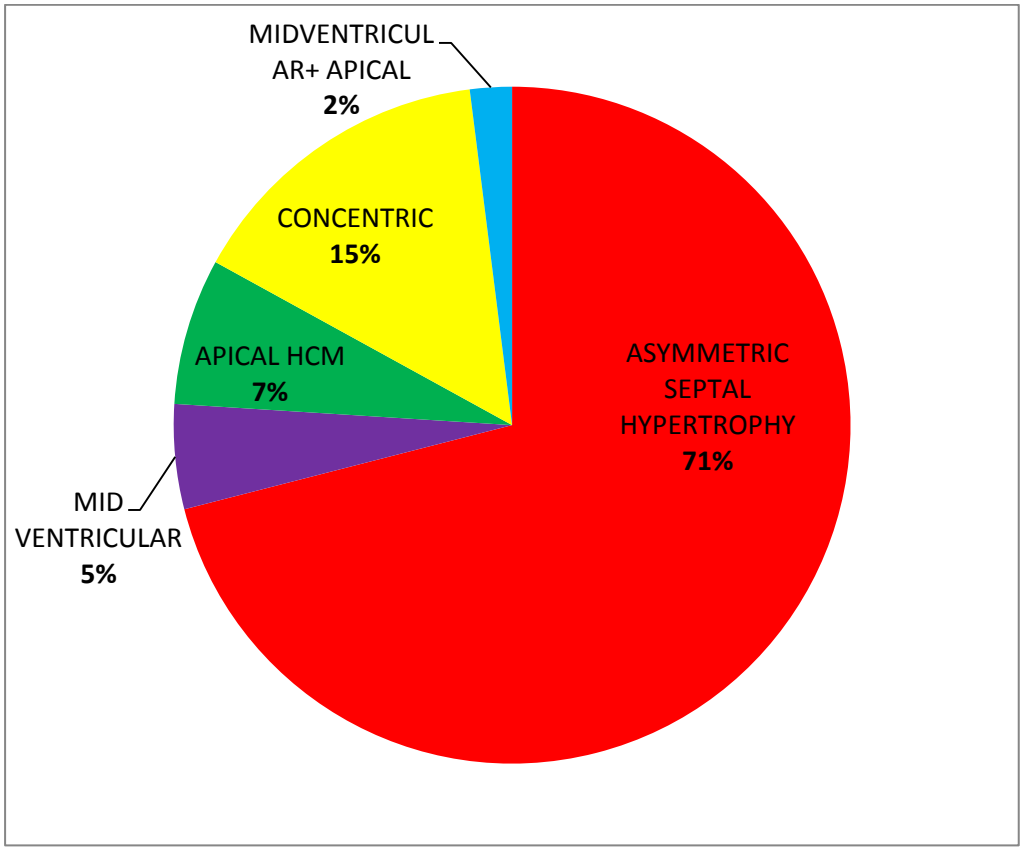


Figure 16: EXTENT OF LV HYPERTROPHY - ALL HCM PATIENTS

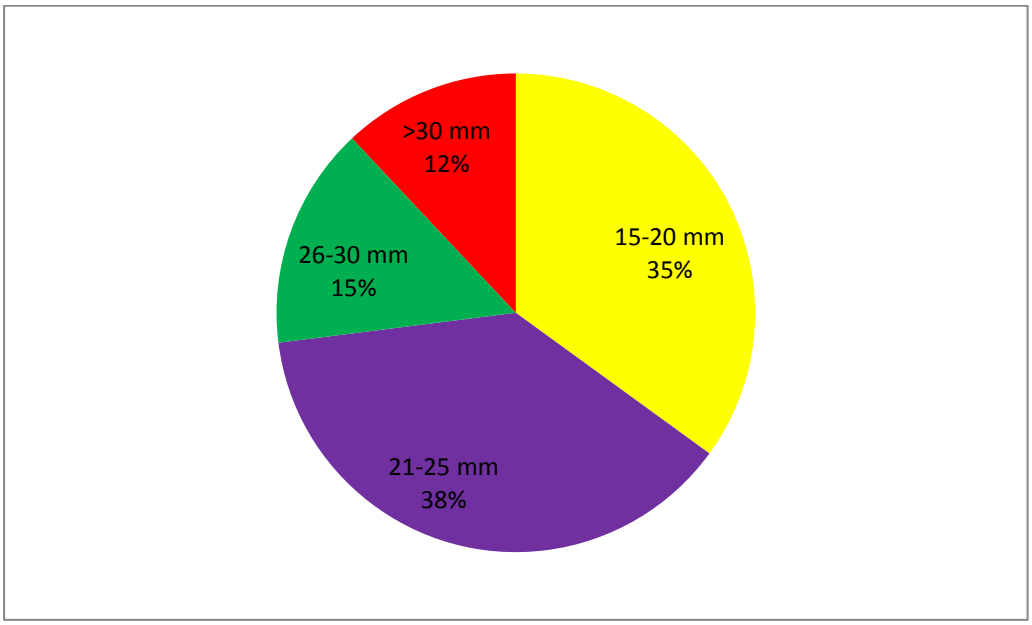


Figure 17: PATTERN OF LGE – ALL HCM PATIENTS

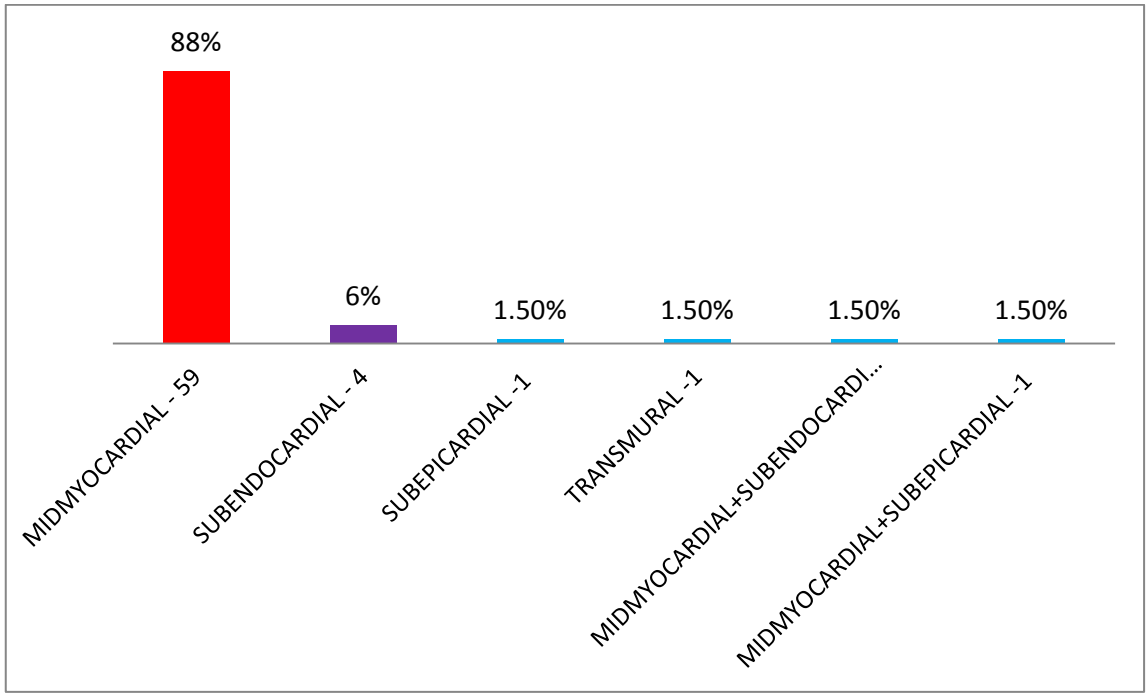
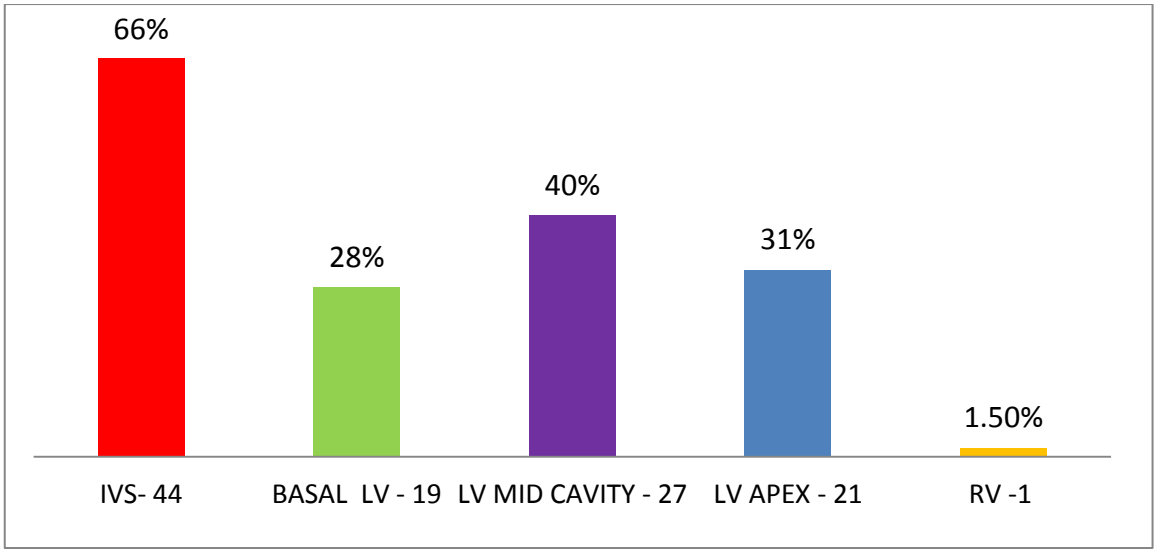


Figure 18: AREA OF LGE INVOLVEMENT – ALL HCM PATIENTS



COMPARISION BETWEEN DIFFERENT GROUPS

Table 3: OBSTRUCTIVE HCM vs NON-OBSTRUCTIVE HCM vs CONTROLS

	HCM (100 pts)	HCM WITH OBSTRUCTION (36 pts)	HCM WITHOUT OBSTRUCTION (64 pts)	CONTROLS (25 pts)
LVEF%	70.1	72.11	68.96	62.26
LGE of myocardium	67%	28(78%)	39(60.9%)	nil
LGE of mitral valve	28%	13(36%)	15(23.4%)	nil
LGE of PM	7%	6(17%)	1(1.5%)	nil
Maximum LV thickness in diastole (mm)	22.9	25.8	21.21	12.68
Mean AML length (mm)	25.83	28.17	24.5	17.92
Mean PML length (mm)	15.75	16.28	15.4	9
SAM of AML Yes No	 46% 56%	 77.8% 22.2%	 28% 72%	 Nil
No of PM 2 3 4	 47% 51% 2%	 17(47%) 18(50%) 1 (2.8%)	 30(46.8%) 32(50%) 2(3.1%)	 23(92%) 1(4%) 1(4%)
PM hypertrophy	82%	29(80.5%)	53(82.8%)	2(8%)
PM bifidity	61%	26(72.2%)	35(54.7%)	2(8%)
Mean indexed myocardial mass (g/mm^2)	99.5 (36 pts)	120(11 pts)	90.48(25 pts)	-

COMPARISION OF OBSTRUCTIVE vs NON OBSTRUCTIVE HCM

Figure 19: PATTERN OF HYPERTROPHY

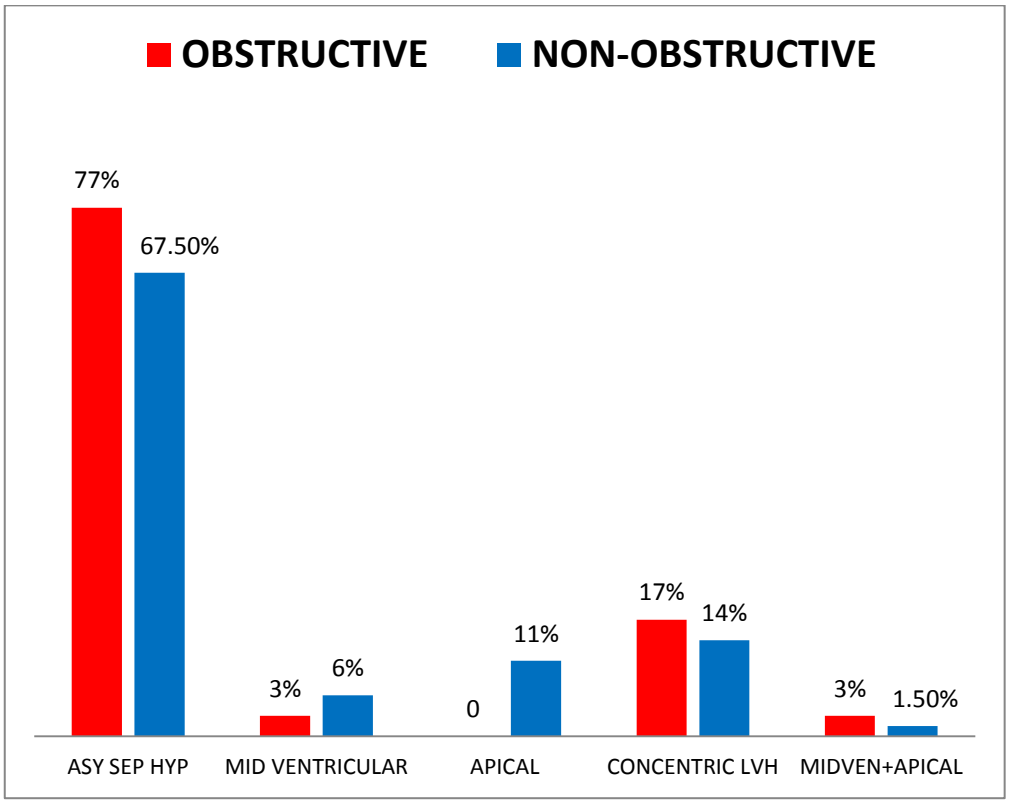


Figure 20: EXTENT OF LV HYPERTROPHY

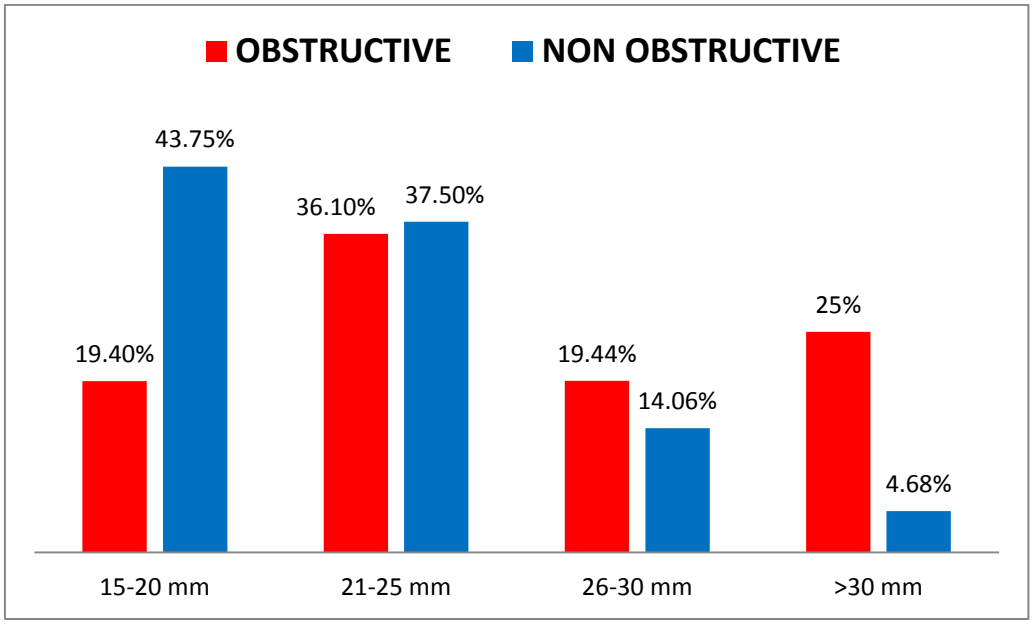


Figure 21: LGE PATTERN IN MYOCARDIUM

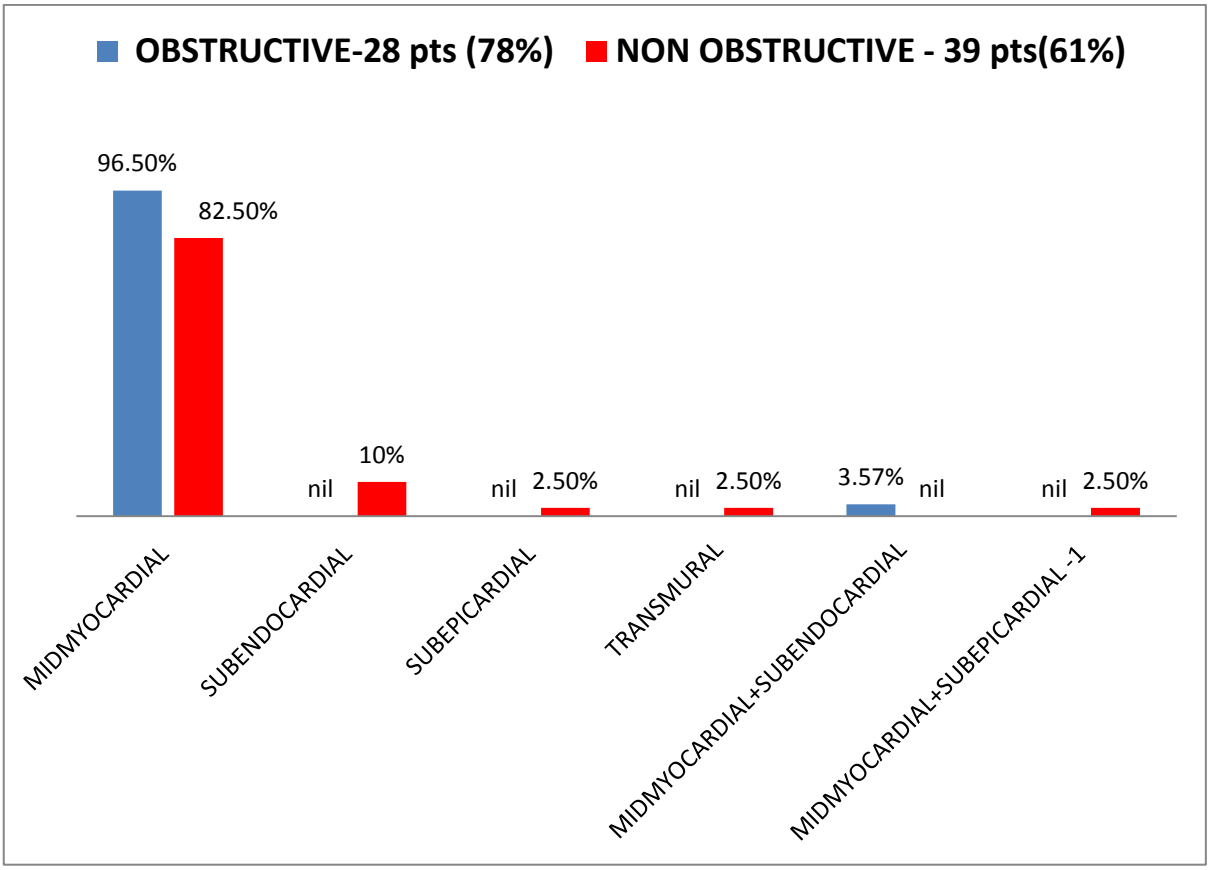
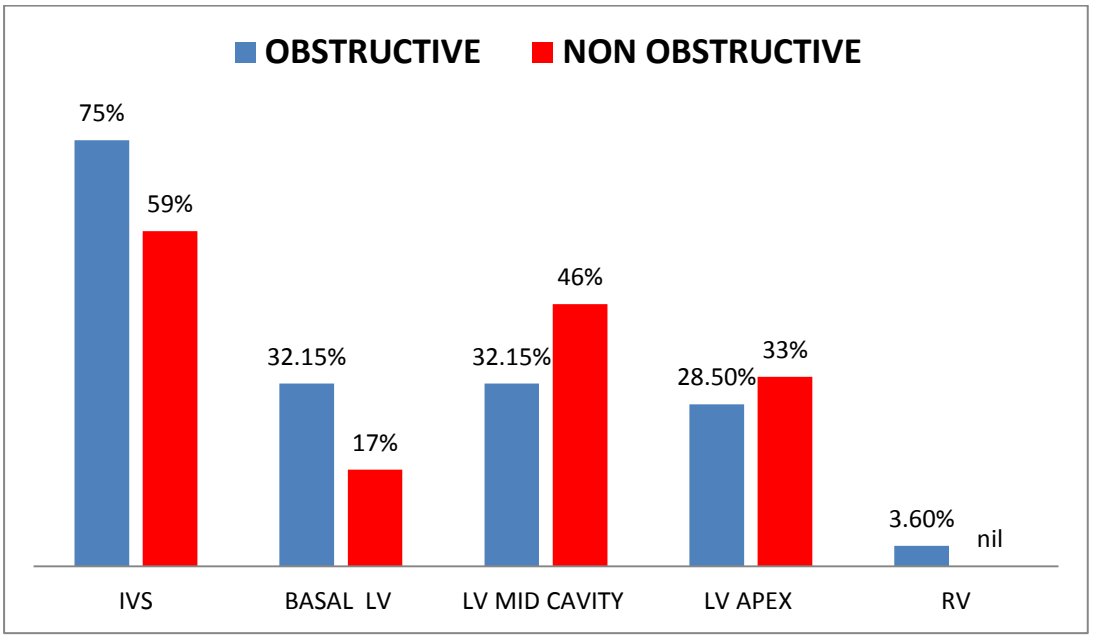


Figure 22: AREA OF LGE IN VENTRICLES



VARIABLES WITH LVOT OBSTRUCTION:

Table 4: AML LENGTH SEVERITY WITH LVOT OBSTRUCTION:					
		LVOT gradient			
		Obstructive	Non-obstructive	Total	
AML LENGTH SEVERITY	<30mm	21	56	77	p value <0.001
	≥30mm	15	8	23	
	Total	36	64	100	

Table 5: SAM OF AML WITH LVOT OBSTRUCTION:

		LVOT gradient		Total	
		Obstructive	Nonobstructive		
SAM OF AML	Present	28	18	46	p value <0.001
	Absent	8	46	54	
	Total	36	64	100	

Table 6: PM HYPERTROPHY WITH LVOT OBSTRUCTION:

		LVOT gradient		Total	
		Obstructive	Nonobstructive		
PM HYPERTROPHY	Present	29	53	82	pvalue 1.0
	Absent	7	11	18	
	Total	36	64	100	

Table 7: PM BIFIDITY WITH LVOT OBSTRUCTION:

		LVOT gradient		Total	
		Obstructive	Non-obstructive		
PM BIFIDITY	Present	26	35	61	p value 0.09
	Absent	10	29	39	
	Total	36	64	100	

Table 8: EXTENT OF LV HYPERTROPHY WITH LVOT OBSTRUCTION:

		LVOT gradient		Total	
		Obstructive	**Non-obstructive**		
EXTENT OF LV HYPERTRPHY (mm)	**15-20**	7	28	35	p value < 0.03
	21-25	13	24	37	
	26-30	7	9	16	
	31-35	9	3	12	
	Total	36	64	100	

Based on the LV thickness in end-diastole, patients were categorized into 4 groups such as 15-20 mm, 21-25 mm, 26-30 mm, >30 mm. Among all HCM patients, LV thickness of 15-20 mm is seen in 35%, 21-25 mm in 38%, 26-30 mm in 15% and >30 mm in 12%. LGE of the mitral valve and papillary muscles was seen in 28% and 7% respectively. Mean AML length in HCM patients was 25.83 ± 4.8 mm and the mean PML length was 15.75 ± 3.06 mm. Systolic anterior motion of AML is seen in 46% of patients. Papillary muscle hypertrophy is seen in 82% of patients. Bifid papillary muscle is seen in 61% of patients.

COMPARISION OF HCM vs CONTROLS

Table 9: BASELINE PARAMETERS

	HCM	CONTROLS	p value
LVEF (%)	70.1	62.26	0.38
LGE OF MYOCARDIUM	67%	nil	-
LGE OF MITRAL VALVE	28%	nil	-
LGE OF PM	7%	nil	-
MEAN AML LENGTH (mm)	25.83	17.92	<0.001
MEAN PML LENGTH (mm)	15.75	9	<0.001
MAXXIMUM LV THICKNESS IN DIASTOLE (mm)	22.9	12.62	0.001

Table 10: SAM OF AML

SAM OF AML	HCM	CONTROLS	
PRESENT	46	1	p value < 0.001
ABSENT	56	24	
TOTAL	100	25	

Table 11: NUMBER OF PAPILLARY MUSCLES

No of PM	HCM	CONTROLS	
TWO	47	23	p value < 0.001
THREE	51	1	
FOUR	2	1	
TOTAL	100	25	

Table 12: PM HYPERTROPHY

PM HYPERTROPHY	HCM	CONTROLS	
PRESENT	82	2	p value < 0.001
ABSENT	18	23	
TOTAL	100	25	

Table 13: PM BIFIDITY

PM BIFIDITY	HCM	CONTROLS	
PRESENT	61	2	p value < 0.001
ABSENT	39	23	
TOTAL	100	25	

Discussion

DISCUSSION

Hundred HCM patients have been categorized into 2 groups; HCM with obstruction (36 patients) and HCM without obstruction (64 patients). 25 normal subjects who underwent cardiac MRI for suspected ARVD or other arrhythmic disorders and found to have normal cardiac MRI study were included as controls for analysis.

MRI CHARACTERISTICS:

COMPARISION OF OBSTRUCTIVE vs NON-OBSTRUCTIVE HCM

Mean LVEF in patients with obstructive HCM, HCM without obstruction was 72.11% and 68.96% respectively. Asymmetric septal hypertrophy was seen in 77% of obstructive HCM patients and 67.5% of non-obstructive HCM patients. Concentric LVH was seen in 17% of obstructive HCM patients and 14% of non-obstructive HCM patients.

Based on the LV thickness in end-diastole patients were categorized into 4 groups such as 15-20 mm, 21-25 mm, 26-30 mm, >30 mm. Among obstructive HCM patients, LV thickness of 15-20 mm is seen in 19.4%, 21-25 mm in 36.1%, 26-30 mm in 19.44% and >30 mm in 25%. Among non-obstructive patients, LV thickness of 15-20 mm is seen in 43.75%, 21-25 mm in 37.5%, 26-30 mm in 14.06% and >30 mm in 4.68%.

LGE of the myocardium is seen in 78% of patients with obstruction vs 60.9% of patients without obstruction. In patients with obstructive HCM, LGE of the myocardium is present in mid-myocardium in 96.5% and 3.5% in mid-myocardial + sub-endocardial regions. In patients without obstruction, LGE of the myocardium is present in mid-myocardium in 82.5%, 10% subendocardial, 2.5% subepicardial, 2.5% transmural and 2.5 % midmyocardial + subepicardial regions. In obstructive HCM patients, LGE of the interventricular septum,

LV base, LV mid-cavity, LV apex and RV were involved in 75%, 32.15%, 32.15%, 28.5% and 3.6% respectively. In non-obstructive HCM patients, LGE of the interventricular septum, LV base, LV mid-cavity, and LV apex were involved in 59%, 17%, 46% and 33% respectively.

LGE of the mitral valve is present in 36% vs 23.4% in patients with and without obstruction respectively. LGE of papillary muscle is seen in 17% vs 1.5% of patients with and without obstruction respectively. The maximum mean LV wall thickness in end-diastole was higher in patients with obstruction (25.8 mm) compared to patients without obstruction (21.2 mm) or controls (21.2 mm).

AML length in HCM patients with obstruction, HCM without obstruction and controls were 28.17 mm, 24.5 mm and 17.92 mm respectively. PML length in HCM patients with obstruction, HCM without obstruction and controls were 16.28 mm, 15.4 mm and 9 mm respectively. SAM was present in 77.8% vs 28% in HCM patients with obstruction and HCM without obstruction respectively. SAM was absent in all controls.

Papillary muscle hypertrophy is seen in 80.5%, 82.8% and 8% in HCM patients with obstruction, HCM without obstruction and controls respectively. Papillary muscle bifidity is seen in 72.2%, 54.7% and 8% in HCM patients with obstruction, HCM without obstruction and control subjects respectively. The mean indexed myocardial mass in patients with obstructive HCM and HCM without obstruction were 120 g/mm^2 and 90.48 g/mm^2 respectively. Accessory papillary muscles (ie.3 PMs) were seen in 53% of patients in obstructive HCM, 50% in non-obstructive HCM and 4% in controls.

FACTORS ASSOCIATED WITH LVOT OBSTRUCTION:

AML length measured at end-diastole in 3-chamber view was divided into two groups <30 mm and ≥30 mm, to assess its correlation with LVOT obstruction. In obstructive HCM patients, 42% of patients had AML length ≥30 mm, whereas in non-obstructive HCM patients, only 12.5% had AML length ≥30 mm ($p<0.001$). SAM of AML is present in 78% of patients in obstructive HCM vs 28% in non-obstructive HCM ($p<0.001$).

Papillary muscle hypertrophy was present in 80.5% in obstructive HCM and 82.8% in non-obstructive HCM patients. Papillary muscle bifidity was present in 72.2% in obstructive HCM and 54.6% in non-obstructive HCM patients (p 0.09).

Based on the extent of LV hypertrophy (maximum LV thickness in end-diastole) patients have been categorized into four groups. 15-20 mm, 21-25 mm, 26-30 mm and >30 mm. Patients with LVOT obstruction with LV thickness of 15-20 mm, 21-25 mm, 26-30 mm and >30 mm were 19.45%, 36.11%, 19.45% and 25% respectively, whereas patients without LVOT obstruction with LV thickness of 15-20 mm, 21-25 mm, 26-30 mm and >30 mm amounted to 43.75%, 37.5%, 14.06% and 4.68% respectively (p 0.03).

AML length >30 mm, SAM of AML and extent of LV hypertrophy were correlated significantly with LVOT obstruction in HCM patients. PM hypertrophy and PM bifidity were not significantly correlated with LVOT obstruction in HCM patients.

COMPARISION OF HCM PATIENTS AND CONTROLS:

Mean LVEF in HCM is 70.1% and in controls is 62.26%. LGE in the myocardium, mitral valve, and papillary muscle were 67%, 28% and 7%. LGE was absent in myocardium, mitral valve and papillary muscle in controls. Mean maximum LV thickness in end-diastole in HCM and controls was 22.9 mm and 12.68 mm respectively.

The mean length of AML in HCM and controls were 25.83 mm and 17.92 mm respectively ($p<0.001$). The mean length of PML in HCM and controls were 15.75 mm and 9 mm respectively ($p<0.001$). SAM of AML is present in 46% of HCM patients and 1 patient in controls ($p<0.001$).

Three papillary muscles were seen in 51 patients and 1 patient in HCM and controls respectively. Four papillary muscles were seen in 2 patients in HCM and 1 patient of controls ($p<0.001$). Papillary muscle hypertrophy was noted in 82 patients of HCM vs 2 patients in controls ($p<0.001$). Papillary muscle bifidity was seen in 61 patients in HCM vs 2 patients in controls ($p<0.001$).

The mean AML and PML lengths were significantly higher in HCM patients compared to controls. The mean maximum LV thickness is higher in HCM patients compared to controls. SAM of AML was absent in controls and present in 46% of HCM patients. HCM patients were characterized by an increased number of accessory papillary muscles. Papillary muscle hypertrophy and PM bifidity were more common in HCM patients than controls.

Limitations

LIMITATIONS

It was a single-center study conducted in a tertiary care center and there is a chance of selection bias. Due to the dynamic nature of the LVOT gradient, it could be affected by a lot of factors, including heart rate, arrhythmia, body position and volume status. LVOT gradient at a particular point of time might not be a true representation of the dynamic LVOT gradient. Since there are no proper standardized methods of assessment of PM morphology or dimensions by MRI and it could be subjected to various errors. SAM of AML could be influenced by various other factors in addition to the mitral valve, papillary muscle, and LV morphology. PM displacement and PM mass of the HCM patients were not included in the study.

.

Conclusions

CONCLUSIONS

The mean AML and PML lengths were significantly higher in HCM patients compared to controls. SAM of AML was absent in controls and present in 46% of HCM patients. HCM patients were characterized by an increased number of accessory papillary muscles. Papillary muscle hypertrophy and PM bifidity were more common in HCM patients than controls.

AML length >30 mm, SAM of AML and extent of LV hypertrophy were correlated significantly with resting LVOT obstruction in HCM patients. PM hypertrophy and PM bifidity were not significantly correlated with resting LVOT obstruction in HCM patients.

Bibliography

REFERENCES

1. Delling FN, Sanborn DY, Levine RA, et al. Frequency and mechanism of persistent systolic anterior motion and mitral regurgitation after septal ablation in obstructive hypertrophic cardiomyopathy. Am J Cardiol 2007;100:1691–5.

2. Gersh BJ, Maron BJ, Bonow RO, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011;58:2703–38.

3. Grigg LE, Wigle ED, Williams WG, et al. Transesophageal Doppler echocardiography in obstructive hypertrophic cardiomyopathy: clarification of pathophysiology and importance in intraoperative decision making. J Am Coll Cardiol 1992;20:42–52.

4. Ro R, Halpern D, Sahn DJ, et al. Vector flow mapping in obstructive hypertrophic cardiomyopathy to assess the relationship of early systolic left ventricular flow and the mitral valve. J Am Coll Cardiol 2014; 64:1984–95.

5. Maron MS, Olivotto I, Harrigan C, et al. Mitral valve abnormalities identified by cardiovascular magnetic resonance represent a primary phenotypic expression of hypertrophic cardiomyopathy.Circulation 2011;124:40–7.

6. Levine RA, Vlahakes GJ, Lefebvre X, et al. Papillary muscle displacement causes systolic anterior motion of the mitral valve. Experimental validation and insights into the mechanism of subaortic obstruction. Circulation 1995;91:1189–95.

7. Halpern DG, Swistel DG, Po JR, et al. Echocardiography before and after resect-plicaterelease surgical myectomy for obstructive hypertrophic cardiomyopathy. J Am Soc Echocardiogr 2015;28:1318–28.

8. Kwon DH, Setser RM, Thamilarasan M, et al. Abnormal papillary muscle morphology is independently associated with increased left ventricular outflow tract obstruction in hypertrophic cardiomyopathy. Heart 2008;94:1295–301.

9. Messmer BJ. Extended myectomy for hypertrophic obstructive cardiomyopathy. Ann Thorac Surg 1994;58:575–7.

10. Minakata K, Dearani JA, Nishimura RA, et al. Extended septal myectomy for hypertrophic obstructive cardiomyopathy with anomalous mitral papillary muscles or chordae. J Thorac Cardiovasc Surg 2004;127:481–9.

11. Hagège AA, Bruneval P, Levine RA, et al. The mitral valve in hypertrophic cardiomyopathy: old versus new concepts. J Cardiovasc Transl Res 2011;4:757–66.

12. Roberts WC. Operative treatment of hypertrophic obstructive cardiomyopathy. The case against mitral valve replacement. Am J Cardiol 1973;32:377–81.

13. Dearani JA, Ommen SR, Gersh BJ, et al. Surgery insight: Septal myectomy for obstructive hypertrophic cardiomyopathy—the Mayo Clinic experience. Nat Clin Pract Cardiovasc Med 2007;4: 503–12.

14. Ibrahim M, Rao C, Ashrafian H, Chaudhry U, Darzi A, Athanasiou T. Modern management of systolic anterior motion of the mitral valve. Eur J Cardiothorac Surg. 2012;41:1260–1270. doi:10.1093/ejcts/ezr232

15. Yacoub MH. Surgical versus alcohol septal ablation for hypertrophic obstructive cardiomyopathy: the pendulum swings. *Circulation*. 2005; 112:450–452.

16. Balaram SK, Sherrid MV, Derose JJ Jr, Hillel Z, Winson G, Swistel DG. Beyond extended myectomy for hypertrophic cardiomyopathy: the resection-plication-release (RPR) repair. *Ann Thorac Surg*. 2005;80: 217–223.

17. Casolo G OI, Manta R, Rega L, Nistri S, Petrone P, Gensini GF. Relationship of echocardiographic maximum left ventricular wall thickness to cardiac mass assessed by magnetic resonance in hypertrophic cardiomyopathy. *Eur Heart J* 2005;26:387.

18. Sipola P, Lauerma J, Jääskeläinen P, et al. Cine MR imaging of myocardial contractile impairment in patients with hypertrophic cardiomyopathy attributable to Asp175Asn mutation in the alpha-tropomyosin gene. *Radiology* 2005; 236:815–824

19. Elliott P, McKenna WJ. Hypertrophic cardiomyopathy. *Lancet* 2004; 363:1881–1891

20. Wigle ED. Cardiomyopathy: the diagnosis of hypertrophic cardiomyopathy. *Heart* 2001; 86:709–714

21. Hughes SE. The pathology of hypertrophic cardiomyopathy. *Histopathology* 2004; 44:412–427

22. Moon JC, McKenna WJ, McCrohon JA, Elliott PM, Smith GC, Pennell DJ. Toward clinical risk assessment in hypertrophic cardiomyopathy with gadolinium cardiovascular magnetic resonance. *J Am Coll Cardiol* 2003; 41:1561–1567

23. Maron MS, Appelbaum E, Harrigan CJ, Buros J, Gibson CM, Hanna C, Lesser JR, Udelson JE, Manning WJ, Maron BJ: Clinical profile and significance of delayed enhancement in hypertrophic cardiomyopathy. Circ Heart Fail 2008, 1:1

Appendix

PATIENT INFORMATION SHEET

TITLE: Morphological abnormalities in Hypertrophic cardiomyopathy – a Magnetic Resonance Imaging based study.

Name of Investigators:

Dr. Vijayan.G, Dr. Ajit Kumar.V.K, Dr. Sanjay.G, Dr. Anoop.A

Dear Patient,

We request you to participate in the study wherein we are planning to assess the ventricular hypertrophy pattern, mitral valve and papillary muscle abnormalities in HCM. We hope to include 100 people from this hospital in the study.

What is Cardiomyopathy?

Cardiomyopathy is defined as a myocardial disorder in which heart muscle is structurally and functionally abnormal without coronary artery disease, hypertension, valvular or congenital heart diseases.

What is Hypertrophic cardiomyopathy?

In hypertrophic cardiomyopathy (HCM) the heart muscle becomes thickened (hypertrophies) in parts of the heart. In the normal heart, the muscle cells are regular and patterned. In HCM the cells of the heart muscle become irregular and disordered.

What are the symptoms of Hypertrophic Cardiomyopathy?

Many individuals with HCM have no symptoms. Symptoms can appear in childhood or adulthood. Symptoms include breathlessness, fatigue or excessive tiredness, dizziness, fainting or collapse during physical activity, strong rapid heart beats which feel like a pounding sensation in the chest (palpitations) and chest discomfort that feels like heaviness in the chest (commonly occurring with exercise). In some cases the first symptom of the disease may be collapse, typically during exercise, which can be fatal.

How is Hypertrophic Cardiomyopathy diagnosed?

HCM is usually diagnosed with echocardiography. This is an ultrasound scan of the heart. Measurements of the thickness of the heart wall can be made. ECGs (Electrocardiograms) are also used. In some cases cardiac MRI (Magnetic Resonance Imaging) is also now be utilized especially where it is difficult to view the heart well with echocardiography.

What is a cardiac MRI?

A cardiac MRI scan is a non-invasive test where magnetic and radio waves are used to create pictures of the inside of the heart. The key difference between echocardiograms and MRI are the ability to better visualize the edges of the heart walls and the advantage of being able to see in the walls of the heart to pick up areas of scar or fibrosis.

Why do I need this procedure?

People with this condition usually do not have symptoms. However, in some people with this condition, there is a risk of developing complications such as failure of the heart to pump blood and sudden death. Currently doctors do not know much about why some people develop these complications. The purpose of this study is to find ways of predicting the risk of developing these problems, so that appropriate treatment can be given. This study will carry out a careful and thorough assessment of people with HCM using MRI to identify markers that are associated with these complications. This information will help doctors to identify people with HCM who are at higher risks of developing complications in the future as a result of the disease.

How long does it take?

The procedure will take about 30-45 minutes.

Is MRI safe?

An MRI study utilizes radio waves to acquire pictures and therefore NO ionizing radiation is required (as opposed to a CT scan, cardiac catherization or X-ray which does require the use

of ionizing radiation). As a result, MRI is a very safe test and no long term ill effects have been reported. Claustrophobia may be problematic in about 2% of patients but often a mild anxiolytic (prescribed by your doctor) prior to the test can prevent this from occurring.

What are the side-effects of Gadolinium contrast used in MRI?

Itchy skin rash may appear in approximately 1 in 1000 patients. Nephrogenic systemic fibrosis (NSF) is a rare condition resulting in skin contractures (or localised skin thickening and tightening) and internal organ damage. It has occurred with some gadolinium-based contrast media in a minority of patients with pre-existing severe kidney function abnormalities.

Do I need to take any precautions?

Patients with pacemakers, implantable cardiac defibrillators (ICD) or retained pacemaker leads cannot undergo the procedure if the device is not MRI compatible.

Permission to collect information from medical records

Details of the treatment including current medical condition and treatment undergone will be obtained for research purposes from your medical records. We seek your permission to take this information.

If you have any further questions, please ask: Dr. Vijayan.G (Principal investigator), Senior Resident, Department of Cardiology (Email: vijayan@sctimst.ac.in **Mobile No: 8334890131**)

For any technical clarifications, please contact - Dr. Mala Ramanathan, Member Secretary(Study independent contact person), IEC, SCTIMST and Additional Professor, AMCHSS, SCTIMST (Email: iec.mem.sec@sctimst.ac.in, Phone no. 0471-2524234

INFORMED CONSENT FORM

TITLE OF THE STUDY: Morphological abnormalities in Hypertrophic Cardiomyopathy - a Magnetic Resonance Imaging based study

Study number: ***100.***

Participant's name: Date of Birth / Age (in years):

I _____ _____,

son/daughter of _____ (Please tick boxes).

[ ] Declare that I have read the above information provide to me regarding the study: **Morphological abnormalities in Hypertrophic cardiomyopathy- an Magnetic Resonance Imaging based study** and have clarified any doubts that I had.

[ ] I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights.

[ ] I also understand that cardiac MRI is a part of the routine workup; I need not have to pay for using this information for this study.

[ ] I understand that the study staff and institutional ethics committee members may be not need my permission to look at my health records even if I withdraw from the trial. I agree to this access.

[ ] I understand that my identity may be not be revealed in any information released to third parties or published.

[ ] I voluntarily agree to take part in this study

.[ ] I received a copy of this signed consent form.

Name: Name of the witness:

Signature: Relationship to participant:

Date: Date:

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

_____ _____ Name and Signature of

Person Obtaining Consent

Dr. Vijayan.G

Senior resident

Mobile no: 8334890131

Dept. of cardiology SCTIMST

22-1-2018

Contact details:

Dr.Vijayan.G Senior resident, Department of cardiology,

Room no 321,

Shristy hostel, SCTIMSTquarters,

Poonthi road, Kumarapuram,

Trivandrum, Kerala.

For any technical clarifications, please contact Dr. Mala Ramanathan, Member Secretary, IEC, SCTIMST and Additional Professor, AMCHSS, SCTIMST (Email: iec.mem.sec@sctimst.ac.in, Phone no. 0471-2524234)

Expenses:

പഠനത്തിനുള്ള സമ്മതപത്രം

ശീർഷകം. ഹൈപ്പർട്രോഫിക് കാർഡിയോമയോപ്പതിയിലെ ഘടനാപരമായ അസാധാരണത്വം. എം. ആർ ഐ അടിസ്ഥാനമാക്കിയുള്ള ഒരു പഠനം

പഠന നമ്പർ 100

പങ്കെടുക്കുന്നയാളുടെ പേര്.....
ജനനത്തീയതി / വയസ്സ് (വർഷത്തിൽ)

ഞാൻ.....പുത്രൻ/പുത്രി.....
..... (കോളങ്ങൾ അടയാളപ്പെടുത്തുക)
പഠന ശീർഷകം.

- എച്ച് സി എമ്മിലെ ഘടനാപരമായ അസാധാരണത്വം. എം. ആർ ഐ അടിസ്ഥാനമാക്കിയുള്ള ഒരു പഠനം എന്ന പഠനവുമായി ബന്ധപ്പെട്ട എന്റെ എല്ലാ സംശയങ്ങളും പരിഹരിച്ചു. [ ]
- എന്റെ ഈ പഠനത്തിലുള്ള പങ്കാളിത്തം പൂർണമായും സ്വമേധയാ ഉള്ളതാണെന്നും എന്റെ ചികിത്സയെയോ നിയമപരമായ അവകാശങ്ങളെയോ ബാധിക്കാതെ പഠനത്തിൽ നിന്നും പിൻമാറാമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- കാർഡികയാക് എം ആർ ഐ പതിവായി ചെയ്യുന്ന പരിശോധനയാണെന്നും, അതുപയോഗിക്കുനനതിന് ഞാൻ പണം നൽക്ണ്ടതില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു.
- ഞാൻ ഈ പഠനത്തിൽ നിന്നും പിൻമാറിയാലും പഠനം നടത്തുന്നവർക്കും സ്ഥാപനത്തിലെ നൈതിക കമ്മിറ്റി അംഗങ്ങൾക്കും എന്റെ ആരോഗ്യരേഖകൾ പരിശോധിക്കുന്നതിന് എന്റെ അനുവാദരേഖകൾ ആവശ്യമില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. അതിനോട് ഞാൻ യോജിക്കുന്നു. [ ]
- എന്നെ തിരിച്ചറിയാനുതകുന്ന വിവരങ്ങൾ ഒന്നും മറ്റുള്ളവർക്കു നൽകുകയോ പ്രസിദ്ധീകരിക്കുകയോ ചെയ്യില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- ഞാൻ സ്വമേധയാ പഠനത്തിൽ പങ്കെടുക്കാൻ സമ്മതിക്കുന്നു [ ]
- സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു കോപ്പി എനിക്കു കിട്ടി [ ]

പേര്
ഒപ്പ്

തീയതി

സാക്ഷിയുടെ പേര്
ഒപ്പ്

(സമ്മതം വാങ്ങുന്നയാൾ)

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനുവേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണപദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകട സാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെ ചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതപത്രം വാങ്ങുന്ന ആളുടെ പേര്

ഒപ്പ്

ഡോ. വിജയൻ ജി (പ്രധാന ഗവേഷകൻ),
സീനിയർ റസിഡന്റ്,
കാർഡിയോളജി ഡിപ്പാർട്ട്മെന്റ്
ഇമെയിൽ: vijayan@sctimst.ac.in ഫോൺ: 8334890131

ഡോ മാലരാമനാഥൻ, മെമ്പർ സെക്രട്ടറി, ഐഇസി SCTIMST
അഡീഷണൽ പ്രൊഫസർ AMCHSS, SCTIMST
ഇമെയിൽ: iec.mem.sec@sctimst.ac.in, ഫോൺ: 0471-2524234)

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)
Grams : Chitramet, Phone : +91-471-2443152, Fax : +91-471-2550728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1176/APRIL-2018 05.06.2018

Dr. Vijayan G
Senior Resident
Department of Cardiology
SCTIMST, Thiruvananthapuram

Dear Dr. Vijayan,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "MORPHOLOGICAL ABNORMALITIES IN HYPERTROPHIC CARDIOMYOPATHY - A MAGNETIC RESONANCE IMAGING BASED STUDY (IEC/1176)" on 21st April, 2018.

The following documents were reviewed:

Original submission

1. *Covering Letter addressed to the Chairperson, IEC, SCTIMST dated 14.03.2018 with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Observation chart*
6. *Patient Information Sheet and Consent Form in English and Malayalam*
7. *CV of Principal Investigator and Co-Principal Investigators*

Revised submission

1. *Covering Letter addressed to the Chairperson, IEC, SCTIMST dated 11.05.2018 with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Observation chart*
6. *Patient Information Sheet and Consent Form in English and Malayalam*
7. *CV of Principal Investigator and Co-Principal Investigators*

The following members of the Ethics Committee were present at the meeting held on 21st April, 2018 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
3.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
4.	Dr. K R S Krishnan	M.E., Ph.D.	Male	Medical Technology	Yes
5.	Dr. S S Giri Sankar	LL.M. Ph.D.	Male	Legal Expert	No
6.	Dr. Aneesh V Pillai	BA. LLB (Hons.), LLM, Ph. D, SET (Law)	Male	Legal Expert	No
7.	Mr. Satheesh Chandran	MSW, PGDPM	Male	Lay person/ NGO/ Social Scientist	No
8.	Dr. Harikrishna Varma PR	Ph.D(Materials Science)	Male	Medical Technology	Yes
9.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
10.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
11.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
12.	Dr. Anand Kumar A	MD, DM	Male	Clinician	No
13.	Dr. V. Raman Kutty	M D, M Phil, M P H	Male	Health Sciences Expert/Clinician	Yes
14.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC

Plagiarism Checker X Originality Report
Similarity Found: 8%

Date: Sunday, July 30, 2019
Statistics: 206 words Plagiarized / 2571 Total words
Remarks: Low Plagiarism Detected - Your Document needs Selective Improvement.

Introduction

Hypertrophic cardiomyopathy (HCM) has a varied clinical course due to its genotypic and phenotypic heterogeneity. Several autopsy studies have shown abnormalities of the mitral valve in some HCM patients. Cardiovascular magnetic resonance (CMR) has become the imaging modality of choice due to its high spatial resolution, well suited to define the diverse phenotypic expression of this complex disease.

HCM has been documented to have various mitral valve abnormalities like an increased length of the leaflets and area, leaflet thickening, impaired mitral leaflet coaptation, and left ventricular outflow tract obstruction (LVOT) due to the systolic anterior motion of the mitral leaflets. Cardiovascular magnetic resonance (CMR) provides an excellent opportunity to assess the papillary muscle (PM) abnormalities like an increased number and mass, bifidity, hypertrophy, antero-apical displacement and LGE of the papillary muscle.

Various guidelines recommend surgical myectomy as the preferred modality for patients with left ventricular outflow tract (LVOT) gradient ≥50 mm Hg who fail to respond to medications or who experience side effects. Alcohol septal ablation (ASA) in patients with mitral valve abnormalities results in persistent SAM, gradients, and mitral regurgitation (MR).

MASTER CHART

Sl.No	AGE	GENDER(MALE-1,FEMALE-2)	LATE Gd ENHANCEMENT OF MYOCARDIUM (YES-1, NO-2)	LATE Gd ENHANCEMENT IN MITRAL VALVE (YES-1, NO-2)	LATE Gd ENHANCEMENT IN PAPILLARY MUSCLE (YES-1, NO-2)	MAXIMUM WALL THICKNESS IN MM at END DIASTOLE	EXTENT OF LV HYPERTROPHY (15-20=1, 21-25=2, 26-30=3, >30=4)	AML LENGTH IN MM	AML LENGTH SEVERITY (<30-1, ≥30-2)	PML LENGTH IN MM	SAM(AML-1, PML-2, BOTH-3, ABSENT-4)	NUMBER OF PAPILLARY MUSCLE	PAPILLARY MUSCLE HYPERTROPHY YES-1,NO-2	BIFIDITY OF PAPILLARY MUSCLE(YES-1, NO-2)	Indexed myocardial mass in g
1	38	1	1	1	2	24	2	21	1	21	4	4	2	1	125
2	55	1	1	2	2	16	1	30	2	20	4	3	1	1	69
3	41	2	1	2	2	22	2	26	1	12	4	3	1	1	65
4	62	2	1	2	2	27	3	18	1	10	4	2	2	2	127
5	19	1	1	2	2	21	2	17	1	11	4	3	1	2	85
6	23	1	2	2	2	23	2	33	2	14	1	3	1	2	55
7	54	2	1	2	2	18	1	28	1	21	4	3	2	1	72
8	61	1	2	2	2	16	1	27	1	19	4	3	1	1	78
9	31	1	1	2	2	29	3	27	1	21	1	2	1	2	132
10	52	1	1	2	2	17	1	30	2	15	4	3	1	1	94
11	31	1	1	2	2	35	4	26	1	22	1	2	1	1	118
12	19	2	1	1	1	32	4	30	2	20	1	2	1	1	147
13	45	1	1	2	2	24	2	24	1	16	4	2	2	2	90
14	39	1	1	1	2	22	2	21	1	14	4	2	1	1	125
15	58	2	1	2	2	22	2	26	1	12	4	3	1	2	78
16	33	1	1	2	2	27	3	17	1	26	4	3	1	1	108
17	47	1	1	2	2	20	1	23	1	16	4	3	2	2	132
18	20	1	1	2	2	25	2	27	1	16	1	2	1	1	81
19	58	1	1	2	2	18	1	13	1	17	1	3	1	1	78
20	59	1	2	2	2	17	1	29	1	17	4	3	1	1	79
21	26	1	1	2	2	25	2	27	1	16	4	3	2	2	106
22	42	2	2	2	2	25	2	21	1	18	4	3	1	1	84
23	70	2	1	2	2	27	3	18	1	15	4	3	1	1	77
24	32	1	1	2	2	37	4	22	1	15	4	2	2	2	296
25	52	2	1	2	2	15	1	28	1	18	4	3	1	2	67
26	50	1	2	2	2	26	3	25	1	18	4	2	1	1	118
27	45	1	1	2	2	25	2	31	2	16	1	3	1	1	144
28	17	1	1	2	2	29	3	21	1	14	1	2	1	1	96
29	57	2	1	1	2	23	2	22	1	16	4	3	2	1	85
30	56	1	1	1	2	23	2	30	2	17	1	3	1	1	150
31	37	1	2	2	1	25	2	28	1	17	1	3	1	2	
32	45	1	2	2	1	17	1	33	2	17	1	3	1	1	
33	61	1	1	1	1	26	3	30	2	14	1	3	1	1	
34	42	1	1	1	1	35	4	29	1	14	1	2	2	2	
35	35	1	1	1	2	29	3	27	1	14	1	2	1	1	
36	42	1	1	1	2	22	2	21	1	16	1	3	1	1	
37	41	2	1	2	2	20	1	33	2	15	1	2	2	2	
38	57	2	1	1	2	30	3	28	1	16	1	2	1	1	
39	38	1	1	1	2	26	3	29	1	16	1	2	1	2	

Sl.No	AGE	GENDER(MALE-1,FEMALE-2)	LATE Gd ENHANCEMENT OF MYOCARDIUM (YES-1, NO-2)	LATE Gd ENHANCEMENT IN MITRAL VALVE (YES-1, NO-2)	LATE Gd ENHANCEMENT IN PAPILLARY MUSCLE (YES-1, NO-2)	MAXIMUM WALL THICKNESS IN MM at END DIASTOLE	EXTENT OF LV HYPERTROPHY (15-20=1, 21-25=2, 26-30=3, >30=4)	AML LENGTH IN MM	AML LENGTH SEVERITY (<30-1, ≥30-2)	PML LENGTH IN MM	SAM(AML-1, PML-2, BOTH-3, ABSENT-4)	NUMBER OF PAPILLARY MUSCLE	PAPILLARY MUSCLE HYPERTROPHY YES-1,NO-2	BIFIDITY OF PAPILLARY MUSCLE(YES-1, NO-2)	Indexed myocardial mass in g
40	50	1	1	1	2	21	2	27	1	18	1	3	1	1	
41	61	1	2	2	2	17	1	28	1	10	4	2	1	1	
42	71	1	1	2	2	22	2	27	1	13	4	2	2	2	
43	59	1	1	2	2	17	1	24	1	14	1	2	2	2	
44	45	1	1	2	2	19	1	18	1	12	4	3	1	2	
45	31	2	2	2	2	19	1	25	1	10	4	2	1	2	
46	59	2	2	2	2	17	1	26	1	12	1	3	1	1	
47	35	1	2	2	2	26	3	27	1	19	1	2	1	2	
48	27	2	2	2	2	18	1	21	1	8	4	2	1	2	
49	58	2	2	2	2	16	1	19	1	17	4	4	2	1	
50	50	1	1	1	2	24	2	21	1	17	1	3	1	1	
51	52	1	1	2	2	22	2	21	1	12	4	2	1	1	
52	47	1	1	1	2	17	1	22	1	12	4	2	1	1	
53	69	1	1	2	2	25	2	20	1	13	4	2	1	1	
54	67	1	1	1	1	23	2	31	2	16	4	3	1	1	
55	50	2	1	2	2	17	1	25	1	18	4	2	2	2	
56	68	1	1	1	2	19	1	30	2	13	1	2	1	1	
57	41	1	2	2	2	20	1	22	1	11	4	2	1	1	
58	28	1	1	2	2	22	2	34	2	16	1	2	1	2	
59	55	2	2	2	2	22	2	23	1	16	1	2	1	2	
60	55	2	2	2	2	18	1	20	1	15	4	3	1	2	
61	61	2	1	2	2	23	2	25	1	16	1	3	1	1	
62	34	2	2	1	2	17	1	25	1	10	1	3	1	2	54
63	63	2	2	1	2	16	1	25	1	10	1	3	1	2	56
64	48	1	1	2	2	24	2	26	1	16	1	3	1	1	
65	52	1	1	2	2	21	2	28	1	17	4	3	1	1	
66	58	2	1	2	2	25	2	20	1	15	4	2	2	2	
67	76	1	2	1	2	25	2	20	1	15	1	2	1	2	
68	55	2	2	2	2	18	1	24	1	12	1	2	1	1	
69	28	1	1	1	2	35	4	38	2	13	4	2	1	1	
70	67	1	1	2	2	25	2	29	1	13	4	3	1	2	
71	66	1	1	2	2	20	1	31	2	15	4	2	1	1	
72	52	1	2	2	2	15	1	30	2	13	4	3	2	1	
73	27	2	2	2	2	21	2	23	1	15	1	2	1	2	
74	46	2	1	2	2	27	3	30	2	16	1	3	1	1	
75	64	1	1	2	2	25	2	35	2	22	1	2	1	1	
76	51	1	1	1	2	35	4	25	1	18	1	2	1	1	
77	36	1	1	1	2	34	4	38	2	16	1	2	1	1	
78	25	1	1	1	2	32	4	32	2	18	1	2	1	1	
79	63	2	2	2	2	21	2	33	2	17	1	3	1	1	

Sl.No	AGE	GENDER(MALE-1,FEMALE-2)	LATE Gd ENHANCEMENT OF MYOCARDIUM (YES-1, NO-2)	LATE Gd ENHANCEMENT IN MITRAL VALVE (YES-1, NO-2)	LATE Gd ENHANCEMENT IN PAPILLARY MUSCLE (YES-1, NO-2)	MAXIMUM WALL THICKNESS IN MM at END DIASTOLE	EXTENT OF LV HYPERTROPHY (15-20=1, 21-25=2, 26-30=3, >30=4)	AML LENGTH IN MM	AML LENGTH SEVERITY (<30-1, ≥30-2)	PML LENGTH IN MM	SAM(AML-1, PML-2, BOTH-3, ABSENT-4)	NUMBER OF PAPILLARY MUSCLE	PAPILLARY MUSCLE HYPERTROPHY YES-1,NO-2	BIFIDITY OF PAPILLARY MUSCLE(YES-1, NO-2)	Indexed myocardial mass in g
80	66	2	2	1	2	18	1	20	1	17	1	3	1	1	
81	34	2	2	2	2	22	2	24	1	16	4	2	1	1	
82	63	1	1	1	2	17	1	21	1	18	1	3	1	1	
83	53	1	2	2	2	18	1	37	2	17	1	3	1	2	
84	43	1	1	2	2	31	4	27	1	18	1	3	1	1	
85	25	1	1	2	2	23	2	24	1	17	4	2	1	2	
86	40	1	1	2	2	23	2	25	1	17	4	3	1	1	
87	19	2	2	2	2	37	4	21	1	14	4	3	1	2	
88	19	2	2	2	2	29	3	24	1	18	4	2	1	1	
89	44	2	1	2	2	22	2	28	1	16	4	2	1	2	
90	70	2	2	2	2	17	1	21	1	16	4	3	1	2	
91	62	1	1	2	2	40	4	31	2	15	4	3	2	1	
92	40	2	2	2	2	29	3	22	1	16	4	3	1	1	
93	38	1	1	2	2	33	4	26	1	17	1	3	1	1	
94	63	2	2	1	2	15	1	25	1	15	1	3	1	2	54
95	52	1	1	2	2	18	1	27	1	12	4	2	2	2	
96	53	2	1	2	2	15	1	28	1	20	4	2	1	1	65
97	55	2	1	1	2	18	1	31	2	15	4	3	1	1	
98	47	1	1	2	2	25	2	27	1	19	1	2	1	2	
99	50	1	2	2	2	26	3	25	1	20	4	2	1	2	118
100	37	1	2	1	1	21	2	25	1	21	4	3	1	1	74