HOCM-OUTCOME FOLLOWING SURGICAL MYECTOMY – A RETROSPECTIVE ANALYSIS

THESIS PROJECT

BY

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DECLARATION

I hereby declare that this thesis entitled, **"HOCM-OUTCOME FOLLOWING SURGICAL MYECTOMY – A RETROSPECTIVE ANALYSIS "** has been prepared by me under the capable supervision and guidance of **Dr.VIVEK .V PILLAI,** Additional Professor , Division of Cardiothoracic and Vascular Surgery,Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram...

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CONTENTS

INTRODUCTION

HOCM is a genetic cardiovascular disease characterized by an increase in left ventricular wall thickness that is not solely explained by loading conditions.It is one of the few ailments which is well studied yet that knowledge is not fully translated into clinical outcome.

Initially described by Teare in 1958

Braunwald was the first to diagnose HCM clinically on 1960

It is the commonest genetic disease with mendelian autosomal dominant inheritance.It is the commonest cause of sudden cardiac death in young adults.

Left untreated it causes significant morbidity and mortality.Incidence of the disease is around 0.1 -0.5 % in the general population.Even though several etiologies has been proposed,genetic remains the most important and with the maximum strength of association.Symtomatology of HCM varies from mild symptoms to sudden cardiac death.Evaluation of these patients starts with symptom analysis to a battery of invasive and non invasive imaging modalities. Treatment strategies for HOCM evolved gradually over years which started with myectomy proposed by Morrow.Since then surgery as well as the medical and invasive methods evolved over years.But still surgical myectomy remains as the gold standard of the treatment.In the present study we will be analyzing the results of the surgical myectomy

Research on HOCM is supported by many factors.

1. It is the commonest genetic heart disease which affects individuals of all age.
2. It is the most common cause of sudden death in young people
3. It is an important cause of heart failure disability.
4. It can taken as a paradigm for the potential opportunities provided by harnessing modern genetic science,which helps in developing treatment for other genetic diseases.

REVIEW OF LITERATURE

Epidemiology

Prevalence of HCM 0.05 – 0.2%

Morphologic evidence of disease is found by Echocardiography in appr 25% of the first degree relatives.

Sex related Demigraphics

Slightly more common in males. The genetic inheritance pattern is Autosomal dominant without sex predilection[4].

HCM usually presents at a younger age in females. Females tend to be more symptomatic and are more likely to be disabled by their symptoms than males([7].

HCM has a bimodal peak of occurance. The most common presentation is in the third decade of life. In children peak incidence is in IInd decade.

Because of delay in phenotypic expression, HCM is not commonly recognized clinically in young children. Greater penetrance is seen in young males([8].

HCM is underdiagnosed clinically in blacks and young women. Yet women tend to present with more marked heart failure than men. There is no overall difference in mortality including sudden cardiac death between men and women[8,10]

ETIOLOGY.

Abnormal myocardial calcium kinetics and abnormal calcium fluxes from an increase in the no of calcium channels which result in increased intracellular calcium concentration which in turn may produce hypertrophy and cellular disarray[10,12].

Genetic Causes

In 1989 Seidman and collaborates first reported the genetic basis of HCM. They detected gene on long arm of chromosome 14.Familial HCM occurs as an AD mendelian inherited disease in approximately 50%[6,9] . Familial HCM is genetically heterogeneous in that it can be caused by genetic defect at more than 1 locus[30,31].

Wider variation exists in the phenotypic expression of a given mutation of a given gene with variability in clinical symptoms and the degree of hypertrophy expressed. Some specific mutations are associated with particular symptoms.

Other possible causes.

Abnormal sympathetic stimulation – Heightened responsiveness of the heart to the excessive production of catecholamines or reduced neuronal uptake[20,23].

1. Subendocardial ischemia – Relates to abnormal cardiac microcirculation that deplete the energy stores essential for

sequesteration of calcium during diastole. Subendocardial Ischemia results in persistent interaction of the contractile elements during diastole and increased diastolic stiffness[6,3].

Cardiac structural Anomalies– Include catenoid configuration of the septum which result in myocardial cell hypertrophy and disarray.

HCM is a genetic disease of sacromere protein with mutations in the genes that encode Beta Myosin heavy chain (MYHT) and myosine binding protiens accounding for 80-85 % of cases .

Mutations in the troponine cardiac troponine T and troponine 1 and alpha tropomyosine accounts for 10-15 % cases.

Myosin light chains and Alpha cardiac actin (ACTCT) are the 8 genes most commonly involved in HCM.

Rare genetic causes

Cardiac tropinC , α myosim heavy chain, MYH6, cardiac myosim light chain kinase 2 (MYLK2) are also implicated in HCM.

Genes that encode nonsarcomere protein include caveolin (CVA3).Calreticulin, junctophilin 2 .

Phospholambdan (PLN) and the mitochondrial tRNA encoding genes MTTG and MTTI produce clinical features that mimic HCM.

Unknown causes

Mutation testing can be uninformative in 3 clinical scenarios.

Hypertrophy that occurs very early in child hood

Hypertrophy that is only recognosed after middle age

Hypertrophy limited to ventricular apex[EJCTS,30,31)]

Disease Mechanics

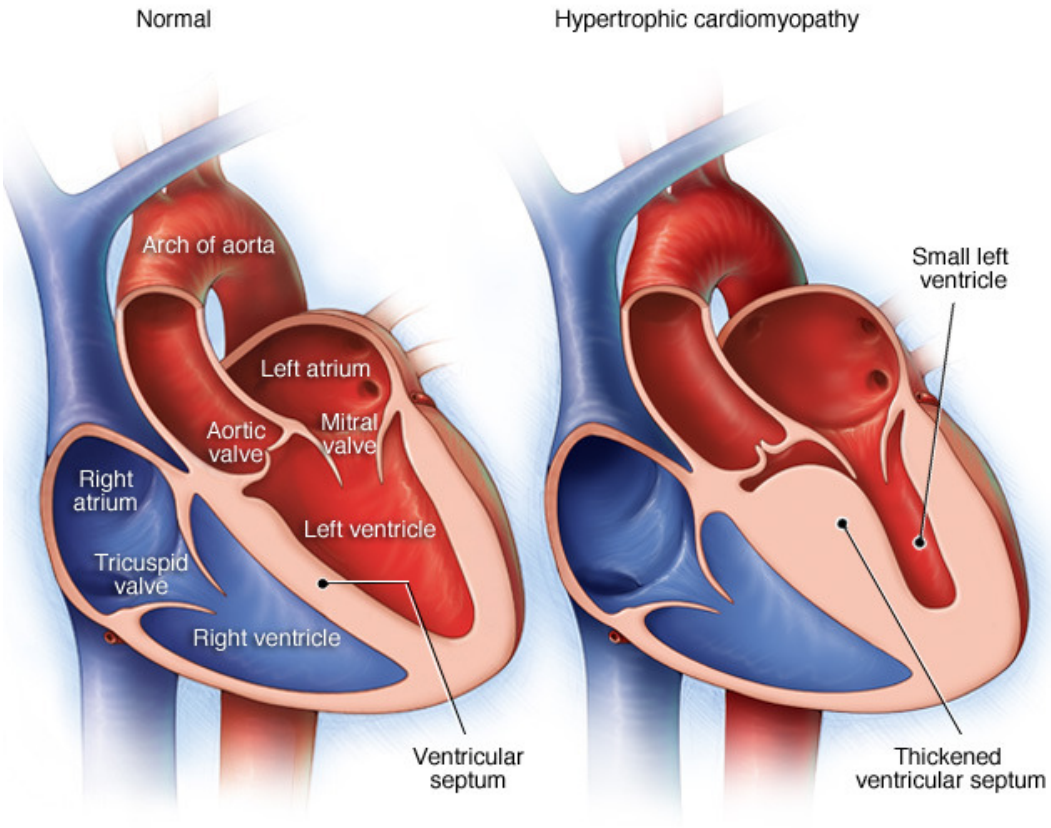
Dominant negative formation (Problems that interfere with the foamtion of a normal allel)

Haplo insufficiency : Insufficient quantity of the normally functioning sarcomere protein.

Impaired myocardial energeties and decreased energy reserve

Pathophysiology

The basic pathology in HCM is hypertrophy of the septum and ventricular wall.



Dynamic obstruction of the LVOT leading to outflow gradient variability

As the thickening gradually increases it leads to Outflow obstruction

A patient may demonstrate a large gradient on one occasion and have none at another time.In some pts without a resting gradient, it may be temporarily provoked.

Three Basic mechanisms has been proposed for this gradient variability. Increased contractility, decreased preload and a decreased after load.

In many patients with HCM the gradient is Midventricular and may be intensified by increased Contractility which exerts a direct muscular

sphincteric action. One of the most potent stimulus for an increased LVOT gradient is a Post extrasystolic potentiation, which may occur after spontaneous premature contraction. (Brokenbrough – Braunwald phenomenon)

Diastolic dysfunction results from impaired relaxation and filling of the stiff and hypertrophied lt ventricle.

Abnormal intramural coronary arteries with thickened walls and narrowed lumen[14,15].

Disorganised left ventricular architecture (cellular disarray)predisposing to abnormal transmission of electrical impulses and thus serving as a substrate for arrhythmogenesis.

TYPES.

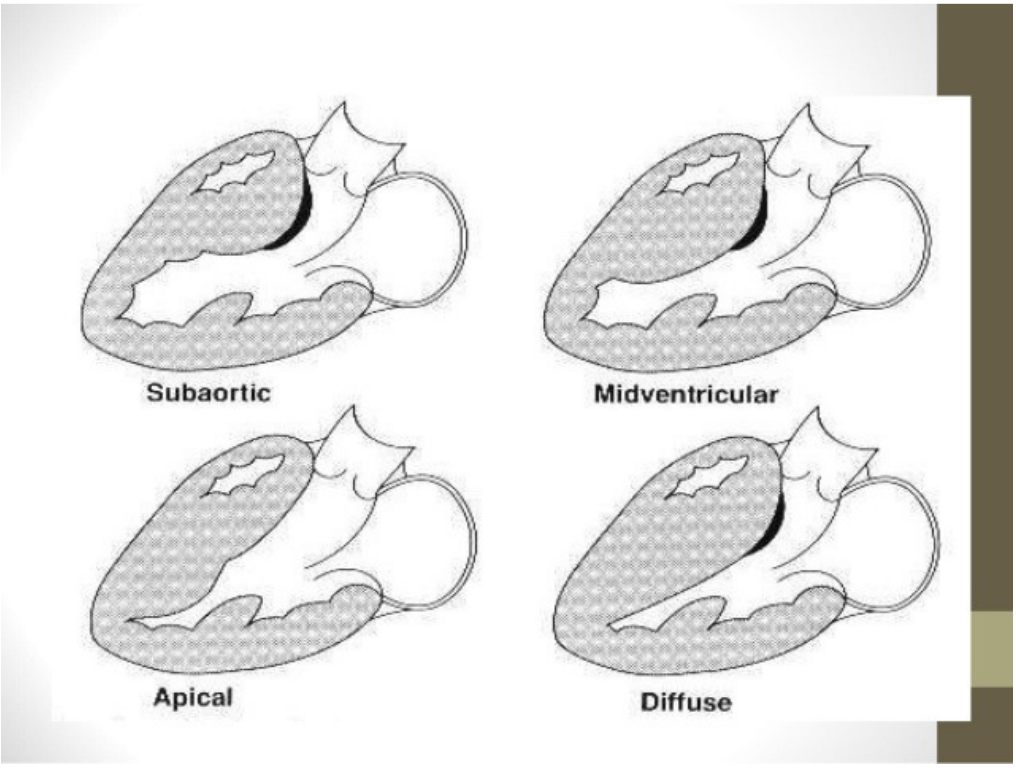
There are mainly four types of HCM.These depend on the type and level of septal hypertrophy and the level of obstruction.Clinical features of each type depend on whether there is any associated LVOTO([3]).

1.Subaortic

2.Midventricular

3.Diffuse

4.Apical



Histological findings.

Whorled pattern : cell to cell disarray & disorganization of the myofibrillar architecture.Fibrosis is prominent

Abnormal intramural coronary arteries with a reduction in the size of the lumen and thickening of the vessel wall.

CLINICAL FEATURES

Following symptoms represents the common presenting features of HCM.

Sudden cardiac death – most devastating presentation.

DYSPNOEA ON EXCERTION – Most common symptom.

Syncope or pre syncope (Diagnostic of LVOTO or Dysrrhythmias).

Angina

Palpitations – ventricular tachycrdia /SVT

Orthopnoea and PND (pulmonary congestion),CHF and Dizzines.

Signs

Double or triple apical impulse

Normal SI, paradoxically split S2,S3 gallop, S4 frequently heard.

Increasd JVP

Double carotid arterial pulse

Forcefull and lateralised apex beat

Systolic Ejection Crescendo-decrescendo murmur without radiation.

PSM of MR at apex and Axilla

Diastotic decrescendo murmur of AR in < 10% patients[9,8].

Work Up

Work up of patients with HOCM mainly consists of history,clinical findings,Echocardiography,Cardiac MRI,Cardiac catheterization,CAG and rarely nucleotide scanning.

Echocardiography

Echocardiographic evaluation forms the main stay and it is the first and foremost investigation required in HOCM

Findings : (a) Abnormal systolic Anterior leaflet motion of mitral valve (b) LVH (c) LAE (d) Small ventricular chamber size (e) Septal to freewall ratio 1.4:1 (f) MVP (g) MR,(h)Decreased Mid aortic flow

2D Echo is diagnostic of HCM. Colour Doppler flow studies typically reveal MR.

Continous wave Doppler studies in patients with obstructive HCM reveal an elevated flow velocity across LV outflow tract. Severe obstructive HCM typically has a flow vetocity greater than 4 m/s and a gradient across LVOT > 50 mm of Hg[3,5].

Echocardiography typically reveals diastolic dysfunction with reduced LV compliance and a mitral valve ratio of E wave to A wave less than 1.Systolic function is typically well preserved and normal and infact LVEF is usually normal or high at the time of diagnosis. A study of Pietro et al suggested assuring the exercise capacity and LV systolic function during exercise echocardiography may aid in determining the risk stratification[21,22,5].

Tissue Doppler imaging is usefull as a screening tool in patients with morphologically normal ventricle and in differntating HCM from and other causes of concentric LVH like Athlet's heart. The Hallmark of the obstructive type of HCM consist of systolic anterior motion of the AML, septal wall thickness > 15mm, ASH with a ratio of septal wall thickness to posterior wall ratio > 1.4:1[22,23].

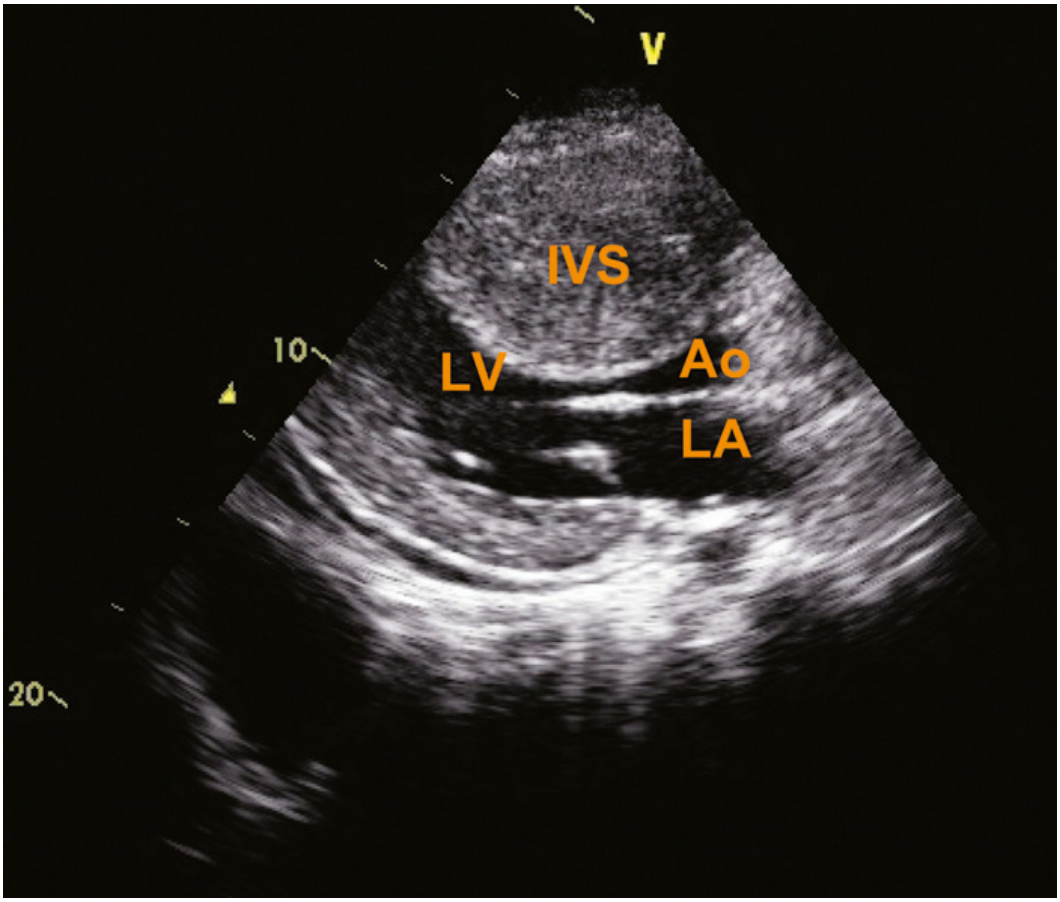
The septum not only is relatively thicker than the posterior wall it is also typically at least 4-6 mm thickness than normal for each age group. Massive hypertrophy with septal wall thickness > 25mm has been noted especially in glycogen storage disease as Pompe's disease[11,13].

1. An unusual echocardiographic pattern consisting of a ground glass appearance has been noted in portion of the hypertrophic Myocardium in some patients. This pattern may be related to the abnormal cellular architecture and myocardial fibrosis that have been observed in pathologic studies[8,9].
2. Narrowing of LVOT contributes to the creation of a pressure gradient. Reduced septal motion and thickening during systole may occur particularly of the upper septum resulting from the disarray of the myocardial architecture and abnormal contractile function[5,8].
3. MVP – a rare echocardiographic finding in HCM may be present.
4. Partial systolic closure or more commonly systolic fluttering of the aortic valve related to the turbulent blood flow in the outflow tract may occur.
5. Theo presence of mitral regulation virtually always is confirmed by Doppler Echo.

Radionucleotide Imaging

With Thallium or Technitium scintigraphy may show reversible defects mostly in the absence of CAD.Thallium or technetium scintigraphy may reveal defect in myocardial perfusion, even in the setting of angiopgaphically normal coronary arteries. These reversible defect evident on radionuclide scanning are more common in children and adolesents with a history of symcope or sudden

death,which suggest that myocardial ischemia is a significant factor in the mechanism of the demise of younger patients with HCM[34,8,9].



Cardiac MRI

Very useful in the diagnosis and assessment with ideal image quality covering both ventricles completely which helps in localisation of the hypertrophy.Is useful when Echo is doubtfull esp.Apical HCM.MRI can visualise LVOT obstruction & SAM.Velocity mapping is useful in the assessment of peak velocities. Improvement in obstruction after septal ablation or myectomy can be demonstrated and also in localisation and size of the associated infarction which are useful for planning repeat procedure.

Cardiac MRI tagging identifies abnormal patterns of strain ,shear and torsion in cases of HOCM, demonstrating significant dysfunction in hypertrophic areas of the ventricle.

Cardiovascular MR Spectroscopy reveals bioenergate defects in HCM, with varying genetic mutations,a fact that supports the underlying substrate for HOCM may be insufficient energy utilization.

The accuracy of the phenotypic determination of HCM by MRI is helpfull for family screening and genetic linkage studies for causative mutation.

The use of Gadolinium Contrast in cardiac MRI is very useful in differentiating HCM from other causes of cardiac hypertrophy and other types of cardiomyopathy such as amyloidosis,athletic heart and fabry's disease.

6. Late Gadolinium enhancement occuring in HCM represents myocardial fibrosis. The greater the degree of later gadolinium enhancement the more likely that the particular HCM patient has 2 or more risk factors for sudden death and more likely the patient has or will develop progression of ventricular dilation toward heart failure, thereby indicating a poor prognosis.

More extensive gadilinium enhancement can be dense or plaque like or diffuse. The larger risk of sudden death in these patients is due to from a reentrant tachyarrhythmia and systolic failure from myocyte replacement. Fabry disease (alpha galactosidase deficiency) which occur in appr 4% show unusual lateral wall gadolinium enhancement[5,12,32].

Cardiac Catherization

Useful to determine the degree of outflow obstruction, cardiac haemodynamics, Distolic characteristics of Lt ventricle and coronary anatomy. The arterial pressure tracing found on cardiac cath may demonstrate a spike and dome configuration similar to carotid pulse recording.

7. Left Ventrography : Typically shows a hypertrophied ventricle and the presence of an outflow gradient, SAM and MR. The LV cavity is small. In patient with apical involvement the extensive hypertrophy may convey a spade like configuration to LT ventricular angiogram.

CAG- LAD and septal perforator may demonstrate phasic narrowing and associated abnormalities of flow during systole[4,23].

Medical Management of HOCM

Beta blockers represent a conerstone of the treatment of symtomatic hypertrophic cardiomyopathy. They are the first line therapy for obstructions and non obstructive forms.

Use of the Beta blockers is supported by the evidence of higher concentrations of epinephrine in the samples of myectomy specimen.

Sympathetic modulation causes the deceleration of the heart rate at rest and after excertion. But corroborative evidence for the improvement is not found. But still prolongation of the diastole improves the coronary perfusion.

Beta blockers cause a reduction in maximal contraction velocity.

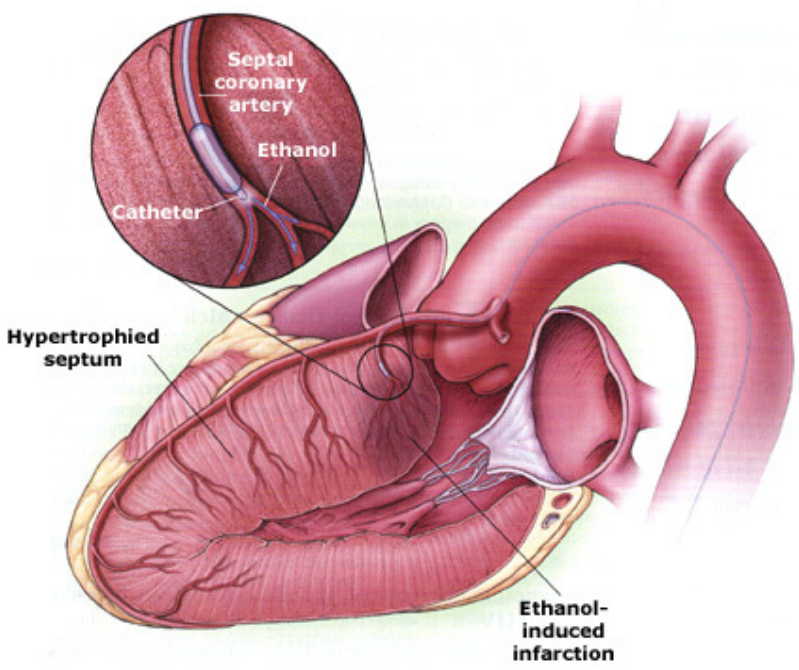
Calcium channel blockers is also used along with beta blockers in patients who show no response with beta blocker alone[31,32,28].

Alcohol Septal Ablation.

ASA introduced in the late 90's as an alternative for septal myectomy.It consists of injecting 1-2 ml of absolute alcohol into the prominent perforator supplying the hypertrophied myocardium.Started by obtaining arterial and venous femoral accesses, using the standard Judkins technique, followed by placement of a 6F temporary transvenous pacemaker lead in the right ventricular apex, a 5F pigtail or multipurpose catheter into the LV, and a 6F or 7F guiding catheter in the ascending aorta. Re-evaluation of the patient's hemodynamics and re-measurement of the intracavitary gradient were then performed and continuously monitored throughout the procedure, through simultaneous pressure measurement in the LV and the aorta. Physiologic provocation of the gradient was assessed with the Valsalva maneuver and checking for the Brockenbrough-BraunwaldMorrow sign by inducing a premature ventricular complex. Coronary angiography was then performed to exclude severe coronary disease and to locate the first septal perforator artery. A 0.014-in. guidewire was advanced to engage, in most cases, the first septal branch of the left anterior descending artery . A slightly oversized, short (10 mm), over-the-wire angioplasty balloon was then introduced into the septal perforator artery, using standard methods; the lumen of this device provides the route for selective delivery of angiographic contrast, echo contrast, and

ultimately alcohol, into the septal artery. After careful fluoroscopic positioning of the balloon (using selective angiography to exclude encroachment onto the LAD, it was inflated and the guidewire removed . A small amount of angiographic contrast was then injected through the balloon lumen to ensure that there was no spill-back into the LAD or collateral recruitment . The balloon should not be placed too distally as this may result in a smaller (and solely right-sided) septal infarct, with a consequent reduction in the effect on the outflow gradient. Subsequently, an echocardiographic contrast agent was injected through the balloon, and the myocardium supplied by the septal artery localized with transthoracic echocardiography.The optimal location within the septum is the point of contact between the anterior mitral valve leaflet and septum in apical four-chamber view. If echocardiographic localization was supportive (no contrast seen outside the thickened basal septum), ablation could proceed. The transvenous pacing wire was re-checked, and intravenous analgesia administered, as the alcohol can cause intense but transient discomfort. Absolute alcohol (1---3 ml) was then administered slowly through the lumen of the balloon, for 3---5 minutes, followed by saline flush under continuous hemodynamic and ECG surveillance. The invasive and echocardiographic gradients were reassessed, a successful procedure being defined as a residual invasive LVOT pressure gradient of less than 50% of baseline value. If the target reduction in pressure gradient was not achieved, alcohol injection was repeated after 5 minutes (1---2 ml) within the same perforator branch. If not successful, the procedure was repeated in a second

perforator branch. Once success was achieved, the balloon was deflated, and coronary angiography was repeated to confirm the occlusion of the septal branch and the patency of the left anterior descending coronary artery (Figure 1D). Following deflation, the balloon and wire were removed. Patients were monitored in an intensive care unit for at least 48 hours after septal ablation, and the temporary pacemaker lead was kept in place for at least 24 hours[21,22].



Surgical Mycetomy

Originally described by Dr. Andrew G Norrow

Dr. N.P Cleland at Hammersmith Hospital was the first surgeon to perform a myectomy but the operation was soon abandoned for decades. There after Dr. Andrew Morrow at National institute of Health, John Kirlkin at Mayoclinic, Wilfred Bigelow and Williams at toronto Pioneered the surgical intervention, permitting, surgical myectomy to emerge as the primary treatment option.

In the early days Myectomy was accompanied by >5% procedural mortality. But over the time mortality is approaching <1%. But Surgery continues to be frequently represented as an outdated and risk prone option by its opponents.

Over the last 15 yrs with the advantage of contemporary cardiac preservation techniques and intraoperative echo cardiograophy,myoctemy had been associated with remarkably low operative mortality, approaching zero at major centres.

In the heart failure benefit

Myoctemy result in immediate and permanent abolishion of Mechanical obstruction to LV outflow with normalization of LV pressures.

The goals of myectomy are

Effective enlargement of LVOT
Excision of thickenened fibrotic endocardium
Correction of long-axis deviation between LV and ascending aorta
Reduction of degree of mitral regurgitation
Avoidance of disease related secondary complications:
AF, VF, VT, syncope, sudden death, arterial embolism, myocardial failure
Intra-, post-operative: laceration of mitral chordae, aortic cusps, total av-block, secondary VSD

Positive influence on early outcome and on long-term prognosis

Principles of Myectomy

The point of LVOTO is determined by the point where the AML contacts the hypertrophied septum. Myectomy is extended below the point of LVOTO to allow the blood flow to track away from the mitral valve.

Subvalvular vertical incisions: near the nadir of the right coronary aortic cusp (RCC); septum beneath the commissure of the RCC and LCC (Bigelow incision)

Septal extension of myectomy after subvalvular connection of both primary incisions in the direction of the apex of the left ventricle (LV) down toward the base insertion of the anterior papillary muscle

Myectomy of the hypertrophied lateral LV wall after retraction of the anterior part of the posterior mitral valve chordae.

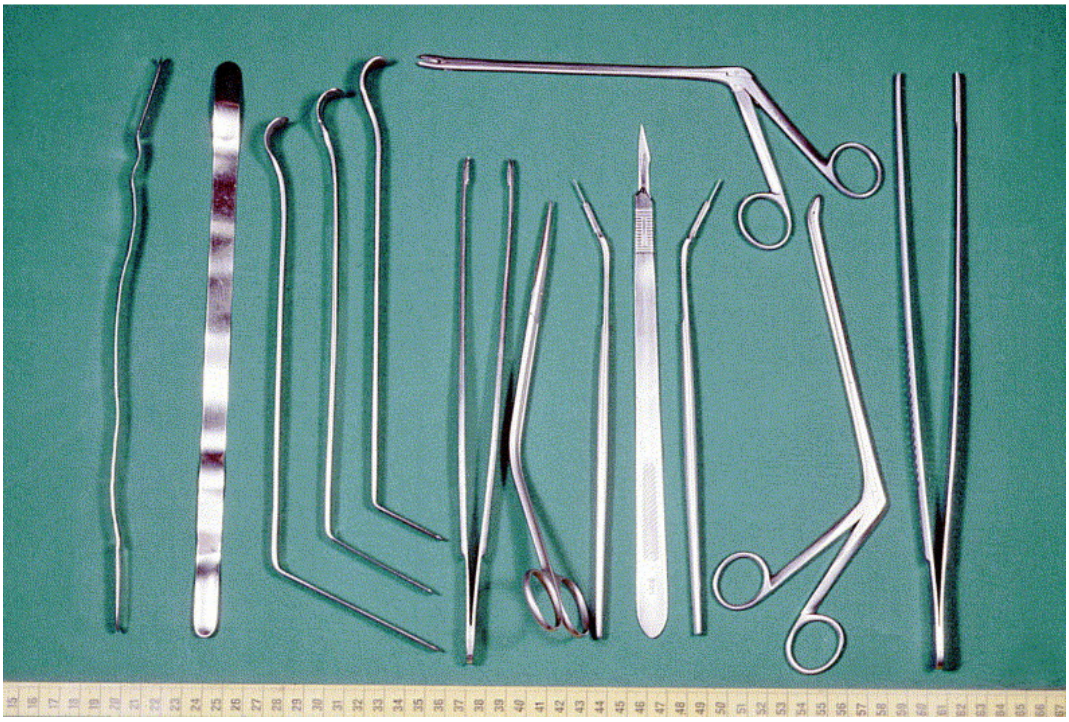
The transverse thickness of the proximal and mid septum determines the depth of septal resection at both levels.

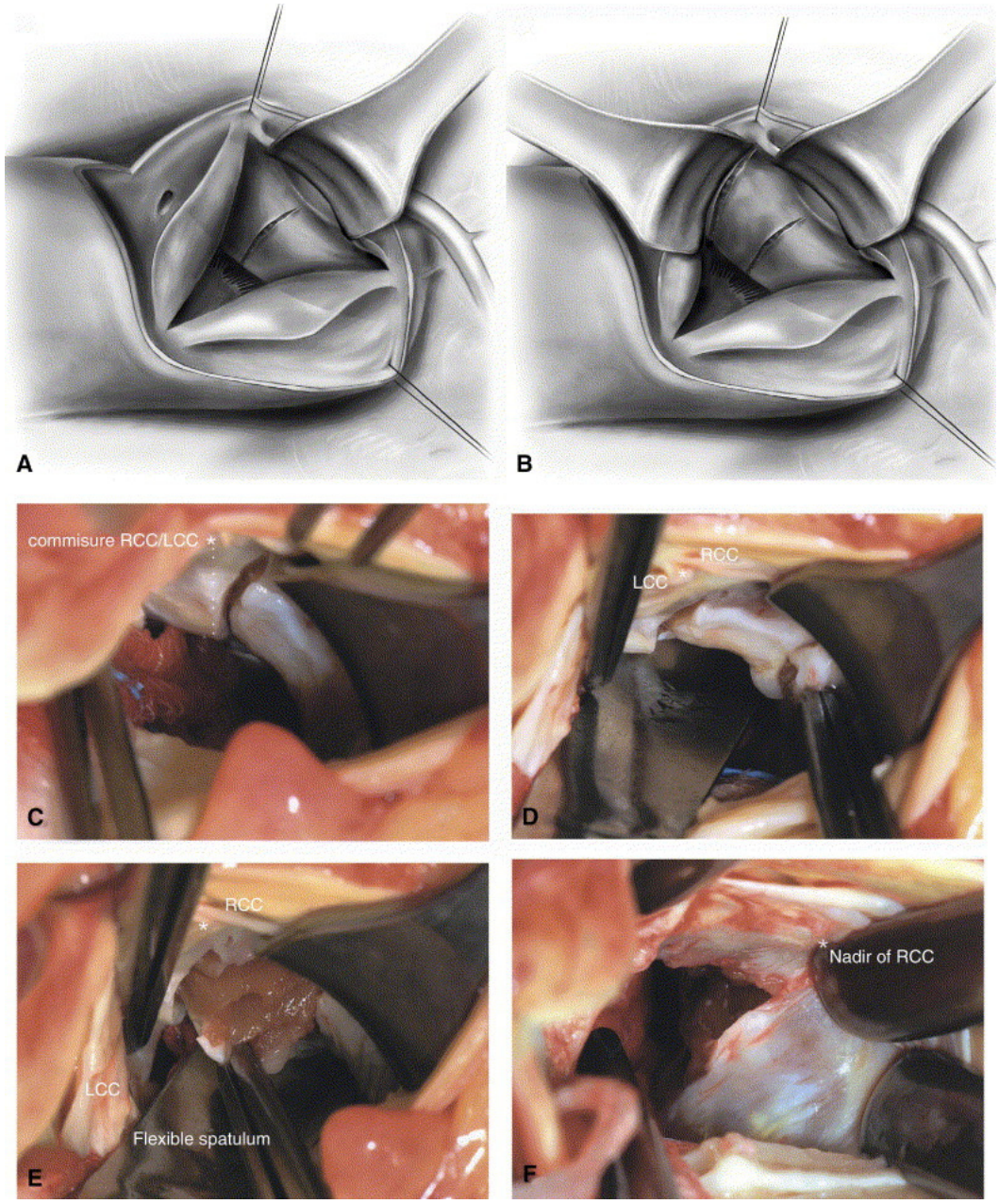
The myectomy should be sufficiently thick and also should extend to atleast 1.5 cm below the mitral septal contact point, often to the base of the papillary muscles to redirect the flow anteriorly and prevent SAM.

Resection is not done medially in the proximal anterior setptum as this region is not involved in the formation of the LVOTO. Moreover resection in this area can lead to ventricular septal defects and conduction blocks.

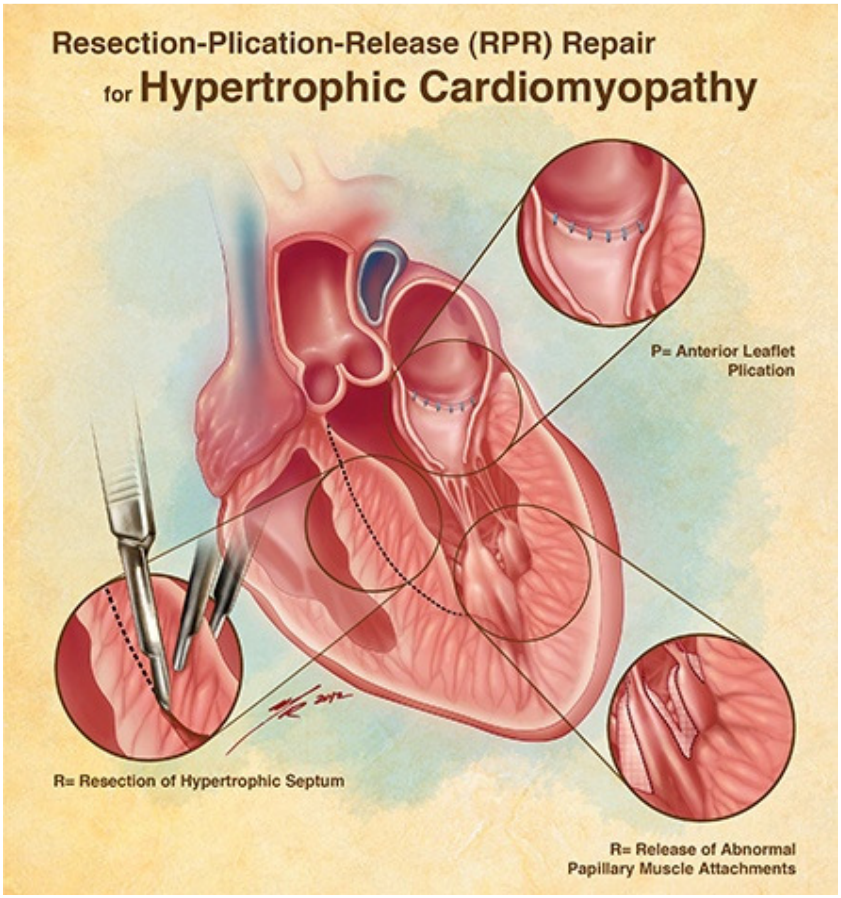
If the subaortic septum is resected only down to the tips of the mitral leaflets, flow is still redirected by the remaining septal bulge so that it comes from a posterior direction leading to persistent SAM.

The proximal incision should be placed away from the Aortic annulus to prevent aortic incompetence.





Based on the current concepts focus has been shifted from just myectomy alone to addressing the mitral valve pathologies.



Current optimal treatment of HOCM is Release placation and resection,hoping to offer a lot foor patients who are suffering from HOCM.

AIMS AND OBJECTIVES

1. To evaluate the outcome of Septal myectomy.

2. To identify preoperative factors involved in affecting the outcome.

3. To evaluate the incidence of post operative complications in terms of mortality, CHB, MVR, Post operative hospital stay.

MATERIALS AND METHODS

Present study is conducted in SCTIMST, Trivandrum. Ours is a premier institute of national importance. Our instituite focus mainly on cardiological and neurological diseases. Instituite has got a world wide reputation interms of research and treatment. Current study is about patients with hypertrophic cardiomyopathy who underwent surgical myectomy as the primary treatment in SCTIMST. Patient samples has been selected over a period of 10 yrs. More than thirty patients underwent myectomy during these period. Out of which only 24 patients has been selected for the present study.Rest of the patients has been excluded as not complying with the inclusion crieteria. Current study is a retrospective descriptive study. Data has been collected from the medical records of the patients, which are entered into the personal computer. Different patient variables has been analysed from preoperative factors to post operative outcome. Statistical analysis was performed using dedicated software (SPSS® version 18.0, 2009). Continuous variables were presented as mean values ± standard deviation; categorical variables were expressed as frequencies. Comparisons were made using a Student's t-test for paired samples.

OBSERVATIONS AND RESULTS

More than thirty patients underwent surgical myectomy in our institute for the last ten years. Out of which only 24 has been included in the present study. Rest has been excluded because not meeting the crieterias.

Patients were divided into four age groups, as less than 20,20-40,40-60 and above 60 yrs. Majority of the pts were in the 40-60 age group(37.5%) closely followed by the 20-40 age group(29.2%).Less than 20 age group has got n incidence of 20.8 % and the least percentage were in the above 60 group(12.5%).So the age pattern in our population also typically follows the universal pattern of incidence. The bimodal peaking of the disease is also typically expressed in our population.

Age of onset of the disease is also scrutinized. This data showed a peak incidence in the < 20 age group(young age).Followed by the 40-60 age group. And in that age group disease has onset of 33.3 %.Very rarely only disease manifested after the age of 60(4.2%).

So the age pattern shows us that all age group can be affected even though it typically follows a bimodal pattern of onset.

Globally the disease affects more males than females, but females tend have a more severe disease. In the present study more patients were female than males(9 vs 15;37.5/62.5%)en. May be the phenotypic expression and severity of the disease will be much more in Indian females. Similar observations has not been reported yet.

Analysing the major symptoms Dysnoe on exertion, syncope ,palpitation, preop arrhythmias, majority of patients were in functional class 3 or 4.But the other presentations were varying among patients. Majority of the patients presented with FC 3(62.5%).7 patients were in FC 2(29.2%).Only 2 patients were in FC-1 and in these patients the presenting symptos were something else.

Syncope were present only in 8 patients(33%).Ten patients had associated palpitations. Preop arrhythmias were present in 29% patients. None of our patients were having any life threatening arrhythmias pre operatively. No patients were on prophylactic ICD or Dual chamber pacing.

Only 5 % of the patients had a strong family history of the disease. Preop arrhythmias were present in 7 (29.2%) patients but the rest 17(70.8%) patients remained in sinus rhythm at the time of surgical admission.

Preop gradients of patients ranged from 60 t0 200 with an average gradient of 115.7.Aerage septal thickness was 16 during systole which ranged from 13-25 mm. Diastolic thickness of the septum ranged from 15 to 27 with an average thickness of 20.25 mm. Posterior wall thickness ranged from 13- 20 with mean of 14.29 during systole. Diastolic thickness of the posterior wall ranged from 15 to 25 with an average of 18.25 mm.

The left ventricular systolic function of all the patients remained good inspite of the severe diastolic dysfunction. Majority of the patients had above the normal ejection fraction which ranged from 60 to 84 % with the mean of

73.21%.Post operative ejection fraction ranged from 54 to 83 with a mean of 69.54%.

Post operative outcomes were quite promising with majority of patients returning to either functional class 1 or 2 without any major late sequele. The major complications reported were CHB requiring permanent pacemakers, non-life threatening arrhythmias, increased rate of conversion to mitral valve replacement and prolonged hospital stay for unforesceen reasons.

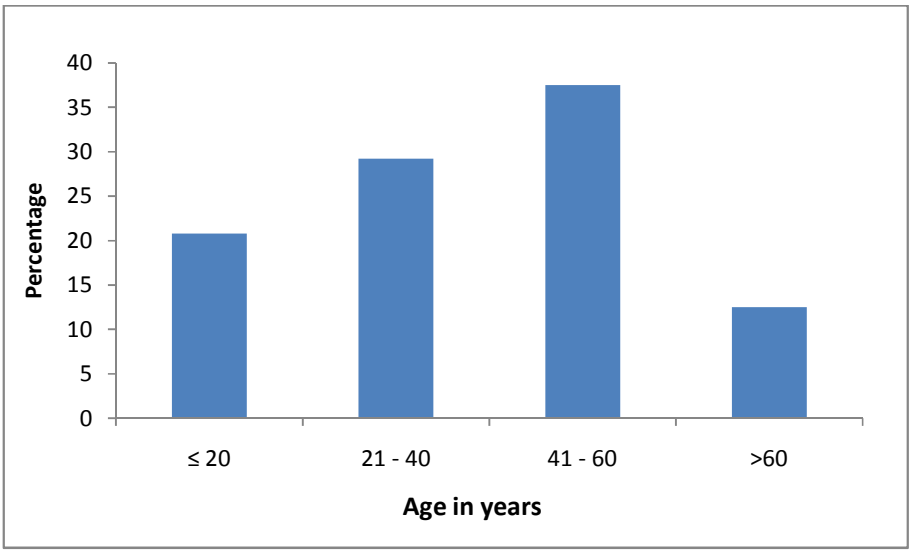
A total of four patients(16.7%) required permanent pacemaker implantation.

Regarding mitral valve almost 12 patients(50%) required mitral valve replacement.RPR techniques were done in some patients. Out of which one patient responded well with AML retension plasty(Walter Delmos technique).

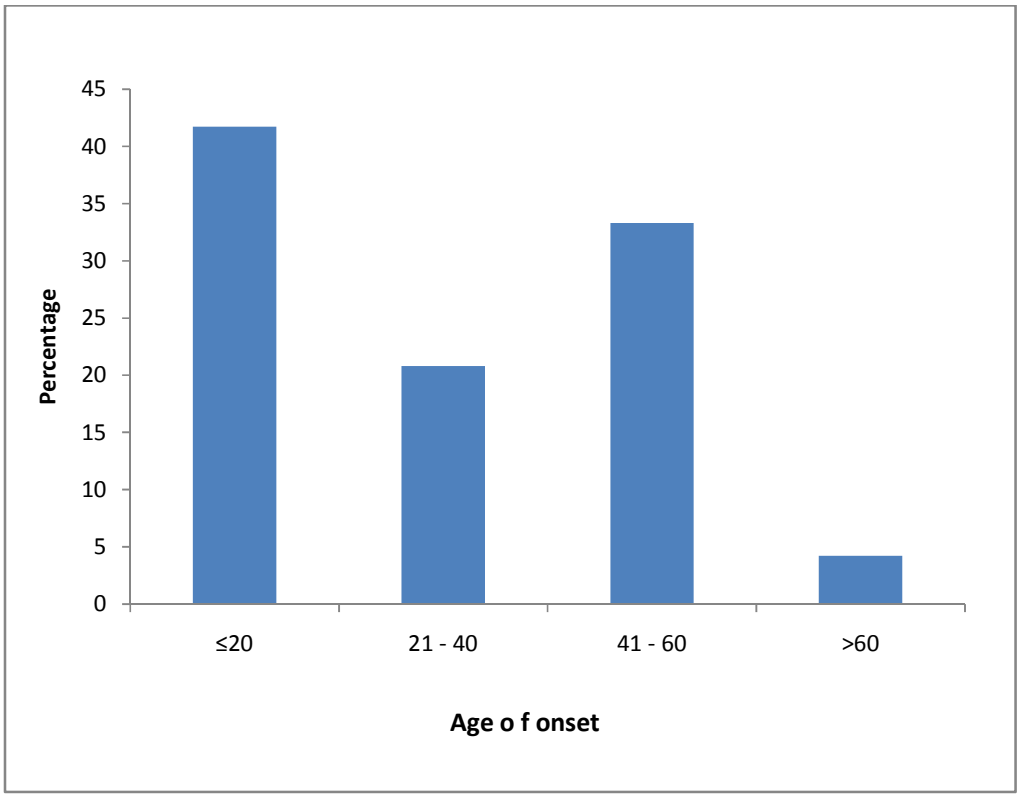
Prolonged hospital stay were present in (20.8%), but the majority of patients 19(79.2%) patients had a normal convalescensce.

Only one patient had a major adverse cardiovascular event leading to death(4%).

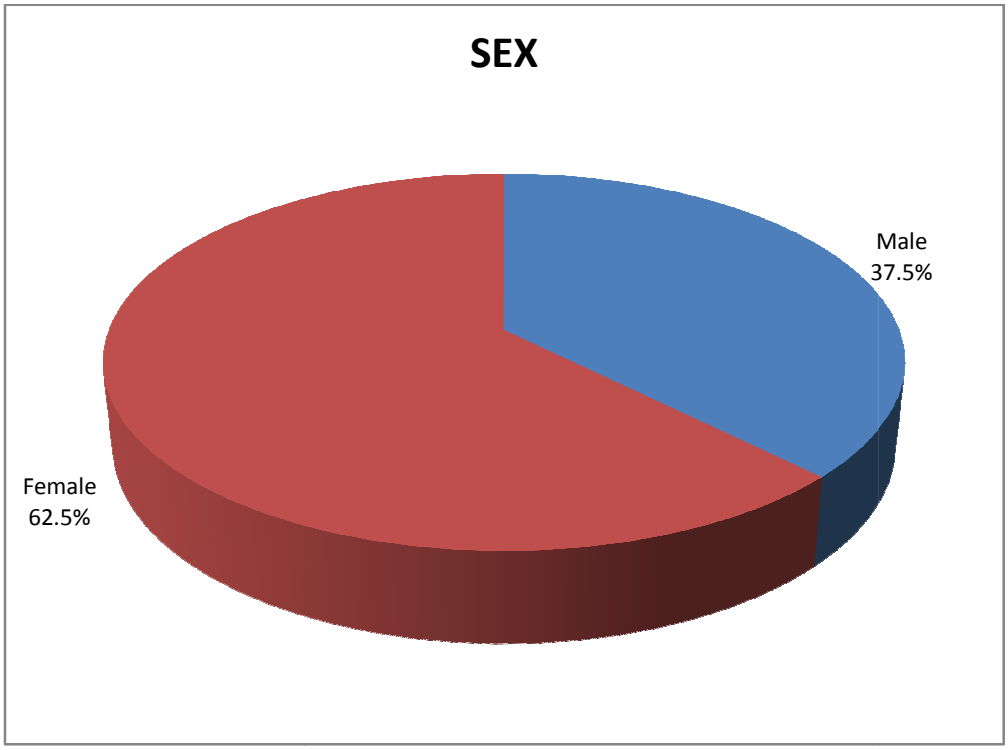
Age in years	Frequency	Percent
≤ 20	5	20.8
21 – 40	7	29.2
41 – 60	9	37.5
>60	3	12.5
Total	24	100.0



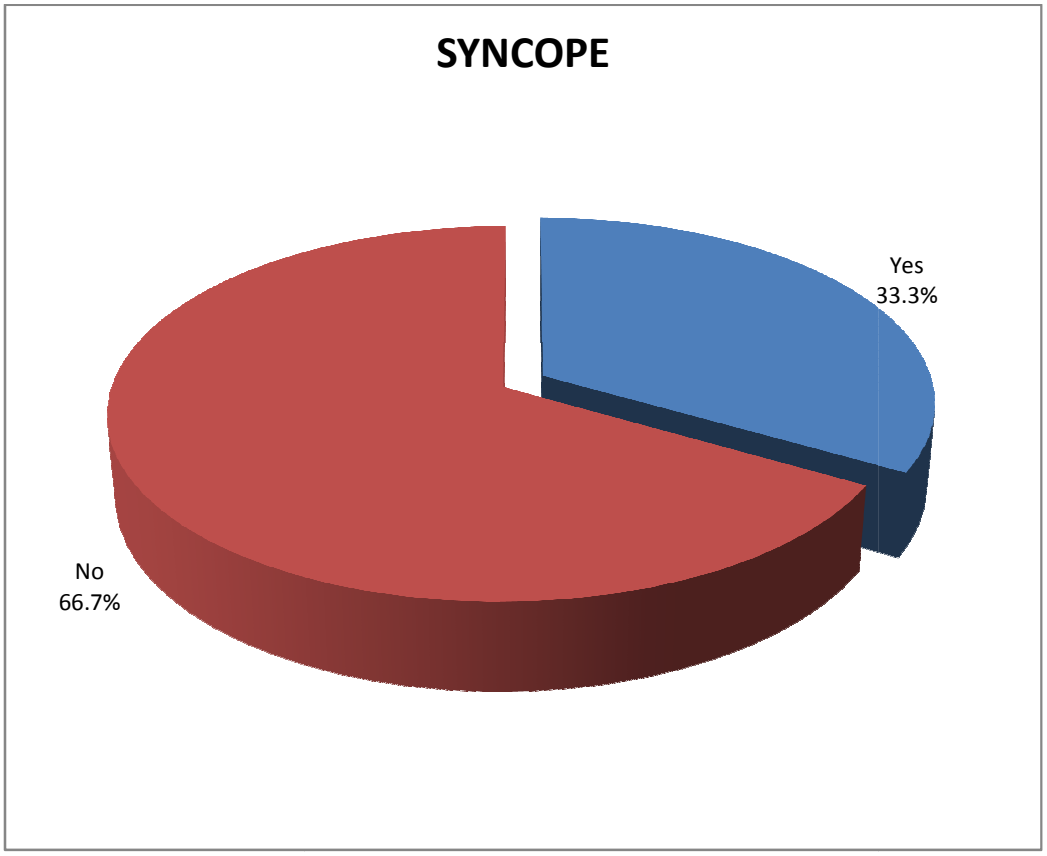
Age of onset	Frequency	Percent
≤20	10	41.7
21 - 40	5	20.8
41 - 60	8	33.3
>60	1	4.2
Total	24	100.0



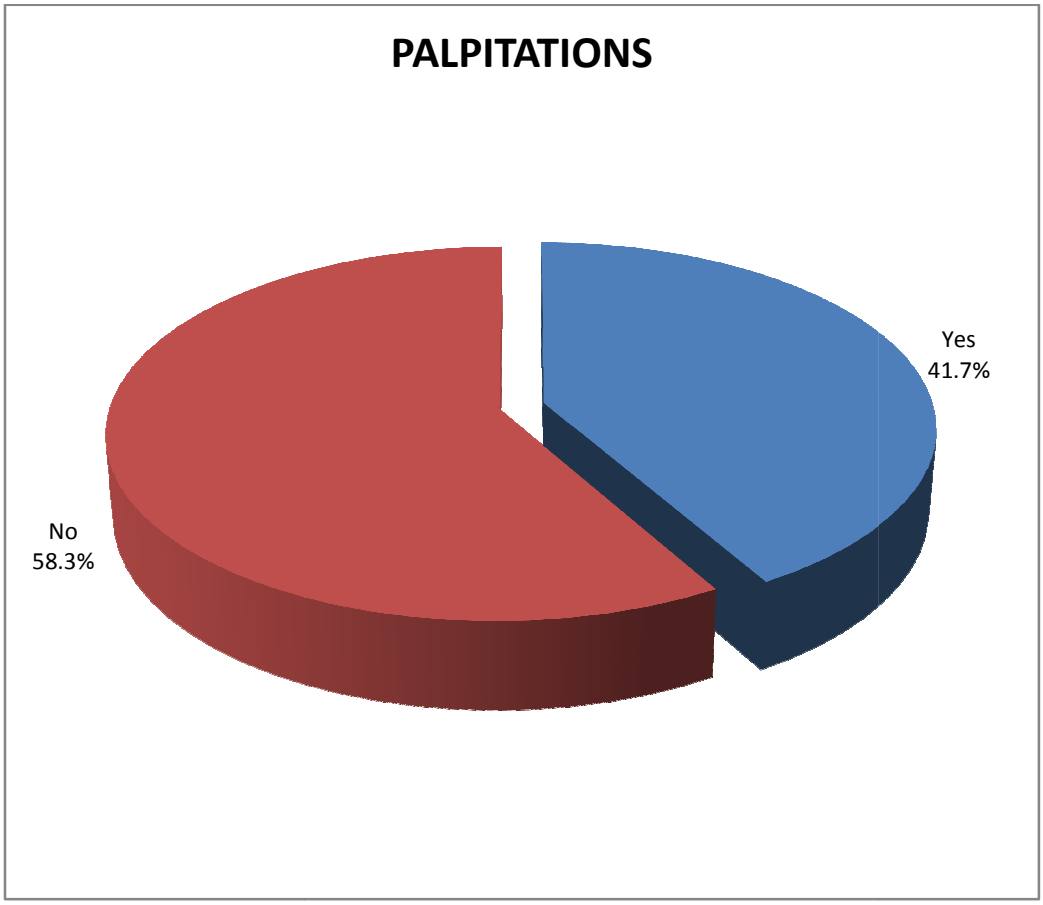
SEX	Frequency	Percent
Male	9	37.5
Female	15	62.5
Total	24	100.0



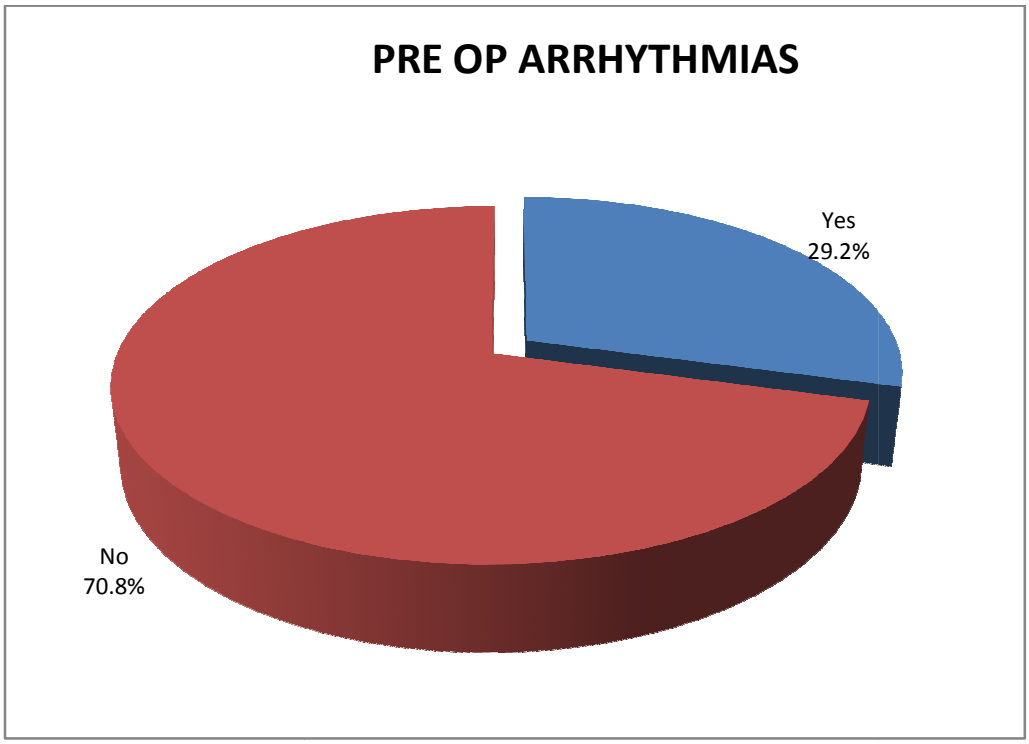
SYNCOPE	Frequency	Percent
Yes	8	33.3
No	16	66.7
Total	24	100.0



PALPITATIONS	Frequency	Percent
Yes	10	41.7
No	14	58.3
Total	24	100.0

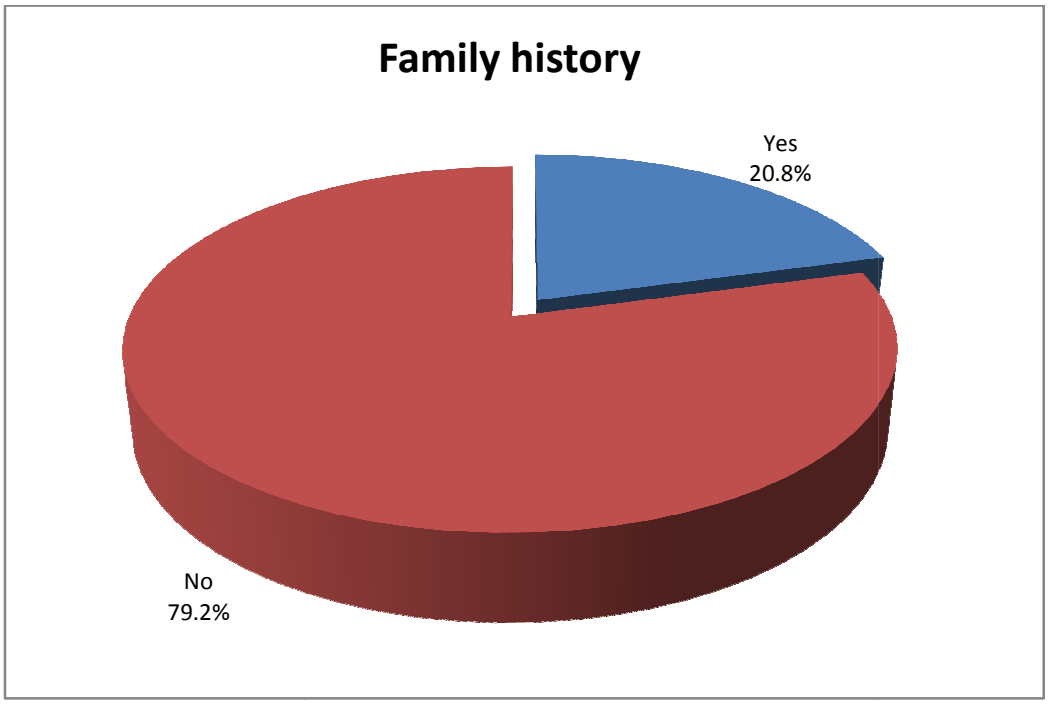


PRE OP ARRHYTHMIAS	Frequency	Percent
Yes	7	29.2
No	17	70.8
Total	24	100.0

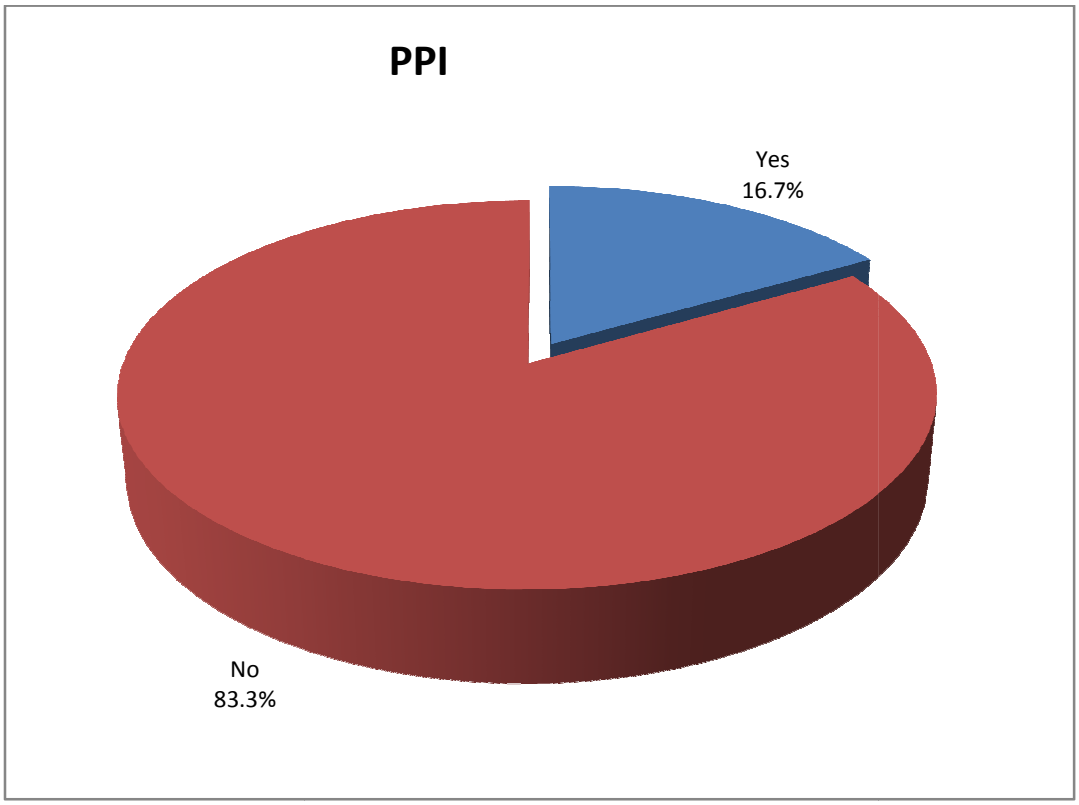


FC	Frequency	Percent
1	2	8.3
2	7	29.2
3	15	62.5
Total	24	100.0

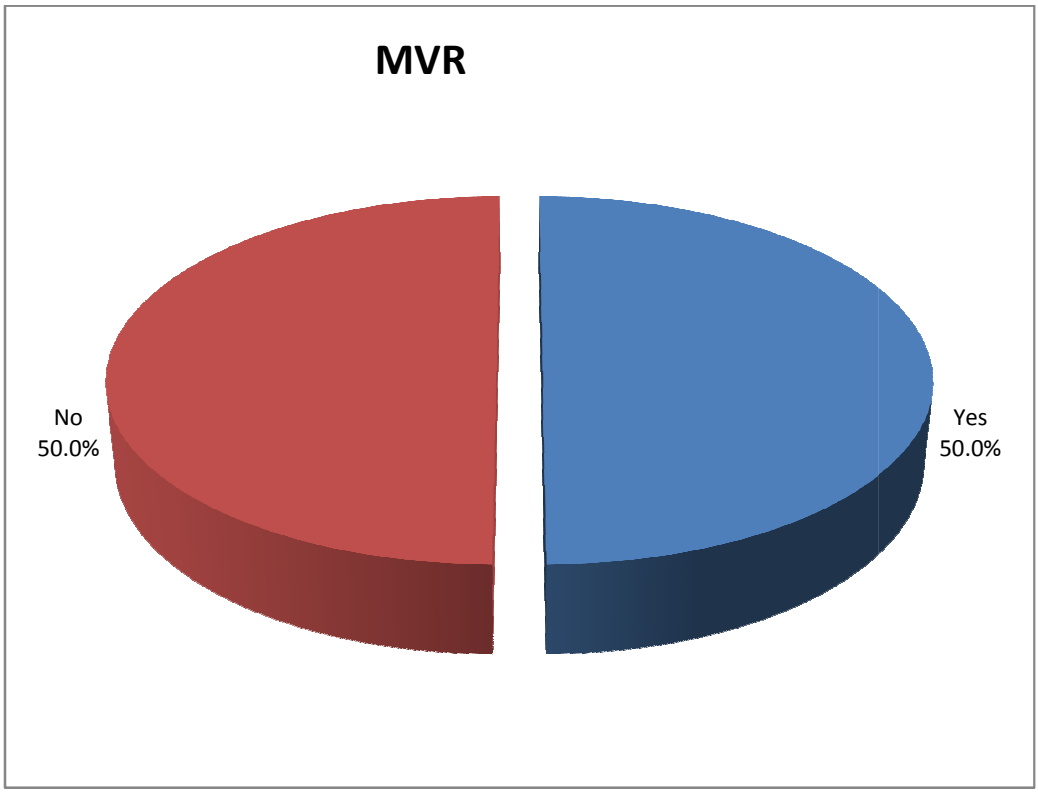
FH	Frequency	Percent
Yes	5	20.8
No	19	79.2
Total	24	100.0



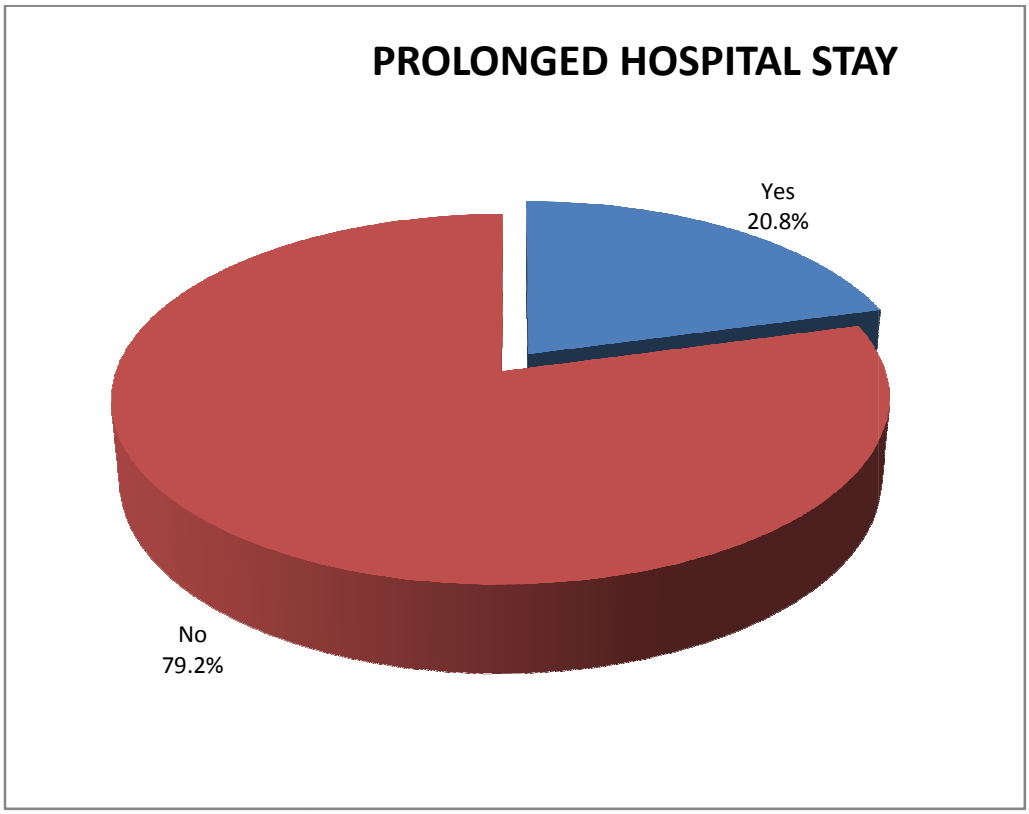
PPI	Frequency	Percent
Yes	4	16.7
No	20	83.3
Total	24	100.0



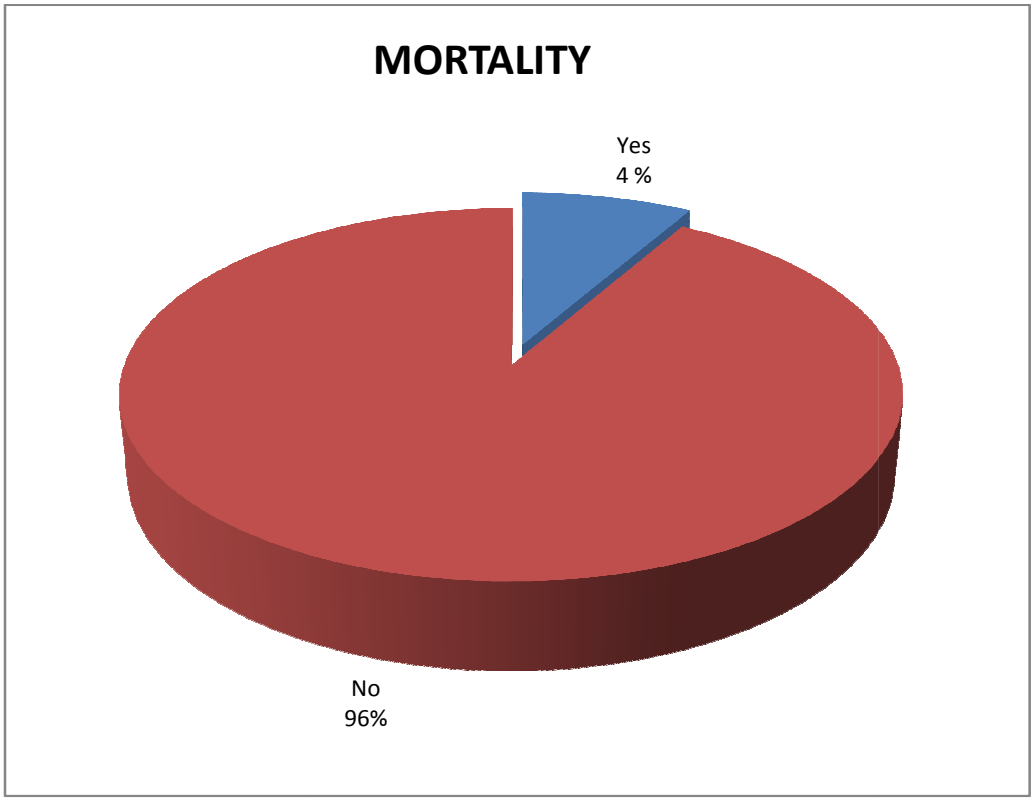
MVR	Frequency	Percent
Yes	12	50.0
No	12	50.0
Total	24	100.0



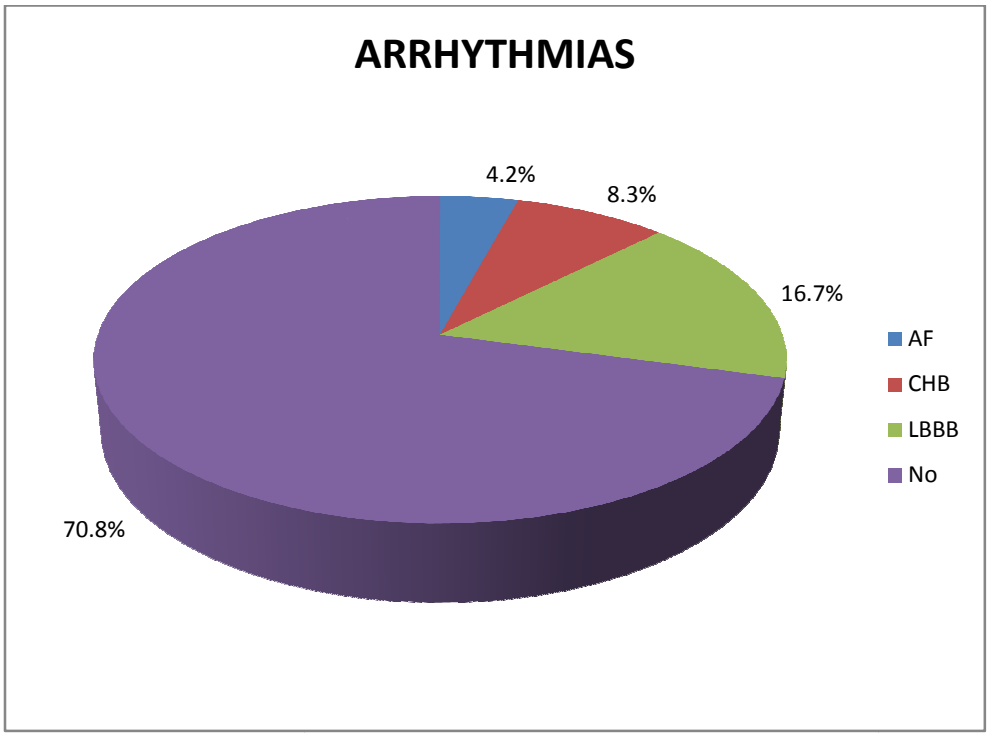
PROLONGED HOSPITAL STAY	Frequency	Percent
Yes	5	20.8
No	19	79.2
Total	24	100.0



MORTALITY	Frequency	Percent
Yes	1	4
No	23	96
Total	24	100.0



ARRHYTHMIAS	Frequency	Percent
AF	1	4.2
CHB	2	8.3
LBBB	4	16.7
N	17	70.8
Total	24	100.0

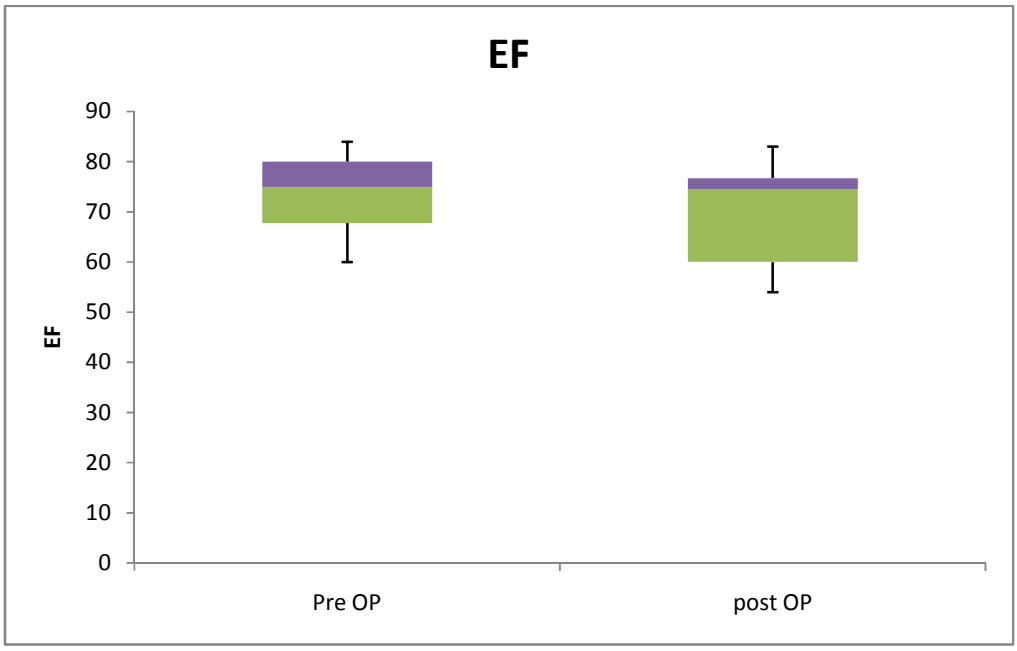


	N	Minimum	Maximum	Mean	sd
AGE	24	10.0	68.0	39.42	18.95
AGE AT ONSET OF SYMPTOMS	24	2	65	31.63	19.77
PREOP GRADIENT	24	60	200	115.17	39.85
IVS	24	13	25	16.04	3.69
IVSdiastolic	24	15	27	20.25	3.79

	N	Minimum	Maximum	Mean	sd
PW s. Pre	24	13	20	14.29	1.99
PW s post	4	8	15	12.25	2.99

EF	N	Minimum	Maximum	Mean	sd
Pre	24	60	84	73.21	7.77
Post	24	54	83	69.54	9.27

t=1.938 p=0.065



	N	Minimum	Maximum	Mean	sd
POPG	24	6	60	22.54	13.80
Posterior wall systolic	12	8	18	14.08	2.75
Posterior wall diastolic	12	13	23	17.50	3.03

DISCUSSION

The diagnosis of HOCM started with its first description by Braunwald. The treatment strategies of HOCM started evolving from 1960's.Initial backbone of the treatment was beta blockers, later followed by additional drugs such as calcium channel blockers,ACE inhibitors and antiarrhythmics (amiodarone, disopyramide).

The definitive treatment of HCM started with the introduction of surgical myectomy by Alfred Morrow in 1963.Since then thousands of patients underwent the procedure with varying functional outcome and mortality. The initial reported mortality was around 5- 10 %.

The surgical procedure itself has underwent various modifications, even though the procedure is still known by its founder Morrow. With refinements in surgical technique, myocardial protection, equipments, understanding the pathophysiology, better post operative care etc all brought down the mortality .Currently the accepted mortality for the procedure is 1-1.5 %.But in high volume centres the mortality is almost approaching zero. Some centres has reported zero mortality for over five hundred cases. Further depths into the pathophysiology has shifted the focus from myectomy alone. Presently higher volume centres are trying for better outcomes in terms of Mitral valve replacement, CHB leading to PPI, and major adverse cardiovascular events.

Coming to surgical indications

1.All patients with a failed medical treatment

2.Symptomatic patients inspite of optimal medical treatment

3.Recurrence of symptoms or residual gradient following alcohol septal ablation.

In conclusion all patients with an LVOT gradient of more than 50 despite medical treatment with beta blockade or calcium channel blockers are accepted as candidates for surgical myectomy. Sub aortc myectomy has become the gold standard to relieve the LVOTO and associated SAM. Myectomy is a safe and effective procedure even though mitral regurgitation, residual LVOTO,SAM are still a problem in a minor group of patients post myectomy.

Mitral valve replacement has been proposed by cooley to solve these problems.But the present day surgeons are in favour of avoiding primary MVR for HOCM. Instead they are resorting to newer methods to address the mitral regurgitation and SAM. We resort primarly to correct the LVOT angulation by adequate myectomy. If the MR and SAM still remains we resort to leaflet placation or the ALPR. All these procedures yielded excellent outcome as evidenced by the no MR/SAM in the immediate post op and midterm followup.

The current study is a single centre experience with surgical myectomy. Our centre is apex centre for cardiac disease with skills and excellence gained over 40 yrs. The outcome analysis shows excellent and promising results. Our results substantiates the results over worldwide. All these results shows that

myectomy still remains as the gold standard for the treatment of treatment for HOCM comparing with the results of PTMSA.

Regarding the functional class almost all patients had a significant improvement in functional class. Majority of patients changed from functional class 3 or 4 to FC 2 OR 1.This corresponds to the decrease in post op gradient. The minimum post op gradient was 6 and maximum 60 with a maen of 22 with a standard deviation of 13.This significant reduction of gradient and enlargement of the LVOT translated into the improvement in functional class.

Our results indicate that myectomy is an effective method for treatment of HOCM. Surgical myectomy leads an acute reduction in LVOT gradient in more than 98 % of patients(70% in PTMSA).Ongoing ventricular remodeling further decreases the gradient and reduction in overall ventricular wall thickness. As the diastolic dysfunction settles effort dyspnoea gradually comes down translating to improved quality of life. The LV remodeling process extends to the entire myocardium leading to regression of LV hypertrophy. Indeed the total LV mass decreases after myectomy and the reduction exceeds that of the septal mass, an indirect evidence of the amelioration of pressure overload. There is an almost complete abolishion of SAM with its associated LVOTO and MR.

The clinical outcomes of the patients were excellent. Regarding functional class more than 98 % of patients had a significant improvement in the functional class. Only one patient remained in functional class 3,rest all were improved to either FC 1 or 11.There were no case of syncope or recurring

angina during the post follow up. The follow up period ranged from 3 months to almost more than 8 yrs.

The complications associated with the procedure were minimal, but it is statistically significant .Four patients required PPI following the procedure which amounted to a statistically significant 16.7 percent. Almost 12 patients required mitral valve replacement(50%). The patient category was complicated with severe mitral regurgitation Majority of these patients had long standing mitral regurgitations which won't respond with myectomy alone. In some patients leaflets were beyond the scope of repair. None of the surgical subset of patients responded with myectomy alone. This indicates that there is an associated mitral leaflet pathology .In last patient operated we could successfully address the severe MR with AML retension and plication.

LIMITATIONS OF THE STUDY.

Study was mainly a retrospective involving only one centre. The patient volume was low because of which the strength of the statistical analysis is low.

CONCLUSION

HOCM is a well studied and well described clinical entity with a varying symptomatology and presentation. Those who are affected by the disease has got a higher risk of sudden cardiac death. Those who survive with the disease has got significant morbidity which affects the quality of life. The treatment strategies are evolved over more than 40 yrs. Mild symptoms can be treated with medical management. Patients with severe disease and with higher risk of sudden cardiac arrest are treated by surgery and or ICD.

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LIST OF ABBREVIATIONS

HOCM	-HYPERTROPHIC OBSRUCTIVE CARDIOMYOPATHY
IVS	-INTER VENTRICULAR SEPTUM
PW	-POSTERIOR WALL
PA	-PULMONARY ARTERY
ASA	-ALCOHOL SEPTAL ABLATION.

TAC APPROVAL

Technical Advisory Committee (Clinical Studies)

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
THIRUVANANTHAPURAM – 695011, INDIA

TAC Registration No: SCT-/S/2015/427 **Date:** 22.03.2016

Project title: HOCM-OUTCOME FOLLOWING SURGICAL MYECTOMY, Retrospective observational study

Principal Investigator:
Name: Dr. Simon Philipose Degree: M.S Surgery, M.B.B.S Address: Senior Resident, Department of CVTS, SCTIMST, Trivandrum.
Co-Principal Investigator(s)
Name: Dr Vivek Pillai Degree: Mch CVTS. M.S Surgery, M.B.B.S. Address: Associate Professor, Department of CVTS, SCTIMST, Trivandrum.
(2) Name: Dr Jayakumar, Degree: MCH CVTS, M.S Surgery, M.B.B.S. Address: Head and Senior Professor, Department of CVTS, SCTIMST, Trivandrum.

Members who participated in the TAC meeting on 08/01/2016
Dr. Rupa Sreedhar (Chairperson)
Dr. Thomas Koshy
Dr. Lissy K Krishnan
Dr. Sylaja P.N
Dr. Krishnamoorthy KM
Dr. Biju Soman
Dr. Bejoy Thomas
Dr. Syam. K
Dr. K. Shivakumar (Member Secretary)

Dr. Thomas Koshy, Dr. Syam K, Dr. Bejoy Thomas and Dr. Sylaja.P.N stayed away from the proceedings when the projects in which they are involved (# 406, 415, 410, 413, 424, 426) as investigators were discussed.

Risk Classification of the project (Minimum/ Moderate/ High): Minimum
Requirement of DSMB: No
Recommended members of DSMB: Not applicable

Recommendations of TAC:
Recommended for consideration of IEC.

The PI may note that there can be no additions / alterations in the documents approved by TAC when they are submitted to the IEC.

Signature of the Member Secretary, TAC (Clinical Studies)

Note for IEC
Copy of the investigator's responses to questions/suggestions from TAC is attached (Appendix-1).

1

IEC APPROVAL

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)

SCT/IEC/919/JUNE-2016 08.09.2016

Dr. Simon Philipose
Senior Resident
Department of CVTS
SCTIMST, Thiruvananthapuram

Dear Dr. Simon Philipose,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "HOCM-OUTCOME FOLLOWING SURGICAL MYECTOMY-RETROSPECTIVE OBSERVATIONAL STUDY (HOCM–HYPERTROPHIC OBSTRUCIVE CARDIOMYOPATHY)" (IEC/919) on 3rd June, 2016.

The following documents were reviewed:

Original submission

1. Covering letter addressed to the Chairperson, IEC, SCTIMST, dated 28.03.2016 with check list
2. TAC Approval Letter
3. IEC Application Form
4. Project Proposal
5. CV of Principal Investigator and Co- Investigators

Revised submission

1. *Covering letter addressed to the Secretary, IEC, SCTIMST with check list*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *CV of Principal Investigator and Co- PI*
7. *IEC Recommendation Letter dated 09.06.2016*

The following members of the Ethics Committee were present at the meeting held on 3rd June, 2016 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Justice Gopinathan. P.S	BSc. LLB	Male	Legal Expert (Chairperson)	No
2.	Dr. Asha Kishore	MD, DM	Female	Clinician (Neurologist)	Yes
3.	Dr. Prabha D Nair	PhD	Female	Basic Scientist	Yes
4.	Dr. Meenu Hariharan	DM	Female	Clinician (Gastro-Enterologist)	No
5	Dr. Rema M. N	MD	Female	Pharmacologist	No
6	Dr. R V G Menon	PhD	Male	Lay Person	No
7.	Dr. V. Raman Kutty	MPH(Harvard) MPhil, MD	Male	Public Health	Yes
8.	Dr. K R S Krishnan	ME, PhD	Male	Biomedical Scientist/Engineer	No
9.	Dr. Kala Kesavan. P	MD	Female	Pharmacologist	No
10.	Smt. Sathi Nair	MA	Female	Lay Person	No
11.	Dr. Christina George	MD	Female	Psychiatrist	No
12.	Dr. Mala Ramanathan	MSc, PhD, MA	Female	Ethicist/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

Simon_Thesis.docx

ORIGINALITY REPORT

2%

SIMILARITY INDEX

PRIMARY SOURCES

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EXCLUDE QUOTES	ON	EXCLUDE MATCHES	OFF
EXCLUDE BIBLIOGRAPHY	ON		

slno	NAME	AGE	SEX	HOSP NO	SYNCOPE	PALPITATIONS	PRE OP ARRHYTHMIAS	FC	FH	PREOP GRADIENT
1	SHAMEER M	22	M	266286	N	N	N	3	N	142
2	VALLIAMMA M	68	F	297701	N	Y	N	3	N	110
3	PREETHA R	36	F	254829	N	N	N	1	Y	120
4	SANABA BEEVI	53	F	353190	Y	Y	Y	2	Y	124
5	GANAPATHY PANDIAN	53	M	354833	N	Y	Y	3	N	140
6	SARANYA M	17	F	9701264	N	Y	N	3	Y	64
7	PREMACHANDRAN PILLAI	53	M	357835	N	N	N	3	N	200
8	AMBIKA THOMAS	54	F	361338	Y	Y	N	2	Y	70
9	THULASIYAMMA	54	F	373616	Y	Y	N	3	N	135
10	SUNITHA PM	35	F	361707	N	N	Y	3	N	100
11	SABU JOSEPH	49	M	360121	Y	N	Y	3	N	120
12	KRISHNAN M	59	M	220477	N	N	N	3	N	119
13	SHIJINA S	17	F	372309	Y	Y	N	2	Y	80
14	LATHA MOL	32	F	8701042	N	Y	Y	2	N	60
15	VIPN K	22	M	9505726	N	N	N	3	N	200
16	ANITHA A	50	F	9900717	N	Y	N	3	N	93
17	PRAKASH	48	M	350724	Y	N	N	1	N	110
18	ATHIRA	12	F	341630	N	N	N	2	N	200
19	OMANA K	63	F	339654	N	N	N	3	N	80
20	AKSHAYA	10	F	311614	N	N	Y	3	N	100
21	SUBAIDA	68	F	307137	Y	Y	Y	3	N	90
22	SANTHI P	38	F	261497	N	N	N	2	N	112
23	AROCKIA DAS	22	M	236717	Y	N	N	2	N	115
24	SAIDALI	11	M	199712	N	N	N	3	N	80

AGE AT ONSET OF SYMPTOMS	IVS	PW	EF	POPG	MR POST	PW	EF	FC	ARRHYTH	PPI	MVR	PROLONGE	MORTALITY
15	17/20	13/16	84	8	8/17	Oct-13		75	N	N	Y	N	N
65	13/18	13/20	60	60				60	CHB	N	N	N	N
17	16/20	14/20	60	10	14/16	15/17		54	LBBB	Y	Y	Y	N
45	18/23	13/18	79	14	13/17	13/18		83	LBBB	Y	N	N	N
38	18/24	16/19	74	22	13/23			78	N	N	Y	Y	N
15	13/17	15/20	73	30				60	N	N	Y	N	N
50	25/27	20/26	67	37	18/22			61	N	N	N	N	N
45	13/16	13/15	60	6	15/13			83	N	N	N	N	N
48	22/26	13/16	84	40	17/19			77	N	N	Y	N	N
30	20/24	13/15	76	12	18/20			59	N	N	Y	N	N
40	22/27	16/19	75	18	14/15	13/16		55	LBBB	ICD	N	Y	N
55	22/26	20/25	70	20				65	N	N	Y	N	Y
15	14/18	14/18	82	10				75	N	N	Y REP	N	N
15	17/19	13/15	80	10	13/18			60	AF	N	Y	N	N
8	14/17	14/18	75	20				70	N	N	Y	N	N
32	15/23	14/19	65	25				60	2 CHB	Y	Y	Y	N
48	13/21	13/17	70	54				74	N	N	N	N	N
5	13/15	13/16	80	30				75	N	N	Y	Y	N
60	13/18	14/18	80	20				75	LBBB	N	N	N	N
2	14/19	13/18	80	24				78	N	N	N	N	N
60	13/18	14/19	60	18				61	N	N	N	N	N
28	13/16	14/16	71	13	13/15			80	N	N	N	N	N
18	14/17	15/18	77	15	13/15			76	N	N	N	N	N
5	13/17	13/17	75	25	N	N		75	N	N	N	N	N