SREE CHITRA THIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY

THIRUVANANTHAPURAM – 695011

PROJECT REPORT

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Month & Year of Submission : October 2009.

CERTIFICATE

I, Dr. Premkumar K.J., hereby declare that I have undertaken the work necessary for the project, under the guidance of the Faculty, Department of Cardiology.

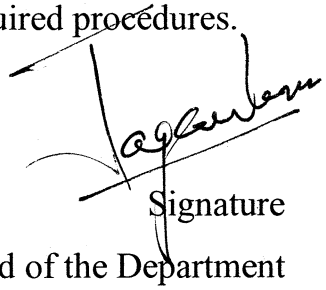
Signature

Name: Dr. Premkumar K.J.

Place: Trivandrum

Date: 13.10.2009

Forwarded: He has carried out the minimum required procedures.



Signature

Head of the Department

LIST OF PROJECTS

1. A Study on Magnetic Resonance Imaging in Endomyocardial fibrosis.
2. A Comparative study of Balloon Mitral Valvotomy and closed Mitral Valvotomy in Juvenile Mitral Stenosis.

Name : **Dr. Premkumar K.J.**

Programme : DM Cardiology

Month &Year of Submission : October 2009.

REPORT I

A STUDY ON MAGNETIC RESONANCE IMAGING IN ENDOMYOCARDIAL FIBROSIS

Introduction

INTRODUCTION

Endomyocardial fibrosis (EMF) is a type of restrictive cardiomyopathy characterised by progressive interstitial fibrosis involving the endo-myocardium of the ventricles. MRI has a definitive role in confirming and characterizing this pathology as compared to catheter angiogram and echocardiography[1,2].

Hypothesis

HYPOTHESIS

In cardiac MRI, in white blood images (Gradient echo) a healthy and a fibrotic myocardium have a similar signal intensity, which looks intermediate (gray), while a thrombus and calcifications will appear as clearly delimited hypointense areas (black)[2].

Immediate Post contrast images will show the fibrotic endocardium hypointense (black) because of hypoperfusion of fibrotic endomyocardium[2].

In Delalyed Enhancement MR (DEMR) images (after 10 mins of contrast injection) fibrotic endocardium will show enhancement while the healthy myocardium will be intermediate (gray) intensity as the contrast has washed out. The late enhancement will continue to persist even after 45mins post contrast in fibrotic endocardium.

In EMF there is fibrotic obliteration of ventricular apex. So in delayed enhancement images of MRI, late enhancement is seen involving the endocardium of ventricular apex.

Review of Literature

skeletal muscle, and is clearly distinguishable from the surrounding bright epicardial fat and the adjacent dark intracardiac blood[1].

The T1 relaxation time of myocardial tissue is about 800 ms, and the T2 relaxation time approximately 33 ms (at 1.5 T). Similar to diseases in other parts of the body, myocardial disorders are often characterized by changes in proton relaxation times. These changes may be helpful, since they can be used, at least to a certain degree, for tissue characterization. For instance, fatty infiltration of the free wall of the right ventricle will be visible as hyperintense intramyocardial spots on T1-weighted SE images, and these abnormalities make the diagnosis of ARVD[1].

Mature myocardial fibrosis or calcification, on the other hand, appears hypointense on both T1- and T2-weighted sequences and can be found in patients with endomyocardial fibrosis. A hyperintense myocardial area on T2-weighted images in a patient with a recent myocardial infarction is suggestive of increased free-water content due to myocardial oedema and/ or necrosis. The latter finding can thus be used for noninvasive localization of the myocardial infarction. However, the changes are non-specific, since other conditions such as acute rejection of a cardiac allograft or myocarditis are equally characterized by an increased water content and a subsequent rise in T2 relaxation values.

But these changes in relaxation times reflect gross morphological changes but are often non-specific. Paramagnetic contrast agents (e.g. gadolinium chelates) can be used for improved detection of myocardial disorders. Differences in signal intensity changes before and after administration of contrast agent between myocardium and skeletal muscle are one way to better detect myocardial pathology such as myocarditis[1].

With the advent of the contrast-enhanced inversion-recovery (CE-IR) MRI with late imaging, superior contrast can be achieved between normal and abnormal myocardium by selectively suppressing or nulling the signal of normal myocardium. This revolutionary idea has led to a whole range of new applications. Nowadays this technique has become the reference technique for myocardial tissue characterization[1].

Myocardial scar is characterized by relative increases in extracellular collagen content[6,7]. On a cellular level, the interstitial space between collagen fibers may be greater than the space between densely packed living myocytes that is characteristic of viable myocardium. This space would be expected to produce an increase in concentration of gadolinium in scar versus normal myocardium due to the expanded volume of distribution.

Histopathology data support this proposed mechanism. In analysis of heart explanted shortly after MRI, moon and collagues[3] demonstrated that

myocardial areas that hyperenhanced on DE-MRI exhibited increased collagen content on histopathology, with a linear relationship between the degree of collagen content and the percentage of hyperenhanced pixels.

A nonischemic DE-MRI scar pattern was diagnosed as mid myocardial or epicardial hyperenhancement, where as ischemic DE-MRI scar pattern was diagnosed as subendocardial or transmural hyperenhancement in a typical coronary anatomic distribution[8]. Although the simple presence of scar was sensitive (94%) for the diagnosis of ischemic cardiomyopathy, specificity was relatively poor (60%). When ischemic or nonischemic-type of scar was considered in as an adjunctive diagnostic criteria, sensitivity remained high (92%), where as specificity was improved (93%) ($p<0.0001$).

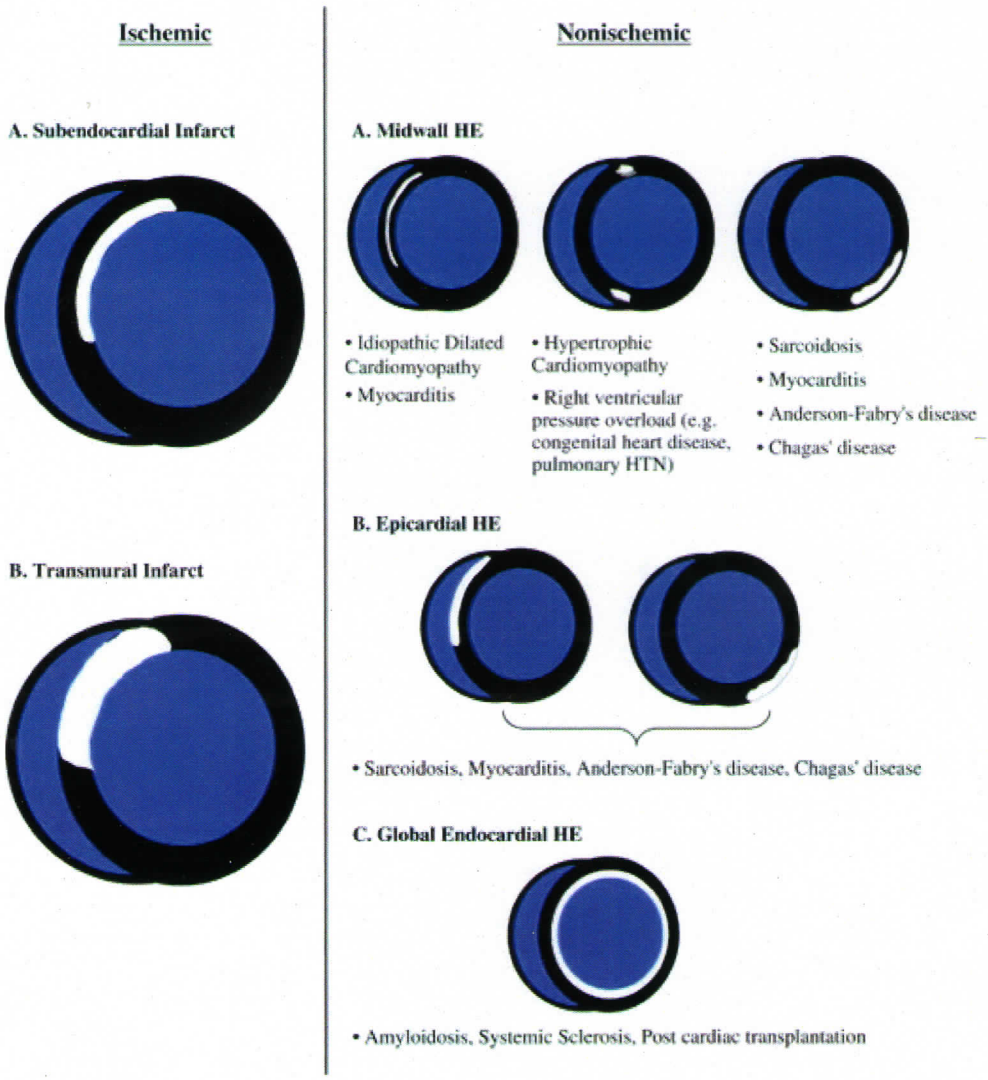
DE-MRI evidenced hyper enhancement can occur in inflammatory conditions such as myocarditis[9,10] infiltrative cardiomyopathies such as sarcoid[11-13] systemic processes such as amyloid[14] or chagas disease[15], and genetic abnormalities such as HCM[16,17] or Anderson-Fabry's disease[18-19]. Each of these conditions results in myocardial dysfunction as a result of diverse pathologic process and has associated differences in hyperenhancement patterns.

For example in the setting of LV hypertrophy, the presence of mid valve hyper enhancement at the junctions of the interventricular septum and

right ventricular free wall is a compelling argument for the diagnosis of HCM, whereas midwall or epicardial hyperenhancement in the inferolateral wall suggests Anderson-Fabry's disease. This is represented in figure below.

Cardiac functional evaluation is another important pillar of the assessment of myocardial diseases. Cine MRI, using the new, balanced steady-state free precession (b-SSFP) techniques, allows for accurate analysis of regional function (wall motion and wall thickening), quantification of global ventricular parameters and myocardial mass, and depiction of abnormal flow patterns (e.g. flow acceleration in a narrowed left ventricular (LV) outflow tract in patients with obstructive HCM and concomitant mitral valve regurgitation).

Velocity-encoded cine MRI is able to quantify flow velocities and volumes, and can therefore be applied to assess the severity of an associated valve abnormality, e.g. mitral or tricuspid regurgitation in a patient with dilated cardiomyopathy (DCM). The same MRI technique is gaining acceptance to assess diastolic function such as in patients with restrictive cardiomyopathy (RCM).



Shah DJ et al, Magnetic resonace of myocardial viability

Analysis of the transvalvular and venous flow patterns enables depiction of impaired myocardial relaxation and/or decreased compliance. Real-time cine MRI techniques have a large potential to assess the influence of respiration on cardiac filling and thus to differentiate patients with restrictive inflow pattern secondary to either restrictive cardiomyopathy or constrictive pericarditis. Other MRI techniques such as MRI myocardial tagging are helpful to explore wall deformation and to better understand the pathophysiology of certain myocardial disorders.

The literature referring to magnetic resonance (MR) findings in endomyocardial disease is scarce, specially related to the use of tissue characterization, new scans and paramagnetic contrast agents. There are no randomised / nonrandomized trials, nor descriptive epidemiological studies on MRI in EMF except for isolated case reports.

Firstly, MRI is very effective to demonstrate the absence of Pericardial thickening on Spin echo images (thickness <4mm) and so useful to diagnose constriction.

Secondly, the different tissue relaxation times corresponding to the nature of each tissue allow to identify precisely the existence of thrombus or calcifications that could be associated with fibrosis, and to differentiate this from other processes, such as tumors. While a healthy and a fibrotic myocardium have a similar signal intensity, intermediate (gray) in the white

blood scans, thrombus and calcifications appear as clearly delimited hypointense areas (black).

Newly, the first step myocardial perfusion scans, that use chelated gadolinium as contrast agent, allow detection of hypoperfused areas (not enhanced, dark) that correspond to areas with fibrosis (can also be due to microvascular affection), and confirms existence of avascular structures, such as thrombus and calcifications that are not perfused.

Finally, the myocardial suppression scans (acquired around 10 min after injection of gadolinium) allow to delimit the disease extension. Gadolinium is an extra-cellular contrast agent that is quickly diffused from the capillaries to the interstice and that presents a rapid wash-out in the healthy myocardium, while persisting longer in the pathologic myocardium with cellular lesions or fibrosis due to contrast kinetic differences in these areas.

This will produce a delayed hyperenhancement of the pathologic areas, independently of their actual thickening. This hyperenhancement is not observed in a healthy myocardium or in non-perfused avascular structures, such as thrombus or calcium deposits.

To begin with, a detailed review on specific macrospcopic and microscopic features of EMF may throw some light on our understanding on

specific patterns of involvement of EMF in MRI. In two series in Kerala and Bombay, the autopsy studies described the EMF hispathology.

The macrospcopic feature of the disease was severe endocardial thickening in the ventricles with effacement of the trabecular pattern. Endocardial fibrosis had either diffuse or focal distribution. In the diffuse type, involving the entire inflow and the apex, the papillary muscles were effaced and the ventricular chamber obliterated by opaque, thick endocardium.

The AV valve leaflets were thin and stretched. Chordae tendinae were often tethered to the thickened endocardium. Actual valve involvement was not a common feature although a rheumatic type of valvular deformity in the mitral valve was occasionally seen. But in Bombay series either the posterior or septal cusp or both cusps of the tricuspid valve were tethered to the ventricular wall. The posterior mitral cusp was plastered to the ventricular wall.

In RV EMF, atriomegaly was present and often the atrium contained a large thrombus. While one ventricle was affected with obliterative fibrosis, focal involvement of the contralateral ventricle involving only the apical region or the base of the papillary muscle was frequently seen.

In the left ventricle, fibrosis involving the inflow tract and the apex was the common finding. Extension of the fibrotic process to the aortic outflow

was seen occasionally. Mural thrombus overlying the thickened endocardium was present. In left ventricle, the process starts below the mitral annulus in the recess between the posterior mitral cusp and ventricular wall and extended over inflow tract and apex, engulfing the subvalvular apparatus. In the right ventricle it occupies the whole cavity from tricuspid and the pulmonary valve.

Microscopically, the thickened endocardium consisted of a superficial compact layer of collagen with occasional hyalinization and calcification, and a deeper, loose spongy layer of fibrous tissue with numerous capillary channels and scanty lymphocytic infiltrates. Of 42 patients, histology showed involvement of Myocardium in 31 patients in the form of Myocytolysis or Myofibre hypertrophy. The myocardium close to the endocardium had strands of vascularised connective tissue. Vacuolation as well as atrophy of few myofibres was seen.

Scarring was infrequent in the outer half of the myocardium. The destroyed muscle fibres were replaced by loose cellular tissue with scanty mononuclear exudates. The subendocardial myofibres frequently showed degenerative changes. Atrophic or severely hypertrophic myofibres were often present in other regions. Intense inflammatory infiltrates, including eosinophils are conspicuously absent in endocardium or myocardium.

Aims of the Study

AIMS OF THE STUDY

1. To assess the usefulness of MRI to diagnose endomyocardial fibrosis.

2. To study the morphological pattern of involvement in endomyocardial fibrosis using MRI.

3. To study the extent of endomyocardial involvement using MRI.

4. To assess the involved ventricular function using MRI.

5. To assess the feasibility of endocardiectomy.

Materials and Methods

MATERIALS AND METHODS

- This is a prospective study of clinically diagnosed EMF cases by using MRI.
- Number of patients studied 19, Duration of study- 32months.
- Pre procedure detailed clinical assessment and Echocardiography done in all cases.
- Catheter angiography and hemodynamic study was done.
- Grading of LV and RVEMF was done as noted below.
- MR Imaging- Cine True FISP in SA(short axis) and 4 Chamber, axial HASTE T2W, axial SE T1W, Velocity-encoded MR (to assess the morphology, ventricular and valvular functions). Phase shift IR scans at 10 - 60 minutes (to assess pattern of enhancement).
- Gadolinium contrast 0.2mmol/kg injection given intravenous.
- Based on clinical and hemodynamic data patients were sent for endocardiectomy with or without AV valve replacement.
- Biopsy report of the surgical specimen were analysed.
- Repeat MRI was done after endocardiectomy
- Endomyocardial Biopsy was done if there was discrepancy between echo/angio and MRI findings.

GRADING OF SEVERITY OF LV EMF BY ANGIOGRAPHY[4,5]

Grade I : loss of the fine trabecular pattern of the LV chamber giving a bald appearance

Grade II : Obliteration of the LV apex

Grade III : More than half of the LV cavity is obliterated resulting in the transverse diameter exceeding the long diameter of the LV.

GRADING OF SEVERITY OF RV EMF BY ANGIOGRAPHY[4,5]

Grade I : Minimal involvement of the RV chamber in the form of alteration in the trabecular pattern at the apex and along the septal border with irregular small filling defects

Grade II : Obliteration of RV apex giving a saucer shape to the RV

Grade III : Obliteration of RV apex and RV inflow near the tricuspid annulus, generally associated with marked RV outflow tract dilatation.

In the severest forms, RV outflow may also be involved but is generally appreciated only at pathological study.

Statistical analysis

Mean and standard deviation are used to represent continuous variables. To compare the significance of difference between discrete variables Fisher exact test and Chi square tests are used. To compare significance of difference between continuous variables Student t test was used. Mann Whitney U test was used to compare variables with different grades. Since the sample size is small, percentage of differences between two groups was also analysed to show the significance.

Observations

OBSERVATIONS

Clinical findings:

Total number of patients - 19. Total number of MRI done 20. Age of patients - 24-60 years (mean- 42.5 years). Male: Female- 2:1 (70%:30%).

Clinically 2 patients were in New York Heart Association (NYHA) Functional Class (FC) IV. 5 patients were in FC III and the remaining were in class II. Functional class II exertional angina was present in 3 patients and 12 patients had a typical chest pain. 5 patients had palpitiation. 3 patients had presyncope and congestive cardiac failure was present in 8 patients.

Only 6 patients were in sinus rhythm, 10 patients were in atrial fibrillation. One patient had atrial flutter. 1 patient had complete heart block and 1 patient had paroxysmal atrial tachycardia with block.

Echocardiographic findings:

In 2D echo cardiography, 12 patient had isolated Right Ventricular Endomyocardial fibrosis (RVEMF). 2 patients had isolated (LVEMF). 5 patients had Biventricular Endomyocardial fibrosis (BVEMF) of which 3 patients had predominantly LV involvement, 2 patients had predominant RV involvement (Table 1).

The mean Left Ventricular Internal Diameter Diastole (LVIDD) was 45mm and mean Left Ventricular Internal Diameter Systole (LVIDS) was 29mm, and Ejection fraction (EF) was 64%. The mean Left Atrial (LA) dimension was 37mm and aortic diameter was 26mm. RVID was 27mm (Table 2). The mean Right Ventricular Systolic Pressure (RVSP) was 44mmHg.

RV apical obliteration was present in 17 patients. LV apical obliteration was present in 6 patients. RV apical calcification was present in 8 patients, LV apical calcification was present in 4 patients. Large RA (Right Atrial) clot was present in 2 patients.

4 patients had severe Tricuspid Regurgitation (TR), another 4 patients had moderate TR and the remaining 11 patients had mild TR. One patient had severe MR (Mitral Regurgitation), 3 patients had moderate MR, 7 patients had mild MR, 6 patients had trivial MR and 2 patients had no MR (Table 3). There was mild (5-10mm) Pericardial effusion in 2 patients, moderate (10-15mm) in 2 patients and Large (>15mm) in 2 patients.

Hemodynamic and Angiographic findings:

Hemodynamic study was done in 12 patients. During hemodynamic study, RA mean was elevated (8-15mmHg in 5 patients, >15mmHg in 3 patients). RVED (RV end diastolic pressure) was elevated (>8-15mmHg in 4 patients, >15mmHg in 3 patients). PA (Pulmonary Artery) mean was mildly

elevated (>25-40mmHg) in 4 patients, no patients had moderate or severe PAH. Other patients had no significant PAH. PA wedge mean pressure was elevated (>12mmHg) in 3 patients. LVED was elevated (>12mmHg) in 5 patients (Table 4).

Table1: Echo cardiographic features of EMF

PARAMETER IN ECHO	No. of Patients
LVEMF(n)	2
RVEMF(n)	12
BVEMF(n)	5
LV>RV(n)	3
RV>LV(n)	2
LV=RV(n)	0

Table 2: Echocardiographic features of EMF

PARAMETER IN ECHO	VALUE
LVIDD(mean)mm	45
LVIDS(mean)mm	29
EF(%)mean	64
LA (mm)	37
AORTA(mm)	26
RVID (mm)	27

Table3: Severity of AV valve regurgitation in ECHO

GRADE	Nil	TRIVIAL-MILD	MODERATE	SEVERE
TR(n)	0	11	4	4
MR(n)	2	13	3	1

Table 4: Hemodynamic variables (n=12)

PARAMETER		
RA MEAN range (mmHg)	8-15	>15
n	5	3
RVED range (mmHg)	8-15	>15
n	4	3
PAMEAN range (mmHg)	25-40	>40
n	4	0
PAW MEAN range (mmHg)	13-18	>18
n	3	0
LVED range (mmHg)	>16	
n	5	

Table 5: Grades of EMF in Angiocardiography (n=12)

Grade of EMF	I	II	III
RVEMF(n)	0	4	6
LVEMF(n)	2	5	1

Table 6:Grading of AVValve regurgitation in Angiocardiography (n=12)

Parameter	Mild	Moderate	Modly-severe	Severe
TR	5	2	0	3
MR	0	4	2	1

In RV angio (AP and lateral view), Grade III RVEMF was present in 6 patients, Grade II RVEMF was present in 4 patients (Table 5). Severe TR was present in 3 patients, Moderate TR in 2 patients, mid TR in 5 patients (Table 6). RV apical calcification was present in 5 patients at fluoroscopy. In 2 patients RA was not entered because of the presence of large RA clot.

In LV angio (RAO 30 and LAO 60) Grade III LVEMF was present in 1 patient, Grade II EMF was present in 5 patients, Grade I in 2 patients. LV was uninvolved in 5 patients. LV calcification was present in 2 patients at fluoroscopic examination.

Regarding associated diseases, MVP of AML was present in 1 patient, 2 patients had CAD (1 patient with Old IWMI and another with old AWMI, Rheumatic Heart disease with moderate-severe Mitral stenosis was present in 2 patients.

Observations in Cardiac MRI:

In Cardiac MRI, Isolated RVEMF (Fig 1) was present in 8 patients and Isolated LVEMF (Fig 2) was present in 2 patients. BIVEMF (Fig 3) was present in 7 patients, of which RV was predominantly involved in 5 patients, LV was predominantly involved in 2 patients, both the ventricles were equally involved in 2 patients.

In cine MR images, RV and LV apex were isointense with normal myocardium. In Post contrast images, during first pass, normal myocardium showed enhancement. There was a rim of apical endocardium which showed hypointensity in first pass images (Fig 2A&B). This pattern was observed in 18 out of 19 patients.

In Post contrast (images taken after 10mins of contrast) normal myocardium showed hypointensity. The rim of apical endocardium (which was hypointense in first pass images) showed delayed hyperenhancement (Fig 2C&D). Late enhancement continued to persist even upto 45mins post contrast. This pattern was also observed in 18 out of 19 patients. The endomyocardial patch which is enhancing post contrast was thick [average 5mm] with mild extension of the enhancement deep into the apical subendocardium (Fig 2).

RVOT dilation was present in 14 patients of RVEMF and BIVEMF with predominant RV involvement. The right atrial thrombus (Fig 5A&B) was present in 4 patients of which 3 patients had calcified thrombus. RV apical thrombus was present in 3 patients. One patient had LV thrombus, but he was classified as BVEMF. Isolated LVEMF patients had no LV thrombus. RV apical calcification was present in 8 patients (Fig 4). LV apical calcification was present in 2 patients.

Moderately severe TR was present in 11 patients. Moderately severe MR was present in 3 patients. Mild PE was present in 2 patients. Moderate PE was present in 1 patient. Massive PE was present in 1 patient. The mean Left Ventricular End Diastolic Volume (LVEDV) was 90ml and Left Ventricular End Systolic Volume (LV ESV) was 50ml. The mean LV EF was 46%. The mean RVEDV and RVESV were 106ml and 70ml respectively. The mean RV EF was 31%.

RV endocardiectomy with Tricuspid Valve replacement were done in 2 patients. RV endocardiectomy with BDG [bidirectional Glenn's shunt] was done in 1 patient. The endocardiectomy samples were sent for histopathological examination in all these 3 patients. Repeat cardiac MRI was done in 1 patient post endocardiectomy. Endomyocardial Biopsy was done in 1 patient.

Table 7 Comparison of MRI findings in RV/LV/BIVEMF

Variables		RVEMF (n=8)	LVEMF (n=2)	BVEMF (n=9)
RV apical obliteration		8	0	7
LV apical obliteration		0	2	3
RVOT dilatation		7	0	7
Calcification		5	0	2(LV) 4(RV)
Thrombus		3	0	1
Mitral regurgitation (Mod- severe)		0	1	2
Tricuspid regurgitation (Mod- severe)		6	0	7
EF%	RV	39		31
	LV	52	46	45

Table 8: Comparison of delayed enhancement

Parameters		RVEMF (%) n=8	LVEMF (%) n=2	BVEMF (%) n=9
Apex	Isolated Endocardial	0	0	4
	Endocardial + Apical Obliterated subendocardium	7	2	5
	Epicardial	0	0	0
	Myocardial	0	0	0
RV free wall				2
LV Posterior wall		0		6
LV posterior Papillary muscle		0		8
RA		5	0	4
LA		3	0	5
IAS		4	0	4
RA clot		1	0	1
LA clot		0	0	0

Figures

FIGURES

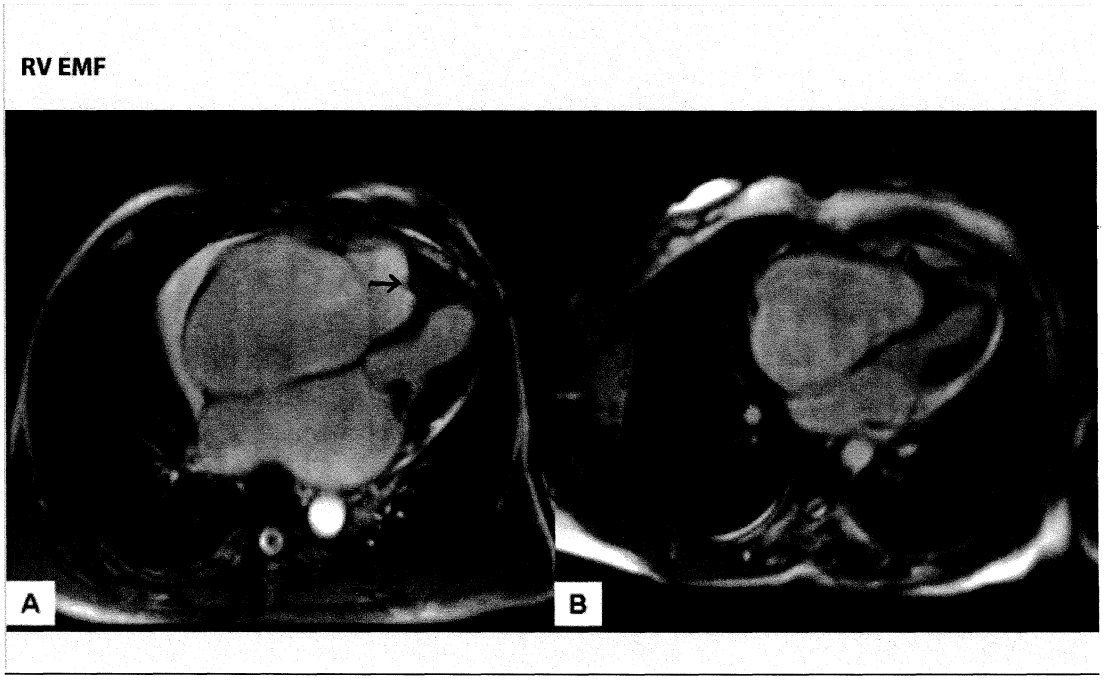


FIGURE 1 A &1 B CINE TRUE FISP IMAGES WITH ARROWS SHOWING RV APICAL OBLITERATION AND RETRACTION OF APEX.

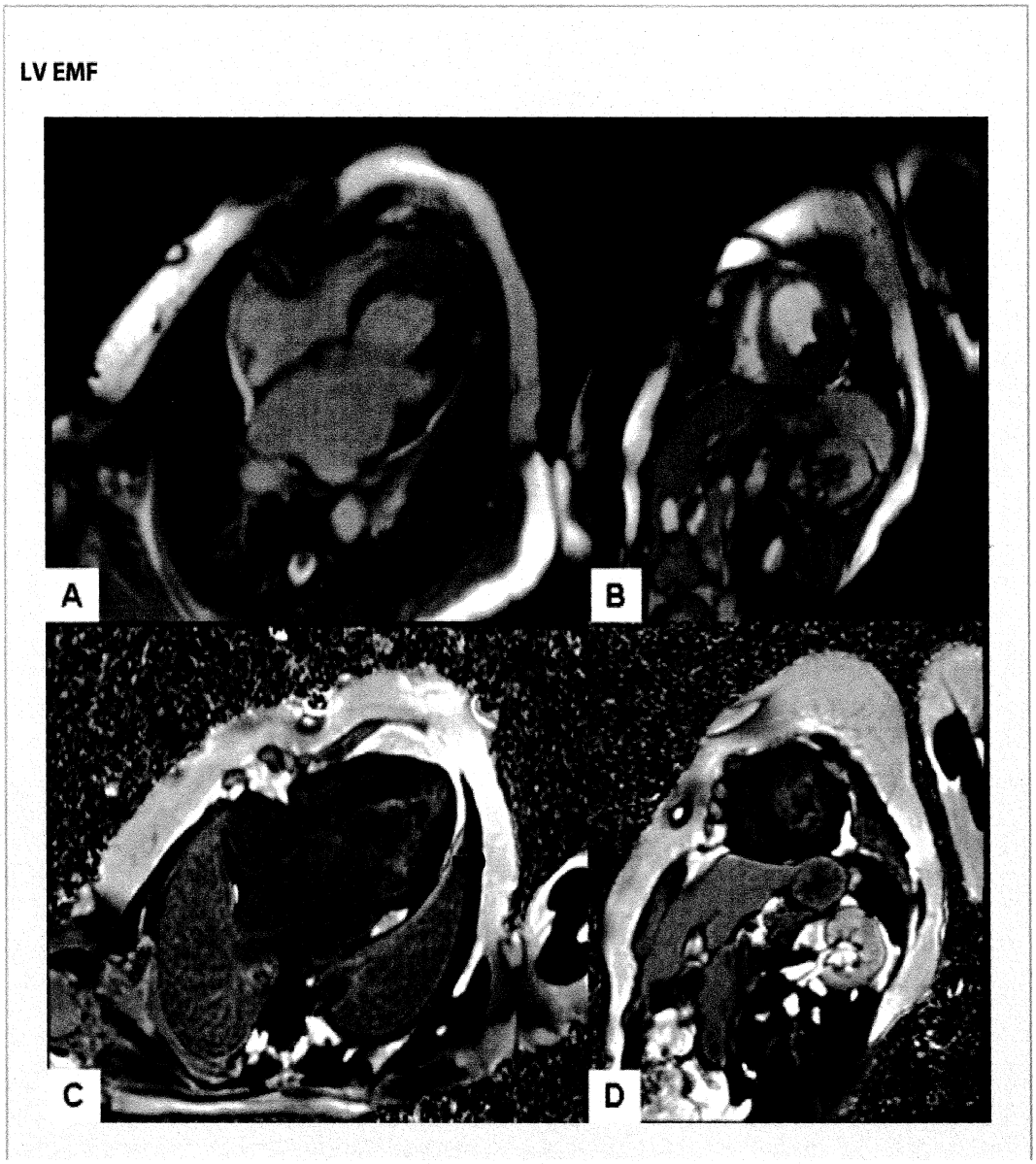


FIGURE 2 A & 2B IMMEDIATE POST CONTRAST PSIR IMAGES IMAGES IN 4 CHAMBER (4C) AND SHORT AXIS (SA) REVEALING LV APICAL OBLITERATION WITH THROMBUS ON ENDOCARDIAL SURFACE. THIS FIGURE ALSO SHOWS HYPOPERFUSION OF APICALMOST ENDOCARDIUM WITH ENHANCEMENT OF NORMAL MYOCARDIUM. FIGURE 2C & 2D POST CONTRAST PSIR IMAGES IN 4C AND SA SHOWING ENDOCARDIAL ENHANCEMENT OF APEX WITH NON ENHANCEMENT OF THROMBUS (ARROW).

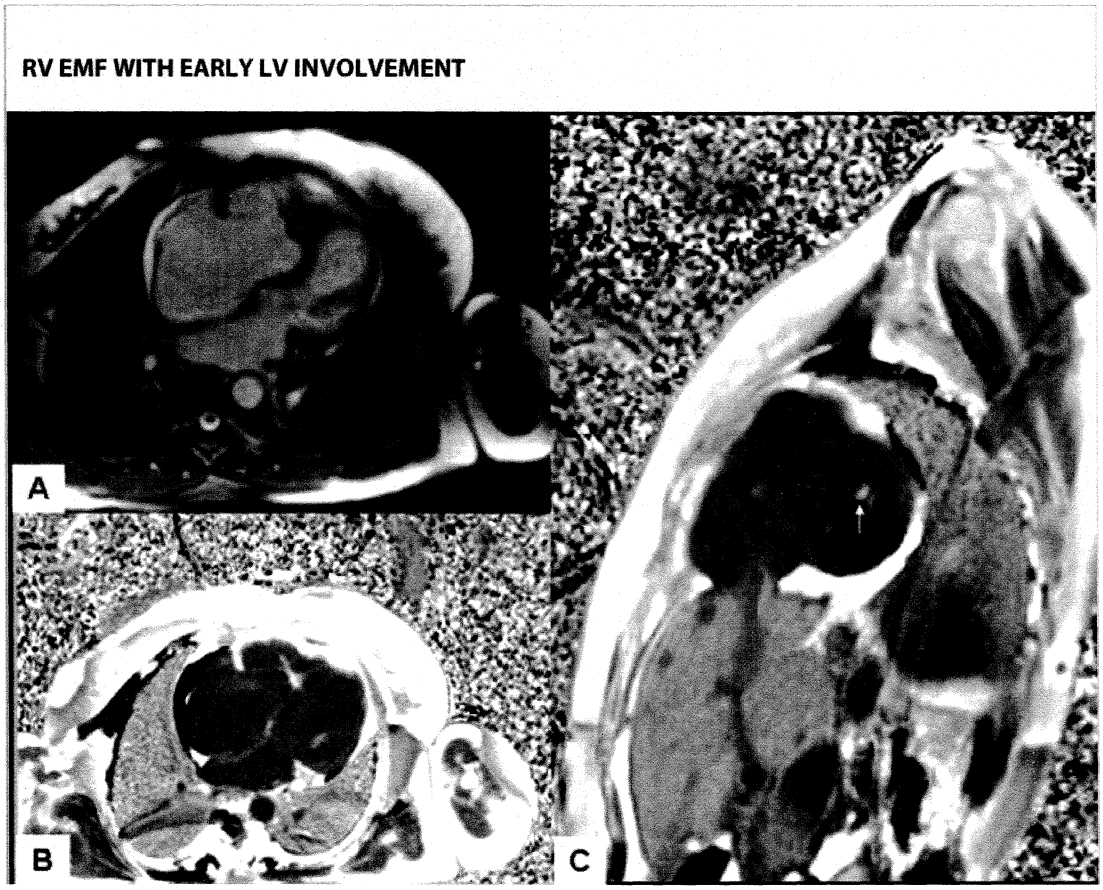


FIGURE 3 A CINE TRUE FISP IMAGE IN 4C VIEW SHOWING RVEMF. B&C) POST CONTRAST PSIR IMAGES DEMONSTRATES RV APICAL ENHANCEMENT (BLACK ARROW) AND ALSO NOTE THE ENHANCEMENT OF PAPILLARY MUSCLE (BLACK ARROW).

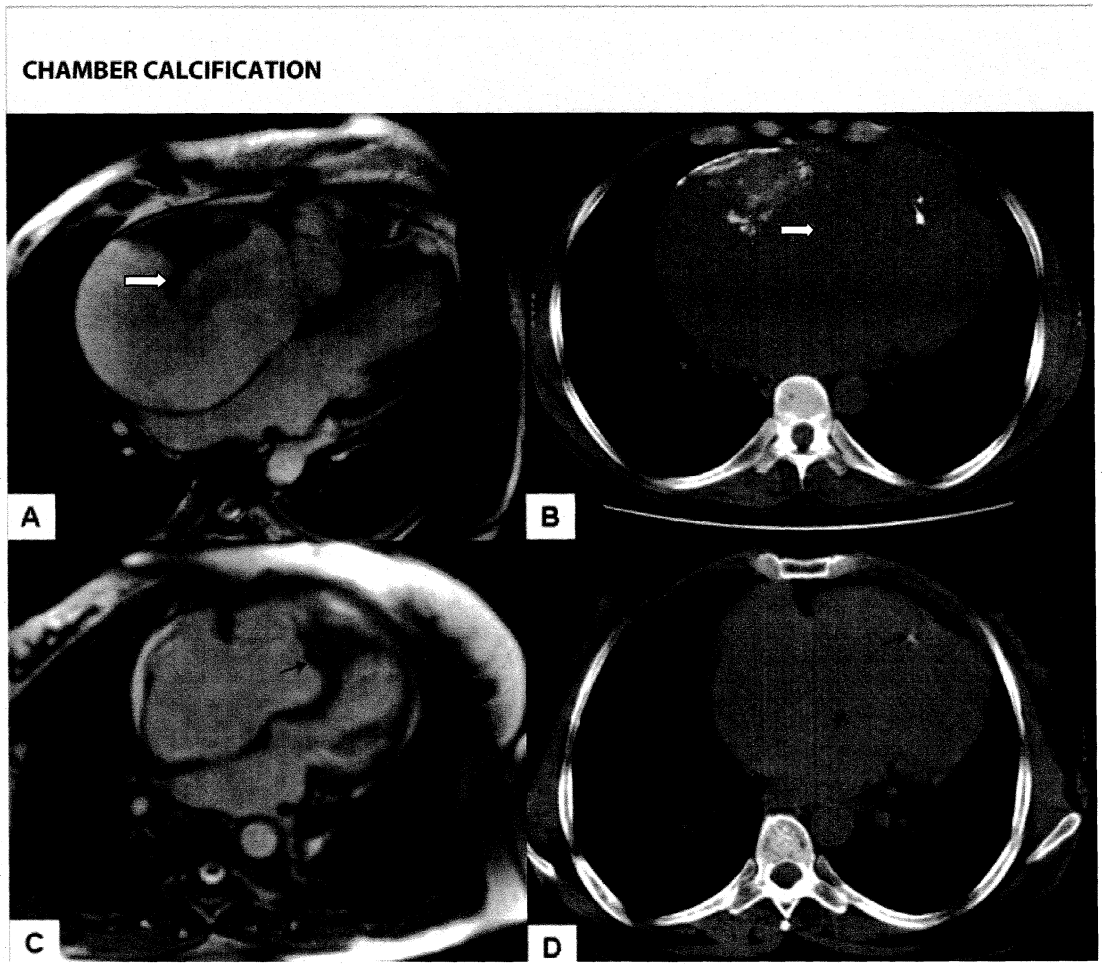


FIGURE 4 A & B CINE TRUE FISP IMAGE IN 4C VIEW AND CORRESPONDING CT AXIAL IMAGE SHOWING RVEMF WITH APICAL CALCIFICATION. ALSO NOTE THE CALCIFICATION OF RIGHT ATRIAL WALL AND THROMBUS (WHITE ARROW). C &D TRUE FISP CINE IMAGE IN 4C VIEW AND CT IMAGE SHOWING RVEMF WITH APICAL APICAL CALCIFICATION (BLACK ARROW).

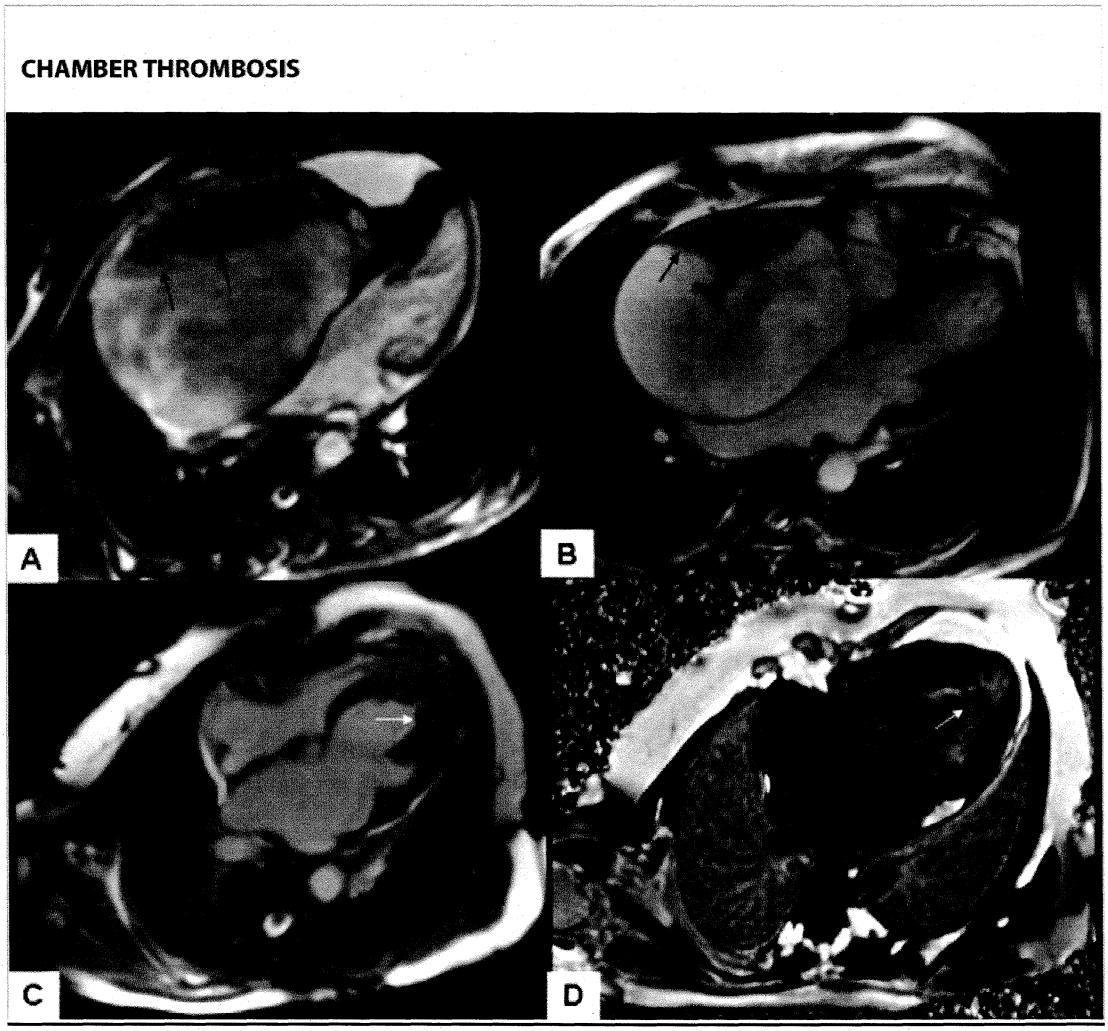


FIGURE 5 A & B) CINE TRUE FISP IMAGES IN 4C VIEW DEMONSTRATES RVEMF CASES WITH RIGHT ATRIAL THROMBUS. C & D) CINE TRUE FISP IMAGE AND POST CONTRAST PSIR IMAGE SHOWING LVEMF WITH APICAL HYPOINTENSE AND NONENHANCING THROMBUS. FIGURE SHOWS ENHANCEMENT OF RIGHT ATRIAL, LEFT ATRIAL WALL AND INTERATRIAL SEPTAL ENHANCEMENT.

VARIOUS PATTERNS OF ENHANCEMENT

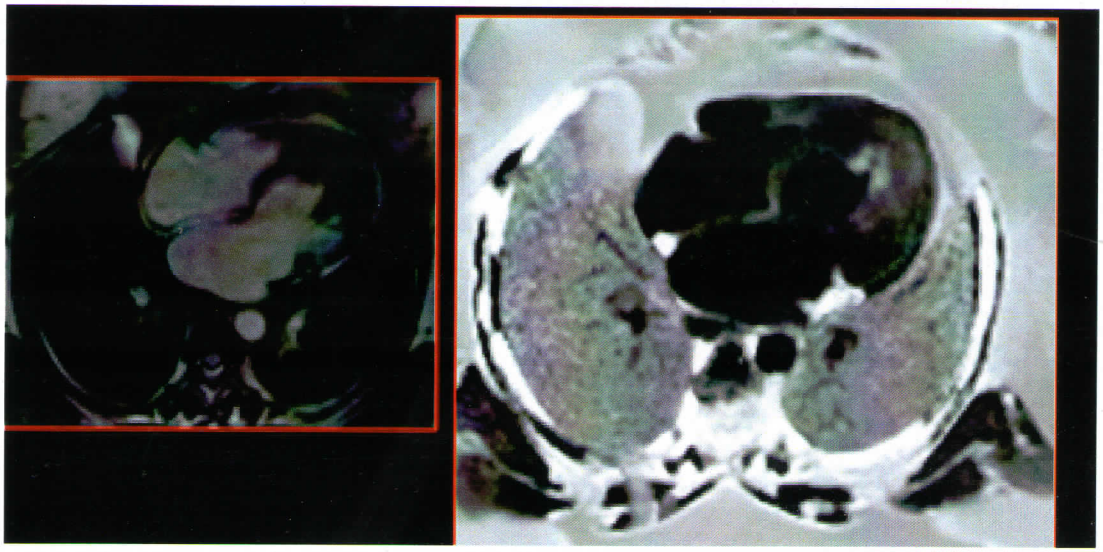


FIG 6(LEFT)CINE TRUE FISP IMAGE OF LVEMF SHOWING HYPOINTENSE AREA IN APICAL ENDOCARDIUM. FIG 6 (RIGHT) POST CONTRAST PSIR IMAGE OF THE SAME PATIENT SHOWING HYPERENHANCEMENT LIMITED ONLY THE APICAL ENDOCARDIUM

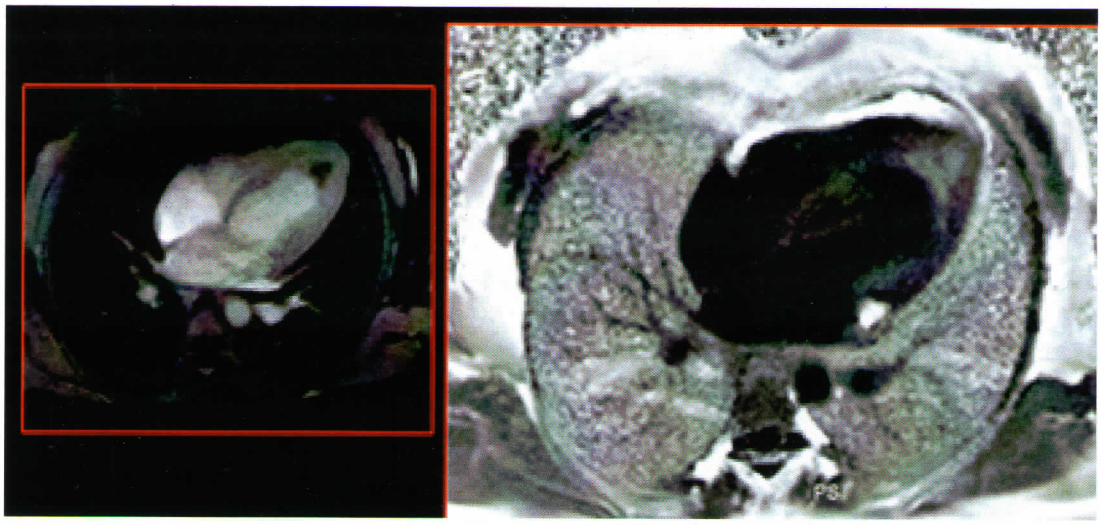


FIG7(LEFT)CINE TRUE FISP IMAGE OF LVEMF SHOWING HYPOINTENSE AREA INVOLVING WHOLE APEX. FIG 7 (RIGHT) POST CONTRAST PSIR IMAGE OF THE SAME PATIENT SHOWING HYPERENHANCEMENT INVOLVING WHOLE OF APICAL ENDOCARDIUM

Discussion

DISCUSSION

Endomyocardial Fibrosis (EMF) is a fascinating disease entity of unknown etiology. It is prevalent in the tropical zone. The essential features are the formation of fibrous tissue on the endocardium and to a lesser extent in the myocardium of the inflow tract and apex of one or both ventricles. It results in endocardial rigidity, atrioventricular valve incompetence secondary to papillary muscle involvement and progressive reduction of the cavity of the involved ventricle leading to restriction in filling and atrial enlargement.[20]

For a long time echocardiography has been the non invasive evaluation regarded as the modality for diagnosis and follow up of patients with EMF. Hemodynamic study and angiocardiography is done when evaluating a patient for endocardiectomy with or without valve replacement. But either investigation modalities cannot identify accurately extent of involvement of ventricles, presence of thrombus and calcification.[2]

Assessment of ventricular function is often difficult and inaccurate by echo and angiocardiography. Cardiac MRI appears to be the ideal investigation to answer these questions. It is well established that cardiac MRI is the gold standard for LV and RV systolic function, as a 3D assessment of the ventricular chamber can be obtained.[21]

In our study, 70% of patients were females. The average age group of our study patients was 42 +/-12 years indicating predominantly a middle aged population. Around 40% of patients in our study were in NYHA FC III-IV with congestive cardiac failure. The average eosinophil count in our study was 11%. Only 2 patients had eosinophil count of >12%. This indicate that hyperesinophilia is not a predominant feature of the tropical endomyocardial fibrosis.

The baseline evaluation (Echo/ Angio) have identified only 5 BVEMF, but in MRI 5 RVEMF patients had mild to moderate involvement of LV qualifying as BVEMF. The identification of early disease in the contralateral ventricle is important because endocardiectomy can be offered for the other side. Bidirectional Glenn (BDG) Shunt as a treatment for RVEMF is contraindicated with significant LV involvement. Also the post surgical patients can be kept on follow up for the progression of the disease in the other ventricle.

The apical obliteration can be identified in cine MR images in all patients. The apical endomyocardium was isointense with the normal myocardium in the free ventricular wall in cine images in all patients. The RV/LV length ratio or LV/RV length ratio was <50% in patients with RVEMF and LVEMF respectively. The average Ejection fraction (EF) in patients with

predominant LVEMF {LVEMF, BVEMF (LV>/=RV)} is 46% in cardiac MRI. But the LV EF in echo was 62%.

Other structural abnormalities like Right atrial dilatation / Left atrial dilatation and RVOT dilatation can be identified better with cardiac MRI as all patients with RVEMF had RA dilatation and RVOT dilatation in cardiac MRI as against echo which has failed to identify because of poor echo window.

Hypercontractile RVOT was seen in 7 out of 8 patients with RVEMF. The mean LA size in echo was 35mm. LA size was underestimated (<35mm) in 3 patients with LVEMF, but in cardiac MRI all patients with LVEMF had LA dilatation. This feature again indicates that atrial dilatation is an early feature of diastolic dysfunction of the ventricle with early involvement. Ventricular calcification was seen in 11 patients with EMF in MRI as against only 5 patients at fluoroscopic examination.

The statistical analysis of variables like diagnosis, RV apical obliteration, LV apical obliteration, and severity of MR did not give statistically significant difference between these investigation modalities. The severe TR was present in significant number of patients in MRI ($p<0.05$) and LV EF was also reduced in significant number of patients in MRI ($p<0.01$). The percentage of difference in observations was also done to adopted for analysis. These are represented in the table 9 & 10 below.

Table 9: Comparison of variables in echocardiography and MRI

		Echo	MRI	p value
DIAGNOSIS	LVEMF	2 (10.5)	2 (10.5)	p>0.05@
	RVEMF	12 (63.2)	8 (42.1)	
	BIVEMF(LV=RV)	0 (0)	2 (10.5)	
	BIVEMF(LV>RV)	3 (15.7)	2 (10.5)	
	BIVEMF(RV>LV)	2 (10.5)	7 (36.8)	
RVAO	Absent	2 (10.5)	6 (31.6)	p>0.05#
	Present	17 (89.5)	13 (68.4)	
LVAO	Absent	13 (68.4)	12 (63.2)	p>0.05#
	Present	6 (31.6)	7 (36.8)	
TR	Nil	0 (0)	2 (10.5)	p<0.05^
	Grade I	0 (0)	1 (5.3)	
	Grade II	11 (57.9)	1 (5.3)	
	Grade III	4 (21.1)	4 (21.1)	
	Grade IV	4 (21.1)	11 (57.9)	
MR	Nil	2 (10.5)	7 (36.8)	p>0.05^
	Grade I	6 (31.6)	2 (10.5)	
	Grade II	7 (36.8)	6 (31.6)	
	Grade III	3 (15.8)	2 (10.5)	
	Grade IV	1 (5.3)	2 (10.5)	
PE	Nil	13 (68.4)	13 (68.4)	p>0.05^
	Mild	2 (10.5)	2 (10.5)	
	Moderate	2 (10.5)	3 (15.8)	
	Large	2 (10.5)	1 (5.3)	
LVEF		64.1±9.4	45.9±16.2	p<0.01@

#Fisher's Exact Test @ chi square ^ Mann-Whitney U

Table 10: Comparison of differences of involvement in MRI, ECHO and ANGIO

			Count	Percent
DIAGNOSIS	MRI-ECHO	Same	11	57.9
		Different	8	42.1
RVAO	MRI-ECHO	Same	15	78.9
		Different	4	21.1
LVAO	MRI-ECHO	Same	16	84.2
		Different	3	15.8
TR	MRI-ECHO	Same	4	21.1
		Different	15	78.9
MR	MRI-ECHO	Same	3	15.8
		Different	16	84.2
PE	MRI-ECHO	Same	11	57.9
		Different	8	42.1

In immediate post contrast images (PSIR) of MRI, enhancement was seen in normal healthy myocardium in 18 out of 19 patients. A thin layer (approximately 3mm in thickness) of apical endomyocardium was seen hypointense in 18 out of 19 patients. After 10 mins of contrast injection normal healthy myocardium was seen hypointense because of normal contrast wash out but the apical endomyocardium which was hypointense in immediate contrast images has shown hyperenhancement in 18 out of 19 patients. This

delayed hyperenhacement was persisting upto 45mins of post contrast images in 18 out of 19 patients.

The delayed hyperenhancement can be explained by slow gadolinium wash out from the fibrotic endomycardium. The persistence of hyperenhancement even after 45mins in the fibrotic endocardium is not a feature of ischemic cardiomyopathy in which contrast washes out after 25 mins of the injection. Loose fibrous tissue and interstitial space with very poor vascularity can explain the prolonged persistence of contrast medium.

Regarding pattern of enhancement, 7 patients in RVEMF, all (two) patients in LVEMF had both endocardial and apical obliterative subendocardial enhancement. In BVEMF 4 patients had only endocardial enhancement and 5 patients had both endocardial and apical obliterative subendocardial enhancement (Fig 6 & 7). No patients had myocardial and epicardial enhancement. The extent of enhancement starts with endocardial and as time passes it extends into deep into subendocardium also. The finding was reinforced by analysis of Histopathology specimens of 3 patients who underwent endocardiectomy.

The other areas of delayed hyperenhancement which were identified are RA free wall, LA wall, interatrial septum, left ventricular posterior wall,

posterior papillary muscle of LV. One patient showed enhancement in interventricular septum also (Fig 5C).

The features which differentiate these patients from ischemic cardiomyopathy are apical obliteration, the extent of delayed enhancement (which does not confine to a coronary artery territory) and unusually prolonged persistence of delayed enhancement.

The exceptional RVEMF patient who had no delayed enhancement even in 45 mins post contrast MR images can be explained in two ways. The patient could have had very dense fibrosis with very poor vascular supply, which hampers the flow of contrast into and out of the fibrous tissue. The other possible explanation is that it can be large apical thrombi. The endomyocardial Biopsy done in that patient was reported as fibrous tissue with interspersed muscle fibres.

MRI was repeated in one patient after endocardiectomy. The thickness of delayed enhancement was mildly reduced, the RV volume has increased with improvement in RV systolic function.

Literature regarding MRI in EMF is limited except for isolated case reports. Jordi et al[22] has identified a similar finding of isointense fibrous tissue in cine images, hypointense in first pass images and DE in late contrast images (>10mins). But the persistence of DE even after 45 mins was not noted in this study.

The DE in areas other than apex of ventricle is noted for the first time in our study. The systolic function in EMF is analysed for the first time in our study. Christian et al[23] has identified the decrease in RV/LV length ratio in RVEMF and viceversa. The result is similar to our study.

Salemi et al[24] has the largest study on MRI in EMF patients. They identified that the core of the apical mass usually is early hypoperfused and late hypoenhanced. They also observed that endocardial surface of the mass becomes late enhanced. In that study they could also detect and quantify the fibrous tissue by DE MR images.

Ricardo et al[25] in a case report has identified the improvement in RV volume and decrease in DE after endocardiectomy. But the repeat MRI done post endocardiectomy in our patient has shown the delayed enhancement thickness mildly reduced. But the RV volumes and Ejection fraction has improved. This can be explained by progression of the disease process (repeat MRI was taken 2 yrs after surgery) or it can be due to inadequate endocardiectomy due to surgical limitation.

The Ideal control for EMF will be Idiopathic hyperesinophilic syndrome. The apical obliteration, diastolic dysfunction, AV valve regurgitation, embolic manifestations are well mimicked by Loeffler's syndrome. But the disease is very infrequent in our country.

Limitations

LIMITATIONS

Small sample size which is a inherent limitation for an expensive investigation.

Descriptive study design: no optimal controls can be taken because the morphology of EMF is different from other restrictive cardiomyophathies except hyperesinophilic syndrome. But hyperesinophilic syndrome is very rare in our country.

Follow up magnetic resonance imaging cannot be done in all post surgical patients because of limitations due to prosthetic heart valve

Conclusion

CONCLUSION

- Cardiac MRI is a good non-invasive imaging modality not only helps in confirming in the diagnosis, but also has a role in determining early disease in contra lateral ventricle in endomyocardial fibrosis when compared to echocardiography.
- Cine MRI is useful in assessing RV and LV systolic function in endomyocardial fibrosis.
- LV systolic dysfunction is found in significant number of patients in endomyocardial fibrosis in MRI when compared to echocardiography.
- Velocity Encoded MRI is useful to assess the degree of atrioventricular valve regurgitation in endomyocardial fibrosis.
- DE MRI is useful in confirming the obliterative process at the apex (fibrosis, calcification, thrombus) in endomyocardial fibrosis.
- Endocardial and apical subendocardial obliteration enhancement is the most common pattern involvement observed in endomyocardial fibrosis
- Fibrotic process in endomyocardial fibrosis involves other areas like LV posterior wall, LV posterior papillary muscles, RV free wall, RA wall, LA wall and Interatrial septum.
- Late enhancement pattern is useful in assessing the extent of involvement of ventricle which can aid in Endocardiectomy.

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Proforma

PROFORMA

Name:

Age/Sex:

District/Place:

Symptoms:

NYHA FC:

R heart failure/ L heart failure:

RHYTHM:

ECHO:LV EMF/ RVEMF:

LV/RV systolic function:

LV/RV diastolic function:

Area / Extent of involvement

MR/TR : severity, central / eccentric jet

RA / LA : dilatation , Size

Angiography:

LV EMF: Extent of involvement : (Grade I-III)

Filling defects , outpouchings

Severity of MR (Grade I-IV),

Pulmonary Hypertension

Coexsisting RV EMF and TR

RV EMF: Extent of involvement : (Grade I-III)

Filling defects , outpouchings

Severity of TR(Grade I-IV),

Coexsisting LV EMF and MR

Pericardial effusion

Pulmonary thromboembolism

MRI PROTOCOL

1) **Morphological analysis**: (True FISP sequences)

   a) RV/LV sizes,

   b) Apical obliteration

   c) RVOT involvement

   d) RA/LA dilatation

   e) Thrombus/ calcification

   f) Pericardial thickeneing/effusion/calcification

2) **Cine images** (True FISP)

   a)RWMA of RV/LV

   b) Systolic function of LV/RV (Argus software)

   → thickineing

   → EDV/ ESV/ EF

   c)Involvement of Mitral/Tricuspid valve

   MR/TR→ Severity, eccentric/central jet

   d) Area/Extent of involvement of EMF

3) **PSIR sequences** (DE MR sequences)

   a) Time from contrast injection :Initial / 5mins / 15mins / 25mins /40mins

   b) Extent of involvement → Subendocardial / Sub epicardial / transmural

   c) Approximate Thickness of the endocardium involved

REPORT II

A COMPARATIVE STUDY OF BALLOON MITRAL VALVOTOMY AND CLOSED MITRAL VALVOTOMY IN JUVENILE MITRAL STENOSIS

Introduction

INTRODUCTION

Mitral stenosis is rarely seen in children and adolescents except in developing countries where rheumatic fever is still endemic.[1–3] Until the mid-1980s, surgical closed or open valvotomy was the only available treatment. However, mitral valve surgery in children and adolescents, in addition to its acute risks, has the added disadvantage that because the initial surgery is performed at an early age, reintervention may be necessary 10 to 15 years later.

In adults, balloon mitral commissurotomy yielded better results than those obtained after closed commissurotomy 4. But there are no studies comparing these procedures in juvenile mitral stenosis.

Review of Literature

REVIEW OF LITERATURE

Juvenile mitral stenosis is predominantly seen in developing countries where rheumatic fever is still very common[16,17]. Mitral stenosis (MS) represents a different pattern of rheumatic fever characterised by a "smouldering" sub-clinical course with the majority of the lesions being diagnosed in older patients (fifth to sixth decade) than mitral regurgitation or aortic regurgitation of rheumatic origin[18,19].

However, in developing countries, MS progresses more rapidly, presumably due to either a more severe rheumatic injury or repeated episodes of carditis due to streptococcal infections, resulting in severe symptomatic mitral stenosis in the early to mid-teenage and early twenties[20]. MS in the under 20 year olds, indicates much more severe rheumatic activity and they exhibit early severe pulmonary hypertension and eventually right ventricular failure and they require early intervention.

Closed mitral commissurotomy had been the most common form of intervention before the advent of BMV. First successful CMV was done in 1923 by Cutler and Levine[21]. Three decades later it was again brought into surgical practice by Harken et al[22].

The largest series of CMV to date is reported by Stanley John et al of CMC, Vellore with a number of 3724 patients form 1956-1980. Of this 25% were ≤ 20 years of age[23]. Probably this series is the largest one for CMV in juvenile MS also. In this series over 40% of juvenile MS had severe malnutrition (<70% based on weight for age). They have noted that patients with juvenile MS represent a unique condition with rapid development of severe pulmonary hypertension and congestive cardiac failure[23]. Restenosis rate in this study varied from 4.2 to 11.4 per 1000 patients per year between 5-15 yr of follow-up. Re CMV for restenosis was accomplished in 130 Patients and excellent symptomatic improvement was evident in 86% of long-term survivors at the end of 15 years. Nevertheless this study was done before the advent of echocardiography in routine cardiac practice and so the follow up is basically clinical. Similarly the data regarding restenosis and re CMV was described for overall patient population, subgroup analysis regarding juvenile mitral stenosis was lacking[23].

Similarly another series from CMC Vellore in 1963 reviewed CMV in juvenile mitral stenosis patients specifically (126 patients)[24]. The description of baseline characteristics of these patients can offer a good description of natural history of Juvenile mitral stenosis. 61% of patients had a total duration of <3 yrs from the initial symptoms including rheumatic fever to time of operation. This was quiet different from western population where the latent

period was 19 yrs from initial attack of acute rheumatic fever to onset of symptoms. 75% patients were in Grade III/IV dyspnea (Wood's grading). 33% had CHF and 79% patients had moderate to severe PAH clinically. AF was seen in only 2% patients and incidence of embolism was low. Mitral valve calcification was seen in 6%. The MVA was <1.0cm2 at operation in 85% of patients. The very interesting fact is that only one patient developed restenosis at 1 to 7years follow up of 70% of patients in this study. This is one of the earliest studies to reveal that young patients do not have higher incidence of restenosis due to active rheumatism. However the limitation is that it is a clinical follow-up study[24].

Regarding recent studies on CMV, Farhart et al,[25] randomized equal number of patients to CMV, OMV and BMV group and found that CMV patients had higher rate of residual MS, restenosis and reintervention when compared to BMV and OMV group. Follow up in this study was both clinical and echocardiographic. But the number of juvenile mitral stenosis in this study was small[25]. Chadha et al operated 136 patients of Juvenile MS and found that CMV achieved satisfying results in terms of valve area achieved and mitral gradient reduction[25-1].

Regarding BMV in Juvenile MS, previous reports have examined small number of patients[26–37] except for Sinha et al[38] who reported a series of 193

patients. Follow-up is often limited to weeks[27,28,33] or months[32,34–37] except for Zaki et al[39] who reported five years follow-up results.

Probably the largest series with longest follow up for BMV in juvenile MS was studied by Gamra et al[40]. The juvenile group was compared to adult population in this study. Juvenile MS patients had less incidence of AF, lesser MV echo score, similar baseline MVA by 2D echo and larger MVA after BMV when compared to adults. Also the younger patients had a higher procedural success (100%). Follow up MVA was higher in younger patients. At 10 years, freedom from restenosis and event free survival was not significantly different from adult patients. It is better to classify the results into immediate and long term results for a detailed review.

Immediate results

Zaki et al[39] reported more than double the MVA after BMV and reduction in peak transmitral gradient to less than one third. The mitral valve score was low in these patients. Similarly Srivatsava et al[34] noted a similar acute result in their study. They also noted no patients with iatrogenic ASD and low incidence of significant mitral regurgitation in their study. Gamra et al[40] found that young patients had significantly larger mitral valve area and lesser complications in comparison to adults. Similarly Bahl et al[33] also found similar immediate results.

In all these studies the good immediate results, larger mitral valve area and lesser complications were attributed to more favourable anatomy in the young as demonstrated by a lower echocardiographic score. Mitral stenosis in young population had significantly smaller left atrial dimension than adults. Furthermore, balloon placement is considerably easier across a pliable than a calcified valve[40].

At last, Gamra et al[40] attempted to find factors other than echo score for better immediate results in Young patients. They analysed the variables between patients with echo score ≤ 8 in both adult and Young population. The analysis revealed similar results to those obtained in whole population. This may suggest a role for factors other than low echo score such as left atrial size.

Long-term results

The long term results of BMV in young can be reviewed under 3 headings namely Restenosis, Reintervention and Event free survival. Among the follow up studies, Zaki et al[39] and Gamra et al[40] has the longest follow up records (5 years and 10 years respectively). So references will be mostly based on these two studies.

Restenosis

Zaki et al[39] noted a restenosis rate of 6.5% and there was no significant change of MVA or the pressure gradient during the follow-up compared with

immediately after BMV. The remaining patients in their study showed persistent improvement in their NYHA FC $\leq$ II. Gamra et al[40] observed a restenosis rate of 12.7% and it was lower but not statistically significant when compared to adult population. Additionally Zaki et al[39] noted that the LA diameter decreased on follow up significantly.

Reintervention

Zaki et al[39] observed no patient going for repeat BMV or MVR inspite of 6.5% restenosis. But sample size in this population is very small (40 patients) in spite of long followup. But Gamra et al[40] observed 14 out of 14 patients sent for reintervention (13 patients sent for re BMV and 1 patient had MVR). The adult population compared in this study had similar restenosis rate but reintervention was required in only 60% of patients. The higher rate of reintervention in the young group was explained by the fact that restenosis is more often symptomatic for patients engaged in physical activity. The mean years of reintervention during follow up was 5-7 years in this study.

Most of the patients with restenosis in Gamra et al[40] were sent for BMV because most of these patients had pliable mitral valve apparatus suitable for repeat procedure. The adult population which was compared had 25% of patients sent for MVR for restenosis because of calcified valves.

Event-free survival

Similarly Zaki et al[39] observed a event free survival of 91%. There were no deaths and reintervention. Few patients had restenosis with worsening of functional class in this study. Gamra et al[40] observed a event free survival of 90% and 74% at 5 and 10 years when compared to 83% and 69% in adult population. But this was not statistically significant. There were no deaths and the only clinical events were related to reintervention procedures for restenosis and/or significant mitral regurgitation in this study.

Many short term and few long term studies have shown that BMV in $\leq$ 20 yrs is effective, safe and provides better immediate results than in adults particularly with regard to acute complications. Mitral valve area post BMV was larger than in adults. Although restenosis rate was similar, the number of reinterventions for restenosis was higher in young patients. The event free survival also not significantly different from adult population.

But there is definite paucity of data regarding the comparison of BMV and CMV in juvenile mitral stenosis

Aims of the Study

AIMS OF THE STUDY

1. To compare the immediate and long term outcomes between BMV and CMV in juvenile mitral stenosis.

2. To compare the event free survival between CMV and BMV in juvenile mitral stenosis.

Materials and Methods

MATERIALS AND METHODS

Design: Retrospective study

INCLUSION CRITERIA:

BMV group: All patients with Mitral stenosis who are ≤ 20 years, who underwent balloon mitral valvotomy from the year 1995 to 2005 were taken for study

CMV group: All patients with mitral stenosis from 1984 to 2000 who were ≤ 20 years who underwent closed mitral valvotomy were taken for study

In each group baseline variables like age, sex, year of procedure were noted.

Socioeconomic status of the patient was assessed by category system which is adopted in our institute (A, B1, B, C and D categories in ascending order of socioeconomic class).

Echocardiographic Evaluation

Transthoracic M-mode, two-dimensional, pulsed, color, and continuous-wave Doppler echocardiographic details were noted before the procedure, immediately after the procedure, at 6-months, 1 year and last follow-up. The echocardiographic score described by Wilkins et al[5] was used

to assess baseline anatomic features of the mitral valve: a score from 0 (normal) to 4 (severely deformed) was assigned to valvular mobility, thickening and calcification and subvalvular thickening. No echocardiographic score was done in CMV group before 1990 as the Wilkins score was not used. 2D echo derived mitral valve area (MVA) was determined through planimetry of the mitral orifice in a two-dimensional short-axis view early in diastole in all patients before and after any commissurotomy. The transmitral pressure half-time (PHT) method was used in all patients at baseline and after the procedure. The mean of 2D and PHT MVA was taken for analysis.

BMV PROCEDURE

The Inoue Balloon catheter is a 12F polyvinylchloride tube with a coaxial lumina. The balloon section is stiffened and slenderized when stretched by the insertion of a metal tube. The balloon size is pressure dependent and consists of 3 portions with slightly different compliance. As pressure is gradually added, the distal portion of the balloon inflates first, followed by the proximal portion. The unique part of the Inoue balloon is its middle waist portion that has the least pressure compliance, with which fixation of the balloon catheter is facilitated and the degenerated fused commissure(s) can be dilated substantially. The ACCURA balloon is similar to Inoue balloon except for a side port used for deflation of the balloon which is absent in ACCURA balloon.

For selecting the appropriate balloon size, some researchers have advocated methods to select balloon size with the patient's height[6] or body surface area[7] as a reference. A simple equation to obtain the reference size (height [cm]/10+10) has been proposed[8].

The procedure was always performed via a femoral approach with a 6F sheath in the vein and a 5F sheath in the artery with the patient under intubated anesthesia. Initially right heart catheterization is performed. Pressures in Right atrium, Right Ventricle, Pulmonary artery were taken. Then a pig tail catheter was introduced into LV and LVed was measured and pull back gradient between LV and Aorta were taken. Then Pig tail catheter was kept in noncoronary sinus of Aortic root and a short hand angiogram is taken in LAO 60 view to delineate to posterior aortic wall.

Transseptal catheterization is performed via a standard Brockenbrough procedure using anteroposterior views. While slowly withdrawing the Brockenbrough catheter from superior vena cava into the interatrial septum, the operator advances the Brockenbrough needle beyond the interatrial septum when the tip of the catheter falls into the fossa ovalis. After advancing the Brockenbrough needle, a coiled-tip (pig tail) guidewire was placed into the left atrium through the Brockenbrough sheath. Then, 100U/Kg of heparin was administered to reduce the risk of a thromboembolic event during the manipulation of catheters and wires in the left atrium.

In the next step, the Inoue/Accura balloon catheter was advanced over the coiled-tip wire. A system for accomplishing PBMV consists of the following devices[9]: Balloon catheter, metallic stiffening cannula (18 gauge, 80 cm in length) for stretching and stiffening the Inoue balloon catheter, guidewire for PBMV (0.028 inches in diameter, 180 cm in length), dilator (14F polyethylene tube with a thinner tip 70 cm in length) for dilating the puncture site of the femoral vein and atrial septum, and a stylet (wire with J-shaped tip, 0.038 inches in diameter, 80 cm in length) for directing the balloon toward the mitral orifice.

Once the balloon catheter has crossed the interatrial septum, the catheter should be placed in the left atrium so that the catheter forms a loop with the tip facing toward the mitral valve orifice. The tip of the balloon was inflated with 1 to 2 mL of contrast media, allowing blood flow to direct the balloon tip into the left ventricle. If advancement of the balloon proves difficult, the stylet was inserted in the balloon catheter, and the balloon catheter with stylet are moved together toward the mitral valve orifice. With the right anterior oblique view, which helps identify the proper line between the base and the apex, the deflated balloon catheter was advanced until the tip of the catheter has crossed the mitral valve into the left ventricle.

Once the balloon catheter has been inserted into the left ventricle, the distal portion of the balloon is inflated with contrast media using a specially

graduated syringe. The catheter was then pulled until resistance was felt. During inflation of the balloon, the appearance of a deformed distal balloon may suggest entrapment in the subvalvular apparatus. In this situation, further inflation should not be performed and the balloon should be repositioned to a location that is more proximal to the mitral orifice to avoid trauma to the subvalvular apparatus (Fig1).

The balloon has a much less compliant portion in its waist that assists in the secure dilatation of the mitral valve orifice. Figure1 shows the typical step-by-step appearance of the balloon catheter. Before placing the balloon catheter, we routinely select the balloon size by which valve orifice was finally dilated, as previously described. After each dilatation, the operator should obtain the left atrial pressure through the second port of the catheter and the left ventricular pressure through the pig-tail catheter simultaneously.

If the pressure gradient between the left atrial pressure and the simultaneously obtained left ventricular pressure does not decrease, the balloon size was increased in 1-mm increments until the pressure gradient decreases or substantial worsening of mitral regurgitation occurs. In addition, 2-dimensional echocardiographic observations are performed after each dilatation.

To assess mitral valve orifice area after each dilatation, planimetry of the valve orifice with 2-dimensional echocardiography was adopted rather than the pressure half-time method on continuous Doppler waveform, because pressure half-time– derived orifice area might be inaccurate in this acute setting[10]. If 1 of the 3 following events was encountered - decrease in the pressure gradient between the left atrium and the left ventricle, occurrence of significant mitral regurgitation and substantial splitting of the commissure, further dilatation was not performed unless critical complications might otherwise ensue[11].

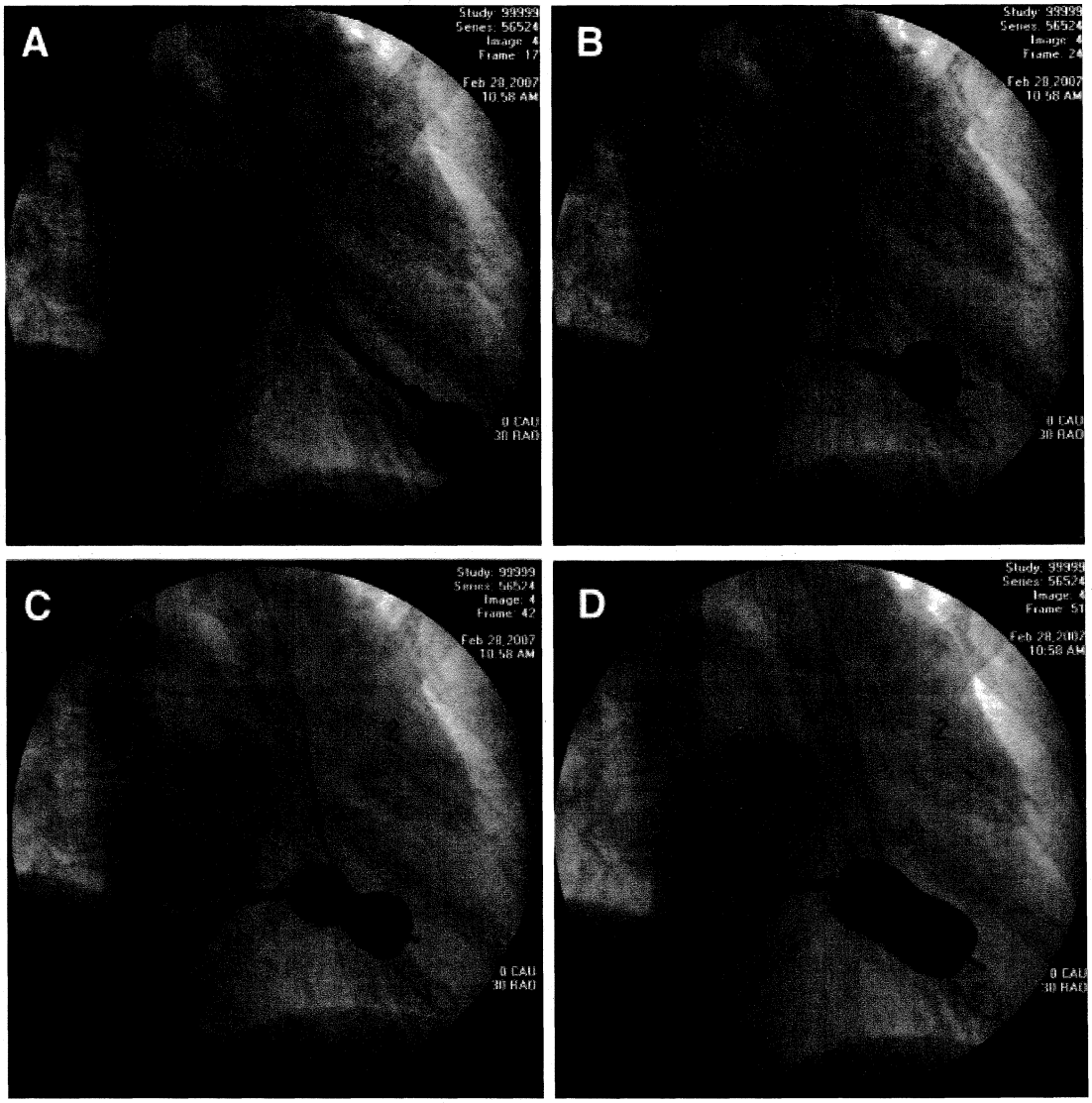


Figure 1 . Manipulation of the balloon catheter. A, Advanced deep into the left ventricle. B, Pulled with the distal portion inflated. C, Inflation of the proximal portion followed by inflation of the middle waist portion of the balloon. D, Properly inflated middle portion of the balloon securely dilates commissural.

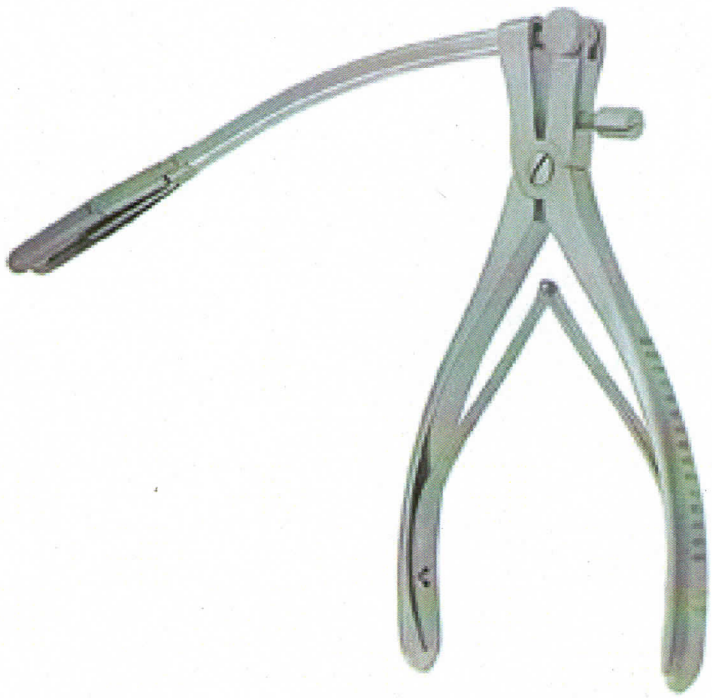
Reference: Nobuyoshi et al 2009, Circulation

CMV PROCEDURE

A left anterolateral thoracotomy approach was used for all patients. The chest was entered through the bed of the fifth rib. Adhesions were separated by sharp dissection to expose the body of the left atrium, adjacent left superior pulmonary vein, and left ventricular apex. Double purse-string sutures of 2-0 Prolene or silk were placed over the body of left atrium, extending onto the entry of left superior pulmonary vein, for introduction of the surgeon's right index finger. Another suture with 2-0 silk was placed at the left ventricular apex adjacent to the previous ventriculotomy site for introduction of a Tubbs dilator (Fig 2). The orifice of the mitral valve was dilated from 2.25 cm dilator to 3.5 cm in diameter[12].

Dilatation was done serially until full opening was achieved or until the surgeon sensed a regurgitant jet[13]. After the procedure, the atriotomy and ventriculotomy sutures were closed. LA appendage amputation was done in few patients. Reexploration was done if large pericardial effusion or tamponade or hemothorax (with large intercostal drainage) and the atriotomy and ventriculotomy sites were examined and resutured.

Fig 2 TUBBS DILATOR



After any procedure, MR was graded on a scale of 1 to 4 with the use of color Doppler echocardiography according to the jet extension in the left atrium. After BMV, color Doppler echocardiography was used to screen left-to-right atrial shunts. Other details like LA diameter in mm, MS gradient (Peak/Mean) in mmHg, status of medial and lateral commissure of mitral valve (fused, fully split, partly split), Aortic stenosis (Peak/Mean) inmmHg, Grade of Aortic regurgitation, Organic tricuspid valve disease (present/absent) and Right ventricular systolic pressure in mmHg were noted.

The type of device (balloon / dilator) used, maximum size of the device used, severity of mitral regurgitation after the procedure, nature of MR (commissural/noncommissural), Acute complications (Vascular access complications, stroke, urgent MVR, infective endocarditis, repeat thracotomy for tamponade and hemothorax) are assessed. The duration of hospital stay in each group was noted.

Additionally in BMV group hemodynamic data pre and Post BMV including Right atrial pressures (a, v, mean), Pulmonary artery pressure (systolic, diastolic, mean), Left atrial pressures (a, v, mean), Left ventricular end diastolic pressures (LVED), Aortic pressure (Systolic, diastolic, mean), Cardiac output in l/min/m2 and Mitral valve area (by Gorlin and Gorlin formula) were noted.

Success of the procedure was defined as final MVA >1.5cm2 and >50% increase in MVA without moderate to severe MR. Restenosis is defined as a valve area < 1.5 cm2 or a >50% loss of the initial gain in valve area achieved. (14). Restenosis in Juvenile MS is defined as a mitral valve area index <0.9 cm2/m2 by 2D echo. The threshold of 0.9 derives from the usual threshold of valve area in adults of 1.5 cm2 divided by the mean body surface area among our adult population which was of 1.7 m2[15].

A clinical event was defined as: (1) death from any cause, (2) mitral valve replacement, (3) repeat balloon mitral commissurotomy, or (4) NYHA FC III or IV.

Statistical analysis

Mean and standard deviation are used to represent continuous variables. To compare the significance of difference between noncontinuous variables Fisher exact test and Chi square tests are used. To compare significance of difference between continuous variables Student t test was used. Mann Whitney U test was used to compare variables with different grades.

Observations

OBSERVATIONS

Preprocedure Variables

Baseline characteristics like age, male: female ratio, socioeconomic status were similar between two groups. The echo parameters like LA diameter, 2D MVA, mean Wilkin's score were similar between two groups.

Among the baseline variables, BMV group had higher mean transmitral gradient. Also this group had more number of patients with higher grade of MR and higher RVSP at baseline. The CMV group had more severe subvalvular pathology. They also had more patients with completely fused medial and lateral commissures (table 1).

Immediate Post Procedure

Procedural success was attained in 93.6% of patients in BMV group and 91% in CMV group with no statistically significant difference. There is no significant difference between the mean MVA achieved, reduction in transmitral gradient. The mean number of patients with fully split medial and lateral commissure was also similar in both the groups. The CMV group had higher grade of MR and higher RVSP post procedure (table 2).

Table 1: Comparison pre procedure variables

	BMV	CMV	t	p
LA diameter	41.6 ± 6.1	41.9 ± 6.7	0.4	0.691
MVA_2D	0.78 ± 0.17	0.83 ± 0.20	1.83	0.310
MVA_PHT	0.81 ± 0.17	0.87 ± 0.19	2.19*	0.029
MS_Peak Gradient	29.9 ± 8.7	26.4 ± 8	3.04**	0.003
MS_Mean Gradient	18.6 ± 6.2	16.3 ± 6.2	1.71	0.410
Wilkins Score	7.7 ± 1.1	7.2 ± 1.2	1.66	0.440
Mobility	2 ± 0.5	1.9 ± 0.4	0.79	0.429
Calcification	0.1 ± 0.4	0.1 ± 0.4	0.71	0.476
Thickening	2 ± 0.3	2.1 ± 0.4	0.66	0.512
SVP	2.8 ± 0.6	3.1 ± 0.6	4.17**	0.000
MC	0.1 ± 0.3	0 ± 0.1	2.52*	0.012
LC	0.1 ± 0.4	0 ± 0.2	3.11**	0.002
MR	0.2 ± 0.7	0.4 ± 0.5	2.8**	0.005
AR	0.3 ± 0.8	0.1 ± 0.5	1.97	0.050
AS_Peak Gradient	0.5 ± 3.6	0 ± 0	1.41	0.160
AS_Mean Gradient	0.2 ± 1.7	0 ± 0	1.27	0.206
RVSP	59.1 ± 25.5	53 ± 26.3	2.06*	0.040

** : significant at 0.01 level * : significant at 0.05 level

Table 2 Comparison of variables at immediate post procedure

	BMV	CMV	t	p
LA diameter	39.3 ± 5.6	39.1 ± 4.2	0.44	0.663
MVA_2D	1.6 ± 0.3	1.5 ± 0.3	1.71	0.087
MVA_PHT	1.6 ± 0.3	1.5 ± 0.3	0.98	0.327
MS_Peak Gradient	13.8 ± 5.3	13.5 ± 4	0.39	0.695
MS_Mean Gradient	6.5 ± 3.5	6.5 ± 2.8	0.03	0.980
MC	1.3 ± 0.8	1.3 ± 0.8	0.46	0.647
LC	1.3 ± 0.8	1.4 ± 0.8	1.1	0.272
MR	1.5 ± 1.1	1.9 ± 0.5	3.64**	0.000
AR	0.4 ± 0.9	0.3 ± 0.7	1.66	0.098
AS_Peak Gradient	0.5 ± 4	0 ± 0	1.26	0.210
AS_Mean Gradient	0.2 ± 1.9	0 ± 0	0.92	0.356
RVSP	32.9 ± 13.7	40.3 ± 17.9	3.88**	0.000

** : significant at 0.01 level * : significant at 0.05 level

Pre and post hemodynamic data in BMV is given in table below. This data is not compared with CMV because it was not available for CMV.

	PRE	POST
RA_M	7 ± 4	6.4 ± 4
PA_S	57.4 ± 23.6	40.8 ± 15.9
PA_D	27.7 ± 12.5	17.7 ± 7.5
PA_M	38.1 ± 15.8	25.7 ± 10.3
LA_A	30.9 ± 7.9	20.4 ± 6.3
LA_V	29.8 ± 9.7	19.6 ± 7.9
LA_M	23.9 ± 7	14.8 ± 5.9
LV	9.5 ± 3.5	12.7 ± 4.6
TMG	16.7 ± 6.5	6.28 ± 2.67
MVA	0.78 ± 0.25	1.51 ± 0.4
CO	3.79 ± 0.96	4.1 ± 1.03

CMV group when compared to BMV group had higher rate of acute complications including 2 deaths and 2 strokes. The mean number of patients with Commissural MR and AML tear were similar in both the groups (table 3 & 4).

Table 3: ACUTE COMPLICATIONS IN BMV

	n=252	
Balloon Used	Accura	142 (57.7)
	Inoue	101 (41.1)
	Inoue & Accura	1 (0.4)
Acute_Complications	AML tear	6 (2.32)
	CFA occlusion	2 (0.8)
	Moderate-Severe Commisural MR	14 (5.5)
	Distal pulse absent	2 (0.8)
	PML TEAR	2 (0.8)

Table 4: Acute complications in CMV patients

Device Used	Tubbs dilator (n=108)	
Acute Complications	Post OP AF	1(0.9)
	Hemothorax	2(1.83)
	Mod-severe Commissural MR	6 (5.45)
	Diaphragmatic palsy	1(0.9)
	Rheumatic activity	1(0.9)
	AML TEAR	2(1.83)
	Death	2(1.83)
	Transient cardiac arrest	1(0.9)
	Stroke	2(1.83)

Follow up after 1 year

The mean LA diameter was lower in BMV group. Higher grade of AR was noted in CMV group. Otherwise variables were not significantly different between two groups (table 5).

Table 5: Comparison of variables at 1 year post procedure

	BMV	CMV	t	p
LA diameter	37.3 ± 6.4	40.5 ± 6.8	2.38*	0.019
MVA_2D	1.4 ± 0.3	1.5 ± 0.3	0.61	0.542
MVA_PHT	1.5 ± 0.4	1.5 ± 0.4	0.7	0.483
MS_Peak Gradient	17.1 ± 7.5	14.5 ± 7.4	1.9	0.061
MS_Mean Gradient	8.7 ± 5	7.7 ± 4.9	1.1	0.274
MR	1.2 ± 1.2	1.4 ± 0.8	1.8	0.073
AR	0.3 ± 0.8	1.8 ± 0.7	11.8**	0.000
AS_Peak Gradient	0 ± 0.1	0 ± 0	--	--
RVSP	42.7 ± 15.7	40.5 ± 12	--	--

** : significant at 0.01 level * : significant at 0.05 level

Last follow up

The mean duration of clinical follow up in BMV group is 6+/-13.1 years and that in CMV group was 12+/-4.2 years. The CMV group had higher LA diameter and lower 2D/PHT MVA on follow up. The severity of AR was also higher in CMV group. The MR severity was higher in CMV group when compared to BMV group but the difference was not statistically significant (table 6).

Table 6: Comparison of variables at last follow up

	BMV(n=189)	CMV(n=99)	t	p
LA diameter	40 ± 5.7	43.5 ± 8.8	4.05**	0.000
MVA_2D	1.44 ± 0.4	1.26 ± 0.4	3.76**	0.000
MVA_PHT	1.51 ± 0.41	1.28 ± 0.44	4.22**	0.000
MS_Peak Gradient	16.6 ± 10.7	18.7 ± 10.3	1.55	0.123
MS_Mean Gradient	8.9 ± 7.1	9.9 ± 6.5	1.2	0.232
MR	1.4 ± 2.26	2.09 ± 3.61	1.88	0.062
AR	0.82 ± 1.11	1.47 ± 0.95	3.07**	0.002
AS_Peak Gradient	2.57 ± 9.38	2.03 ± 12.05	0.36	0.721
AS_Mean Gradient	0.91 ± 4.49	0.86 ± 5.58	0.08	0.938
RVSP	43.7 ± 13.3	46.1 ± 19	1.07	0.285

** : significant at 0.01 level * : significant at 0.05 level

Restenosis

The restenosis rate in BMV was 15.2% and 18% in CMV group. Inspite of higher restenosis rate in CMV group, the difference is not statistically significant. This restenosis rate was calculated after adjusting for the longer follow up duration in CMV group by logistic regression.

Reintervention

The mean duration in year to reintervention in BMV group was 5.6+/-2.1 years and that for CMV group was 10.3+/-4.6 years (Table 7).

Table 7: Comparison of reintervention in BMV and CMV

Restenosis (%)	15.2%	18%	p 0.13**
Nature of reintervention n (%)	31 (14.8)	37 (37)	p<0.000**
BMV(n)	29	23	
CMV(n)	0	7	
MVR(n)	2	6	
DVR(n)	0	1	
Mean duration to reintervention (yrs)	5.6 ± 2.1	10.3 ± 4.6	p<0.000**

** significant at 0.01 level

Discussion

DISCUSSION

Previous reports of balloon mitral valvotomy in young populations examined small number of patients[26,27] except for Sinha et al.[38] who reported a series of 193 patients. Follow-up is often limited to weeks[27,28,33] or months[32,3437] except for Zaki et al.[39] who reported five years follow-up results. Longest follow up of 10 years was obtained with Gamra et al (2003). Our study also had a fairly long follow up (6 ± 13.1yrs).

Regarding CMV group the median follow up period was 12 ± 4.2years. In 1961, Borman et al (Israel) followed up 12 patients for 12 years. Cherian et al (1963) reported to follow up 70% of their patients for 1-7 years. But as previously mentioned those studies had only clinical follow up. There are no recent long term follow up studies on CMV in juvenile MS. We have followed up 92% of patients which probably represents a large follow up data for CMV in juvenile MS.

Immediate results

Multiple studies have proved that the immediate results of BMV in young were better than in adults with a significant larger mitral valve area and fewer complications with no statistically significant difference between most of hemodynamic variables.[26-39] Although we have not compared juvenile MS

with adult MS, the hemodynamic response to BMV is dramatic. The study shows a significant fall in PA pressures, LA mean pressures (>2/3rd) and transmitral gradient (TMG) from 16.7 ± 6.5 to 6.28 ± 2.67 and doubling of MVA form 0.78 ± 0.25 to 1.51 ± 0.4 cm^2 . The procedural success was obtained in 93.6% of patients. The procedural success obtained in CMV group was 91%. This is similar to Farhart et al[41], but the number of juvenile mitral stenosis patients in that study was small.

Juvenile mitral stenosis has a better immediate response to intervention because of the favourable anatomy in the young as demonstrated by a lower echocardiographic score. Furthermore, balloon placement is considerably easier across a pliable than a calcified valve. All of these factors make the procedure easier, smoother and shorter in young patients.

Our results are comparable to other reported by others[31,32,38,39]. The immediate results in CMV patients was assessed only by echocardiography as hemodynamic study results were not available in CMV patients. The mean 2D MVA in CMV patients increased from 0.8 ± 0.2 to 1.5 ± 0.3cm2. There is no statistical difference between final valve area achieved in both the groups.

Turi et al[42] found no difference in MVA (catheterization) achieved after BMV and CMV. But there was no comparison of 2D MVA in that study and the patients aged below 20 years was also very few. Ben Farhart et al[41] found

a larger 2D MVA attained after BMV than CMV. The reasons they propose was that the blades of the Tubb's dilators always open in the same plane, whereas commissures are not; pressure is applied by the blades at two diametrically opposite points of the mitral orifice, whereas it is applied on the overall mitral orifice by the inflated balloons so were more likely to split commissures and to a greater extent and whenever immediate hemodynamic measurements taken during BMV indicated unsatisfactory relief of mitral obstruction, it is easy to redilate with larger balloons[41]. But as already noted juvenile MS was very less in this study. Also in our study patients had favourable Wilkins score with a pliable mitral valve and so the method of splitting of the commissures probably did not produce difference in final valve area achieved.

Regarding the acute complications, common complications like AML tear and moderate- severe commissural MR was not different statistically. But CMV patients had 2 mortalities. Of which one patient was taken on emergency, and another patient had severe comorbidites at the baseline (severe Biventricular dysfunction with CHF). Also 2 patients in CMV population had stroke. This is due to the fact that when CMV was started initially, transesophageal echocardiography was not available to rule out LA clot. Probably the event may be related to occult LA clot.

More number of patients had MR in CMV group (significant). This could be due to higher degree of MR seen in baseline echocardiography in CMV group. Also it can be due to higher degree of Subvalvular pathology noted in baseline characteristics in CMV group (significant).

Also noted in our study is that the reduction in RVSP in immediate post procedure echo was less in CMV (significant). First it can be due to higher degree of MR in CMV post procedure. Another cause could be due to lesser MVA achieved compared to BMV group.

Long-term results

Restenosis and Reintervention

Restenosis rate was lower in BMV when compared to CMV 15.2% Vs 18%. The reintervention rate was also higher in CMV group (37% vs 14.8%). BMV was done in 29 out of 31 patients who had symptomatic restenosis because all of them had a pliable mitral valve apparatus suitable for a repeat procedure. The remaining 2 patients had severe SVP and significant MR and was sent for MV replacement. In CMV group 7 patients underwent re CMV and 23 patients underwent BMV because of symptomatic restenosis. 6 patients were sent for MVR due to significant MR and 1 patient underwent DVR due to associated significant AR (table7).

The higher degree of restenosis in CMV group can be partly explained by higher subvalvular pathology to start with in CMV group. Another possibility is that the duration of follow up is much longer than BMV group which can explain the progression of the disease by natural history itself rather than modification by the procedure. The follow up duration between BMV and CMV were matched by logistic regression during statistical analysis.

The higher number of patients sent for MVR in CMV group can be explained by higher grade of MR in CMV group in immediate post procedure and last follow up. Similarly natural history of RHD could explain the higher number of patients with AR in CMV group who did not have significant AR to start with before the procedure.

Event-free survival

In our study event free survival at 1, 3 and 5 years are 89.7%, 87.3% and 82.9% in BMV group and 97.2%, 93.6% 87.2% in CMV group respectively. The difference is statistically significant. The difference is statistically significant ($P<0.05$). In spite higher number of reinterventions the event free survival is favourable for CMV because the mean duration of reintervention after CMV is longer than BMV (5.6 ± 2.1 Vs 10.3 ± 4.6 years). In the event free survival table the survival for CMV started declining from 11 yrs onwards (table 8). In previous studies event free survival was 90% and 74

% at 5 and 10 years respectively[40]. Zaki et al also found an event-free survival of 91% at 5 years in juvenile MS. Our results are also similar.

Table 8: Distribution of event free survival

Clinical follow up	BMV		CMV	
	Count	Percent	Count	Percent
1 yr	226	89.7	106	97.2
3 yr	220	87.3	102	93.6
5 yr	209	82.9	95	87.2
7 yr	197	78.2	85	78.0
9 yr	187	74.2	73	67.0
11 yr	180	71.4	63	57.8
13 yr	171	67.9	53	48.6
15 yr	164	65.1	51	46.8
17 yr	-	-	50	45.9
19 yr	-	-	49	45.0
21 yr	-	-	41	37.6
23 yr	-	-	29	26.6
25 yr	-	-	27	24.8
29 yr	-	-	26	23.9

Limitations

LIMITATIONS

This is a retrospective study.

The procedures which are compared were done at two different periods (investigations like echocardiography was not commonly used in cardiological practice when CMV was started).

The duration of follow up in CMV is very long when compared to BMV. Inspite of control used to adjust for the difference between the two groups, the statistical analysis is limited to predict the results.

Conclusion

CONCLUSION

- In juvenile mitral stenosis, balloon mitral valvotomy is effective, safe and provides similar immediate results as closed mitral valvotomy.
- Balloon mitral valvotomy produce less mitral regurgitation and earlier reduction in pulmonary arterial hypertension than closed mitral valvotomy.
- Closed mitral valvotomy has higher rate of acute complications.
- Restenosis rate was similar in closed mitral valvotomy and balloon mitral valvotomy.
- Reintervention rate was higher in patients who underwent closed mitral valvotomy.
- Event free survival at 5 years was better in patients who underwent closed mitral valvotomy inspite of higher reintervention rate because the CMV group had more number of reinterventions from 5 years onwards.

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Proforma

A COMPARATIVE STUDY ON BMV AND CMV IN JUVENIL MITRAL STENOSIS

Name / Age / Sex/ Cat: Hos No:

CMV/BMV Date: Re BMV/CMV Date:

Duration of follow up: Ht / Wt / BSA:

Parameters	Pre BMV	Post BMV	6 Months	1 Year	Last ( )
CATH Data					
PAP					
LA					
LV					
TMG					
MVA					
CO					
ECHO data					
LA dia					
MVA (2D)					
MVA(PHT)					
MS Grad					
Wilkins					
Mobility					
Calcification					
Thickening					
SVP					
MC					
LC					
MR(0-4)					
AR(0-4)					
AS Grade					
OTVD					
RVSP					
Clin & lab					
FC					
Rhythm					
ESR					
TC / ASO					
DC/ADNB					
CRP					

Dilator /Balloon Used :

Size :

No. OF dilatations :

MR Severity :

Acute complications:

Length of Hosp Stay: