SREE CHITRA TIRUNAL INSTITUTE FOR
MEDICAL SCIENCES AND TECHNOLOGY
THIRUVANANTHAPURAM

DEPARTMENT OF CARDIOLOGY

IMMEDIATE AND LONG TERM OUTCOMES OF BALLOON MITRAL VALVOTOMY IN JUVENILE MITRAL STENOSIS IN COMPARISION WITH ADULT MITRAL STENOSIS

A THESIS SUBMITTED FOR THE DEGREE OF

DM CARDIOLGY

DR. SHRUSTHI WALAD

AUGUST 2020

DECLARATION

I, Dr. Shrusthi Walad, hereby declare that the project in this book, titled "Immediate and long term outcomes of balloon mitral valvotomy in juvenile mitral stenosis in comparison with adult mitral stenosis " was undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

Thiruvananthapuram

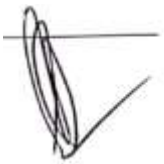
Date
31/8/2020

Dr. Shrusthi Walad

DM Trainee

CERTIFICATE

I hereby certify that the work in this dissertation titled “Immediate and long term outcomes of balloon mitral valvotomy in juvenile mitral stenosis in comparison with adult mitral stenosis” is a certified record of original research work undertaken by Dr. Shrusthi Walad in the Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology in partial fulfilment of requirement for the purpose of award of D.M. Cardiology degree.



Dr. Krishnamoorthy K M

Professor and Head

Dept of Cardiology

Sree Chitra Tirunal Institute for Medical Science and Technology,

Trivandrum-695011

CERTIFICATE

I hereby certify that the work in this dissertation titled " Immediate and long term outcomes of balloon mitral valvotomy in juvenile mitral stenosis in comparison with adult mitral stenosis" is a certified record of original research work undertaken by Dr. Shrusthi Walad in the Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology in partial fulfilment of requirement for the purpose of award of D.M. Cardiology degree under my guidance and supervision.

Guide:

Dr. Harikrishnan S

Professor

Dept of Cardiology

Sree Chitra Tirunal Institute for Medical Science and Technology

Trivandrum-695011

TITLE

"IMMEDIATE AND LONG TERM OUTCOMES OF BALLOON MITRAL VALVOTOMY IN JUVENILE MITRAL STENOSIS IN COMPARISON WITH ADULT MITRAL STENOSIS"

Primary Investigator

Dr. Shrusthi Walad
Senior Resident, Department of Cardiology, SCTIMST

Guide

Dr. Harikrishnan S, MD, DM
Professor, Dept of Cardiology,
Sree Chitra Tirunal Institute for Medical Science and Technology, Trivandrum

Co-guide

Dr. Sanjay G, MD, DM
Additional Professor, Dept of Cardiology,
Sree Chitra Tirunal Institute for Medical Science and Technology, Trivandrum

CONTENTS

ACKNOWLEDGEMENTS

It is with deep sense of gratitude, satisfaction and with the divine blessings of GOD that I submit this dissertation. I take this opportunity with much pleasure to thank all who contributed in many ways for the success of this study.

I would like to express my deep sense of thanks and gratitude to Dr. Harikrishnan S for giving me the idea of conducting such a research project and his contributions and suggestions during the entire work.

I am greatly indebted to my co guide Dr. Sanjay G for the continued support, guidance and advice he has extended to me throughout my work towards this thesis.

I am grateful to Dr. Krishnamoorthy, Professor and head, Department of Cardiology, SCTIMST for providing valuable suggestions and his constant support that helped to make this study better.

My sincere thanks to Dr Ajit Kumar V K, Dr. Sivasankaran S for their constructive inputs. I would also like to sincerely thank all the faculty members of Department of Cardiology, SCTIMST for their guidance.

I would like to thank Dr Deepanjan, for guidance in the statistical analysis and constantly supporting me all the time in my work.

I have no words to express my heartfelt gratitude and love to my parents, my husband and my sister who provided the most precious support.

I would like to thank my colleagues for their valuable suggestions.

Finally, my sincere thanks to all the patients who were included in the study.

Dr. Shrusthi Walad

ABBREVIATIONS

BMV	-	Balloon mitral valvotomy
RHD	-	Rheumatic heart disease
MS	-	Mitral stenosis
PTMC	-	Percutaneous transvenous mitral commissurotomy
CMV	-	Closed mitral valvotomy
PMV	-	Percutaneous mitral valvotomy
MVR	-	Mitral valve replacement
NYHA	-	New York Heart Association
MVA	-	Mitral valve area
AF	-	Atrial fibrillation
PA	-	Pulmonary artery
MR	-	Mitral regurgitation
BSA	-	Body surface area
Fr	-	French
IBMC	-	Inoue balloon mitral commissurotomy
PMMC	-	Percutaneous metallic mitral commissurotomy
AML	-	Anterior mitral leaflet
PML	-	Posterior mitral leaflet
IBMV	-	Inoue balloon mitral valvotomy
PAH	-	Pulmonary artery hypertension
Qp/Qs	-	Pulmonary blood flow/ systemic blood flow
MPAP	-	Mean pulmonary artery pressure
PVR	-	Pulmonary vascular resistance
PBMV	-	Percutaneous balloon mitral valvotomy
LA	-	Left atrium
MV	-	Mitral valve

MVAI	-	Mitral valve area index
PAW	-	Pulmonary artery wedge
TEE	-	Transesophageal echocardiography
ASD	-	Atrial septal defect
ESR	-	Erythrocyte sedimentation rate
TLC	-	Total leucocyte count
PHT	-	Pressure half time
SD	-	Standard deviation
AR	-	Aortic regurgitation
AS	-	Aortic stenosis
TS	-	Tricuspid stenosis
TR	-	Tricuspid regurgitation
SEC	-	Spontaneous echo contrast
EF	-	Ejection fraction
TMG	-	Transmitral gradient
RVSP	-	Right ventricular systolic pressure
PASP	-	Pulmonary artery systolic pressure
LV ed	-	Left ventricular end diastolic pressure
CO	-	Cardiac output
CI	-	Cardiac index
SVT	-	Supraventricular tachycardia
TIA	-	Transient ischaemic attack
DVR	-	Double valve replacement
hs CRP	-	High sensitivity CRP

SYNOPSIS

Introduction: Percutaneous mitral valvotomy(PMV) has shown good results even in the juvenile mitral stenosis(MS). Immediate and intermediate outcomes of PMV in juveniles are in par with adults, but there is no study which compares long term outcomes of PMV in juvenile with adult MS.

Aim: To study the immediate and long term outcomes of PMV and compare the rate of restenosis in juvenile with adult MS.

Methods: Retrospective analysis of 156 juvenile MS (age < 20 years) who underwent PMV in our institution between 1/1/1995 and 31/12/2017 were compared with 156 adult MS between 21 to 50 years of age. The clinical, echocardiographic and hemodynamic parameters at the time of BMV and clinical and echocardiographic data post PMV at 6 months, 1-3 years, 5 years upto the last follow up were analysed. Rate of restenosis between the two groups were compared.

Results: Mean age in juveniles was 15.87 ± 2.97 and in adults was 32.32 ± 7.65. 33.3% were males in the juvenile group and 16.6% adults were males (p=0.001). 3.2% and 14.1% were in AF in the juvenile and adult group, respectively (P=<0.05). Wilkin's score was 6.25 ± 1.73 and 6.91 ± 1.94 in juveniles and adults, respectively (p=<0.05). Procedural success seen in 89.1% juveniles and 87.8% adults. Adults had larger LA size, but the indexed left atrial size was higher in the juvenile group. Though MVA and MVAI by 2D did not vary among the groups, MVAI by catheterization was higher in juveniles. Mean transmitral gradient was higher in juveniles. PA pressures did not vary between the groups and significant fall noted post procedure in both the groups. Immediate complications were similar between both the groups. Mean follow up was 10.83± 6 years (range-0.25-23.6 years). 50.64% juveniles and 37.82% adults had restenosis. Time to 1st restenosis in juveniles was 6.46 ± 4.23 years and in adults was 10.32 ± 6.21 years. Age, previous commissurotomy, PA pressure and MR predicted restenosis.

Conclusion: PMV is safe and effective in juvenile MS with good immediate and intermediate results. Freedom from restenosis was much higher in adults at 5,10 upto 23 years as compared to juveniles.

What is already known?: Immediate and intermediate results in juvenile MS are comparable to adults. No significant difference in restenosis between the two groups.

This study adds: Restenosis rates in juveniles are significantly higher as compared to adults over a long time period.

INTRODUCTION

INTRODUCTION

Mitral stenosis first described by Vieussens in 1705, first disease to be diagnosed by echocardiography[1] and the first valve lesion to be treated by surgery[2] and balloon mitral valvotomy(BMV)[3]. It is highly prevalent in developing countries because of high prevalence of rheumatic fever. In India, school survey between 1940-1983, the prevalence of rheumatic heart disease was 6 per 1000 children (1.8 to 11/1000 children), and from 1984 to 1995 it was reported to be from 1 to 3.9 per 1000.vs 0.5 per 1000 in developed countries[4]. In the largest school survey conducted to date at Vellore during 2001-2002, a total of 2,29,829 children between 6-18 years of age were screened as part of a school health programme[5]. The prevalence of RHD was 0.68/1,000 school children, which showed a declining prevalence of RHD in rural children in India. In developed countries, prevalence detected by echocardiography is about 0.02-0.2%.[6]

Juvenile mitral stenosis is defined as pure or predominant mitral stenosis of rheumatic origin under the age of 20 years as described by Roy et al[7]. Male predominance, lesser atrial fibrillation and high prevalence of pulmonary hypertension were charcteristics of juvenile mitral stenosis. Mishra et al. in their study of prevalence of RHD in 378 children below 19 years, mean age was 15.1 ± 4.4 years[8]. The male to female ratio was 4:1. Mild mitral stenosis (MS) was diagnosed in 34.9% and severe MS was diagnosed in 33%.

Percutaneous transvenous mitral commissurotomy (PTMC), first described by Inoue[3] in 1984 has now gained widespread acceptance and is the preferred method of treatment for symptomatic patients with rheumatic mitral stenosis. BMV has outreached CMV in the management of mitral stenosis because of short hospital stay and lack of scar. The procedure has proven to be safe and effective in large series of adult patients[9,10]

Similar to adults, it has shown good result in symptom relief and effective orifice area even in juvenile mitral stenosis. Immediate results and intermediate outcomes of PMV in juveniles are in par with adults, but there is no study which compares long term outcomes of BMV in juvenile vs adult patients.

In this study, we aim to study the immediate and long term outcomes of PMV and the rate of restenosis in juvenile and adult patients.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Juvenile mitral stenosis defined as pure or predominant mitral stenosis of rheumatic origin in < 20 years of age. Roy et al.[7] included 754 patients of rheumatic heart disease out of which 171 were below the age of 20 years. Of those 171, 108 had pure or predominant mitral stenosis. 66 were boys and 42 were girls. 71 (66%) had atleast one attack of rheumatic fever and 30 (28%) of them had more than one attack. 50 (70%) of the 71 patients with history of rheumatic fever developed symptoms within five years of first attack. 9% of the patients were asymptomatic, 78% had significant exertional dyspnea. Congestive heart failure was seen in 45% and atrial fibrillation in 6%. 12% had angina. Predominant mitral stenosis with or without regurgitation was seen in 63%, out of which isolated mitral stenosis was seen in 40%, being the commonest single lesion. Mitral stenosis with slight regurgitation in 33% and moderate regurgitation in 8%. Only mitral regurgitation was seen in 7%, mitral and aortic valve disease in 18% and pure aortic regurgitation in 3%.

ECG showed moderate right ventricular hypertrophy (R/S in lead V1 >1) in 38 patients and severe (R/S ratio in V1 >5) in 26 patients. The prime R in V1 exceeded 12 mm in 13 patients. X ray features of moderate to severe degrees of pulmonary hypertension was seen in 68 patients. Rheumatic activity was seen in 24 patients. In over two thirds of the catheterized patients the resting mean arterial pressures were considerably raised, occasionally even beyond systemic arterial pressures. In 60%, resting mean pulmonary artery wedge pressure exceeded 20 mm Hg. Cardiac output was normal in 80% of patients. The pulmonary vascular resistance was abnormal in almost two-thirds of patients. The estimated valve area was < $1cm^2$ in most. At operation,17 of the 23 patients had large and turgid pulmonary arterial trunk, calcification and mural thrombi was seen in 1, and 18 out of 23 had stenosed mitral valve enough to obstruct passage of the tip of surgeon's index finger. Prominent features in lung biopsy specimens were pronounced medial hypertrophy; intimal thickening of small muscular pulmonary arteries, arterioles and venules; alveolar capillary sclerosis and hypertrophic smooth muscle bands in distal respiratory passages.

Shaw et al.[11] studied the clinical and hemodynamic profiles of young, middle aged and elderly patients with mitral stenosis undergoing mitral balloon valvotomy. Of 405 patients who had mitral balloon valvotomy, 19 were aged under 40 years, 101 aged 40– 54, 173 aged 55–69, and 112 were 70 years old or more. Medical co-morbidity and Parsonnet score for risk at surgery increased notably with age. Older patients had greater symptomatic limitation and a more severe degree of mitral

stenosis, with more valve degenerative change. The incidence of atrial fibrillation, mitral reflux, left ventricular impairment, coronary artery disease, and aortic valve disease increased progressively with age. Before balloon dilatation the right ventricular systolic and left atrial pressures were similar in all age groups, but younger patients had a higher transmitral gradient and cardiac output. After balloon dilatation the younger patients achieved a greater increase in valve area. Complications of balloon valvotomy were more common in the older patients. At five years after balloon dilatation the percentages of patients in each age group who were in New York Heart Association classes I and II were 87%, 63%, 36%, and 19%, respectively. Mortality at five years was 0%, 5%, 31%, and 59%. Percutaneous balloon valvotomy gave a good haemodynamic and symptomatic result in patients under 55. In older patients improvement was less pronounced and less sustained, but a well tolerated palliative treatment for those unsuitable for surgery.

Gamra et al.[12] compared 110 patients of juvenile mitral stenosis with 554 adults. Juvenile patients had lesser atrial fibrillation and lesser mitral valve deformities. There was no difference in the mitral valve area index between the two groups prior to the procedure but the indexed mitral valve area was higher in the juvenile group after the procedure. There were more complications, particularly ≥ moderate mitral regurgitation in adult group compared to the juvenile group. Procedural success was seen in all the patients with juvenile group but in 92% of patients with adult group with significant p value. Follow up indexed mitral valve area was 1.16cm^2/m^2 in adult group compared to 1.34 cm^2/m^2 in juvenile group. At 10 years, there was no significant difference in the freedom from restenosis and event free survival between the two groups. Cinical event was defined as death from any cause, mitral valve replacement, repeat balloon mitral commissurotomy or NYHA class III or IV. Mitral valve restenosis was defined as a mitral valve area index <0.9cm^2/m^2 by 2D echo.

Fawzy et al.[1113] compared 57 children ≤ 18 years to 474 adult patients who underwent balloon mitral valvotomy and were followed up for a mean of 8.5± 4.8 years. Juvenile group had lower mitral echo score and doppler mitral valve area and higher mitral valve gradient compared to the adult group. Immediately after procedure juvenile group had larger mitral valve area both by catheter and doppler in comparison with adults. Complication rates were similar in both groups. Restenosis was defined as a >50% loss of the original increase in MVA, with follow-up MVA <1.5 cm^2. At mean follow up of 8.5 ± 4.8 years (range 1.5-18 years), no difference in restenosis between the two groups. Echo score >8 was a predictor of restenosis in children whereas echo score and previous surgery were predictors of restenosis in adults.

Actuarial freedom from restenosis at 10, 15, and 18 years for juvenile and adult groups were 78% ± 7%, 64% ± 9%, and 18% ± 14% and 77% ± 2%, 43% ± 4%, and 17% ± 4%, respectively (P = 0.26). Event-free survival was defined as survival with freedom from redo BMV, MVR, death, or

NYHA functional class III or IV. Event-free survival rates at 10, 15, and 18 years were 87% ± 6%, 62% ± 1%, and 20% ± 2% versus 87% ± 1%, 51% ± 4%, and 20% ± 5% for juvenile and adult groups, respectively (P = 0.51). Post procedure MVA < 2.0 cm^2 (P = 0.043) and previous surgery (P = 0.03) were identified as predictors of events in children. Echo score > 8 and pre valvuloplasty AF were the predictors of events in adults. At baseline pulmonary artery systolic pressures were equal in both groups and significant drop in PA pressures in both the groups just after the procedure. Regression of pulmonary hypertension though seen immediately after percutaneous valvuloplasty, it decreases slightly with further substantial regression over 12 months.

Similar study of "Balloon mitral valvotomy in juvenile rheumatic mitral stenosis: Comparison of immediate results with adults"[14] included 40 juvenile and 40 consecutive adult patients who underwent balloon mitral valvotomy using Accura balloon. No significant differences in gender distribution, NYHA functional class and Wilkin's score between the two groups. Atrial fibrillation and left atrial enlargement was higher in adult group, though right atrial enlargement was seen in 22.5% and 12.5% of juvenile and adult groups respectively. Though the juvenile group had smaller mitral valve area prior to procedure their indexed mitral valve area was no much different, however immediate gain in the indexed mitral valve area was much higher in the juvenile group. Transmitral gradient pre and post procedure was higher in the juvenile group. Juvenile patients had higher pulmonary artery systolic pressures prior to procedures and significant fall off PA pressures in both the groups post procedure though there was no significant difference in the absolute post procedure PA pressure.

Shrivastava et al [15] showed the safety and effectiveness of mitral valvotomy in juvenile mitral stenosis using the Inoue balloon. Stepwise dilatation was done starting with a balloon size 2 mm less than that calculated by the formula (Balloon size= height of the patient in cm/ 10 +10). After each dilatation, transmitral gradients were recorded and cardiac auscultation was done to look for new onset or increase in pre-existing mitral regurgitation. Valve was dilated with stepwise 1 mm increment in balloon size until transmitral gradient decreased to less than 5 or if there appeared to be new or increased gradients in pre-existing mitral regurgitation. The final balloon size was never >2 mm above that calculated by the formula. Immediate results were good with significant decrease in mean pulmonary artery wedge, transmitral gradient, mitral valve area and indexed mitral valve area, mean pulmonary artery pressure. Cardiac index increased significantly though there was no significant fall in PVR. None developed tamponade or systemic embolism. 1 developed severe mitral regurgitation underwent mitral valve replacement and died in the peri-operative period. No patient had clinical evidence of restenosis upto 2 years of follow up. As there is lower incidence of atrial septal defect reported with Inoue balloon (10-25%), their series had 1 case with catheter based Qp/Qs ~1.5, but no atrial septal defect with colour doppler.

Harikrishnan et al.[16] compared long term results of Inoue balloon technique with with Cribier metallic commisurotome in juvenile mitral stenosis. Procedural success was defined as increase in mitral valve area of at least 50% from the basal or a final valve area of more than 1.03 cm^2/m^2 (equal to 1.5 cm^2/ mean BSA of adults with mitral stenosis, 1.45 cm^2), in the absence of MR requiring surgical intervention. The metallic commissurotome consists of a distal metallic head (5 cm long, 5 mm in diameter) comprising two 15-mm long hemicylindrical bars. It is fixed at the tip of a 12-Fr catheter and connected by an internal cable to a proximal hand-operated device, which can open the arms gradually to 33, 35, and 37, up to a maximum of 40 mm. Extent of bar opening was based on the body surface area and the mitral valve morphology. The initial bar opening was set at 37 or 40 mm if the patients had a BSA of more than or equal to 1.5 m^2 and if they had no significant calcium in the mitral valve. Patients with smaller body frames had bar opening set to 33 or 35 mm and increased to 35, 37, or 40 mm, according to the result after initial dilatations. Follow-up evaluations were done at 1 month, 6 months, and then yearly. Follow-up evaluation at 1 month included clinical examination only. Mitral re-stenosis was defined as a loss of >50% initial gain in valve area with reappearance of symptoms.

Out of the 33 patients who underwent PTMC in each group, the procedure was successful in 31 patients in each group. One patient in the PMMC group had crossover to IBMC, as LV could not be entered using the floatation balloon. IBMC technique in that patient gave a successful result. One patient in the IBMC group developed cardiac tamponade because of perforation of LA and underwent repair of the tear with CMV. One patient in each group developed tear of anterior mitral leaflet (AML) and severe MR, and had to go for emergency mitral valve replacement . Procedural success was similar in both groups. The average procedural time was 58 min for PMMC compared with 51 min for Inoue Balloon technique. One patient in IBMC group and two patients in PMMC group had >1.4:1 shunting by catheterization though there was no shunt by colour flow. No deaths or major complications upto 41 months of follow up. There was no difference of NYHA class and number of commissures remaining open on follow up among the two groups.

PMMC required two experienced operators (one for holding the beaded wire and another person for pushing the device), whereas IBMC could be managed with one experienced operator. The catheters were reused. Whether the Inoue balloon was reused or not the PMMC was much more cost effective compared to the IBMC. There was no reported infective endocarditis or any complication related to infection. Hence they showed that both IBMC and PMMC had similar procedural success and complication rates. PMMC resulted in higher MVA immediate post procedure, which was not apparent at follow-up. Patients in both groups had sustained symptomatic relief on follow-up, and the restenosis rates were similar. PMMC was more cost-effective than IBMC.

Joseph et al.[17] compared 107 children aged <18 years who underwent percutaneous mitral commissurotomy with 450 adults. Percutaneous mitral commissurotomy was done using Inoue balloon. There were significantly higher number of males in juvenile group compared to the adults. Higher atrial fibrillation in adult group. Subvalvar fibrosis did not vary between the two groups. There was no difference in the mitral valve area between the two groups before and after the procedure. Though they didn't index the mitral valve area. Absolute pulmonary artery systolic and mean pressure was significantly higher in the juvenile group compared to the adults though there was significant fall in the PA pressures after the procedure. Balloon size was significantly smaller in the juvenile group. Mitral regurgitation and mitral valve replacement didn't vary significantly between the groups. The outcome was similar in both groups. Children were found to have significantly higher pulmonary artery pressure compared to adults. They showed PTMC using an Inoue balloon is effective and safe in children. In a mean follow up of 14 months, 2 patients (1.8%) developed restenosis.

In our previous study by Dohra[18] we analysed immediate and intermediate term results of percutaneous transmitral commissurotomy of 92 patients with juvenile mitral stenosis. All patients were in sinus rhythm. Inoue balloon was most commonly used during PTMC in 75 (82%), Accura balloon in 12 (13%), Cribier's metallic commissurotome in 4 (4%) & Mansfield balloon in 1 (1%) patient. Procedural success was achieved in 76% cases with optimal increase of mitral valve area and absence of any complication. After PTMC mean transmitral gradient decreased from 15.8 ± 5.3 to 5.6 ± 2.3 mmHg. Mitral valve area as determined by Gorlin's formula increased from 0.70 ± 0.24cm^2 to 1.52 ± 0.43cm^2. There was significant change in the mitral valve area from 0.76 ± 0.19 cm prior to PTMC to 1.62 ± 0.33cm^2 as measured by echo planimetry. After PTMC systolic pulmonary artery pressure decreased significantly by 29%. 17.3% patients developed moderate mitral regurgitation and 3.2% patients developed severe mitral regurgitation after PTMC. Moderate mitral regurgitations were mainly commissural and did not progress during follow up. Three patients developed severe MR requiring mitral valve replacements constituting only 3.2% of the total population undergoing PTMC. Death, cerebrovascular accident or any other major complications were not reported. In this study two patients underwent balloon tricuspid valvotomy due to significant tricuspid stenosis with a good immediate result.

In a mean follow up of 4.2 ± 2.5 years, the mean 2D mitral valve area remained at 1.64 ± 0.47 cm^2. 5 patients developed mitral valve restenosis of which 3 had unsatisfactory result after initial PTMC with mitral valve area (2D MVA) of less than 1.5 cm^2.These patients underwent repeat PTMC with 90% increase in mitral valve area. At the study period the result remained unchanged. They showed the result of PTMC in restenosed valve to be satisfactory but the number was small. Follow up moderate mitral regurgitation was present in 15% patients and severe mitral regurgitation was

present in only 2.1% patients. Considering the presence of moderate mitral regurgitation immediately after PTMC of 17%, there was no significant progression of commissural MR resulting after PTMC. At follow up 91.3% of patients remained in NYHA functional class I. 6.5% patients remained in class II and 2.2% patients remained in class III. No patients were in functional class IV at follow up. All the patients remained in sinus rhythm at follow up.

Sinha et al[19] included 193 patients with juvenile rheumatic MS who were compared with adults, with specific reference to the effect of IBMV on hemodynamics and pulmonary vasculature in patients with severe PAH. Mitral valve areas were smaller (0.76 +/- 0.22 versus 0.81 +/- 0.22 cm2), while mean pulmonary arterial pressure (MPAP) (44.5 +/- 16.5 versus 38.4 +/- 15.1 mmHg) and pulmonary vascular resistance (PVR) (5.5 +/- 4.6 versus 4.41 +/- 4.04 Wood units) were greater in juvenile patients when compared with adults. There was a 99% procedural success. Juvenile patients showed an overall greater fall in MPAP and PVR when compared with adults. The incidence of severe PAH was much higher (32%) among juveniles than adults (16%). Only 5% of patients with juvenile MS with severe PAH had residual severe PAH immediately after IBMV, compared with 17% in older patients. Hemodynamic benefits (echocardiographic mean transvalvular gradient and mitral valve area) were sustained at a mean follow up of 29 months, and there was no documented case of restenosis after successful IBMV.

Gupta et al[20] analysed 614 consecutive patients undergoing balloon valvotomy and identified 84 patients (13.7%) with mitral restenosis following prior surgical valvotomy (Group I). The remaining 530 patients (86.3%) had not undergone previous surgery (Group II). The incidence of atrial fibrillation (19% vs 5.6%), mitral valve calcification (50% vs 30.6%) and total echo score >8 (54.8% vs 24.15%) was significantly higher in Group I. Both groups were comparable in terms of functional class, technique of valvotomy, mitral valve area (0.87 ± 0.18 vs 0.87 ± 0.15cm^2 , P=ns), mean transmitral gradient (19.63 ± 6.01 vs 19.21 ± 5.67 mmHg, P =ns), and mean pulmonary artery pressure (42.2 ± 19.0 vs 40.8 ± 14.4 mmHg, *P=ns).* After percutaneous balloon mitral valvotomy, the final mitral valve area (1.67 ±0.28 vs 1.69 ± 0.29 cm^2, P=ns), mean transmitral gradient (6.12 ±3.68 vs 5.02 ± 3.21 mmHg, P=ns) and mean pulmonary artery pressure (31.0 ± 15.2 vs 28.5 ± 11.1 mmHg, P=ns) were comparable. The success rate (93% vs 95.3%, P=ns*)* was similar in both groups. Significant mitral regurgitation was seen in four (4.8%) patients in Group I and 22 (4.1%) patients in Group II (P=ns). There were two deaths (2.4%) in Group I and five (0.9%) in Group II (P=ns). The clinical and echo Doppler follow up (8-40 months) studies showed that both groups were of similar NYHA class, and had similar mitral valve area (1.65 ± 0.21 vs 1.66 ± 0.3 cm^2) and transmitral gradients (7.1 ± 3.8 vs 5.9 ± 3.5 mmHg). They concluded that percutaneous balloon mitral valvotomy was safe and effective in patients with mitral restenosis following surgical valvotomy; the beneficial

acute outcome was sustained as shown at intermediate-term follow-up and was similar to that of patients undergoing balloon mitral valvotomy as an initial procedure.

Rafla et al[21] analysed whether the presence of calcium in the MV commissure predicted restenosis at 3 years follow-up after PBMV. 220 consecutive patients with rheumatic MS who underwent successful PBMV by using the Inoue balloon catheter were studied prospectively. Commissural calcification was present in 70 patients (32%). Commissural splitting occurred immediately after PBMV in all the 220 patients. Bilateral commissural splitting was present more significantly in patients without commissural calcification than in patients with commissural calcification ($P < 0.001$). 140 patients presented at 3 years follow-up. Commissural calcification was present in 35 patients (25%) while the other 105 patients (75%) had no commissural calcification. Bilateral commissural splitting was present more significantly in patients without commissural calcification than in patients with calcification ($P < 0.001$). Severe MR was present in 20 patients (14.3%). It was present more significantly in patients with calcification than in patients without ($P < 0.001$). Restenosis occurred in 30 patients (21.4%). Patients with commissural calcification had a lower incidence of bilateral commissural splitting; higher incidence of severe MR at one year and at 3 years follow-up after PBMV. Old age, large LA diameter, high total echo score of the MV, MV score ≥ 8, lower MV area before PBMV, low incidence of bilateral commissural splitting, low MV area after PBMV and the presence of commissural calcification were significant predictors of restenosis at 3 years follow-up.

Bahl et al.[22] studied 270 patients with rheumatic mitral stenosis who underwent PTMC using Inoue balloon. 81 (27%) had juvenile mitral stenosis (age < 20 years, range 9-20 years, mean 14 +/- 5), 48 were males and 33 females. All patients were symptomatic, NYHA class III in 61and class IV in 20 patients. Following PTMC, the mitral valve area increased from 0.8 +/- 0.4 to 2.2 +/- 0.5 cm^2 ($P < 0.001$) and the cardiac index increased from 2.4 +/- 0.8 to 3.0 +/- 0.8 $L/min/m^2$ ($P < 0.001$). Mean transmitral gradients decreased from 24 +/- 8 to 4 +/- 3 mm Hg ($P < 0.001$). Three (4%) patients had an increase in mitral regurgitation by 1 grade (grade 2/4); none required surgery. Significant left to right atrial shunt ($Qp/Qs > 1.3: 1$) on oximetry was detected in 8 (10%) patients. Overall results were compared to the rest of adult patients (n = 189, 100 females and 89 males). Adults ranged from 21 to 44 years (mean 32 +/- 11 years). The percentage increase in MVA was higher in juvenile as compared to adult patients. A larger final MVA was achieved in the juvenile group (2.2 +/- 0.5 vs. 1.9 +/- 0.3 cm2, $P < 0.05$). However, the incidence of increase in mitral regurgitation by 1 grade was similar in two groups (6% vs. 4%, P = NS)

Zaki et al.[23] assessed the late functional and morphologic results after BMV in children and adolescents. BMV was performed in 46 children and adolescents (mean age 15.5 ± 3.2 years, range 7 to 19; 19 males) with rheumatic mitral stenosis. Long term results of the procedure was analysed

during a follow-up period of 66 ± 6 months. The mitral valve score was 6 ± 2/16. BMV was successful in 45 patients (98%). There was a significant increase of the mean mitral valve area index (MVAI) (0.65 ± 0.14 vs 1.54± 0.23 cm^2/m^2, p <0.001) and a significant reduction of the mean transmitral pressure gradient (16.1± 2.9 vs 5.13.1± mm Hg, p <0.001) from pre to post-BMV, respectively. There was no significant change of MVAI or the pressure gradient during the follow-up compared with immediately after BMV (1.51 ± 0.31 cm^2/m^2 and 4.9 ± 2.5 mm Hg, respectively). No deaths or mitral valve replacement occurred during the follow up period. Restenosis (loss of >50% of the achieved increase in MVAI) occurred in 3 patients (6.5%). All other patients remained in their New York Heart Association class (<II). The event-free survival with good functional results was seen in 42 patients (91%) at the end of the follow up period. The left atrial diameter decreased from 4.6 ± 0.9 before BMV to 3.7± 0.6 cm at follow up (p <0.05). They concluded that BMV had excellent intermediate term results in children and adolescents with a relatively low mitral valve score.

Kothari et al[24] reported 45 children (aged 7–12 years, mean 11.0 ± 1.2 years) with severe rheumatic mitral stenosis (MVA 0.64± 0.14 cm^2) who underwent PTMC. The pulmonary artery wedge pressure (PAW) decreased from 24.3 ± 8.6 to 14.7 ± 7.2 mmHg (P= 0.0001) and mean diastolic gradient decreased from 24.3 ± 7.7 to 7.9 ± 5.9 mmHg with the final MVA of 1.63 ± 0.45 cm^2 (P = 0.0001). Complications included significant mitral regurgitation (MR) in three children and atrial shunting in two patients. No procedural death, systemic embolism, and cardiac tamponade were encountered and concluded that it was safe and effective in them.

Twenty-four children had maximum balloon size (MBS) same as recommended balloon size (RBS) derived according to the height (group I) and 21 children had MBS 1–3 mm less than RBS (group II). Despite the lesser maximum balloon size, the final results were comparable in both groups and the incidence of significant MR was similar. On follow-up of 20.4 ± 16.3 months (range 3–56 months), one child developed restenosis. They concluded that the smaller balloon size than the RBS derived from height may be equally effective and possibly safer.

AIMS

AIMS

- To evaluate the safety and efficacy of percutaneous mitral valvotomy in juvenile mitral stenosis in comparison with adult mitral stenosis.
- To compare the clinical, echocardiographic and hemodynamic profile of juvenile mitral stenosis with adult mitral stenosis.
- To compare long term outcomes and restenosis between juvenile and adult mitral stenosis undergoing PMV.

HYPOTHESIS

Results of BMV in juvenile MS are similar to adults but the rate of restenosis is greater in the juvenile group due to recurrent rheumatic activity or chronic subclinical low grade of infection.

MATERIALS & METHODS

METHODS

This is a retrospective prospective analysis of 156 juvenile mitral stenosis patients (age < 20 years) who underwent percutaneous balloon mitral valvotomy in our institution between 1st January 1995 and 31st December 2017. These patients were compared with 156 adult patients of mitral stenosis between 21 to 50 years of age who underwent percutaneous balloon mitral valvotomy within two to three days of the juvenile group.

INCLUSION CRITERIA

Patients with MS who have undergone BMV as per standard indications and guidelines of BMV between the period 1/1/1995 to 31/12/2017

GROUPS : JUVENILE GROUP < 20 years

ADULT GROUP : 21-50years

EXCLUSION CRITERIA

- Patients who have undergone BMV in emergent situations
- Patients who have undergone BMV during their pregnancy
- Patients who have undergone BMV after 50 years of age

METHODOLOGY

The clinical, echocardiographic and hemodynamic parameters of the two groups at the time of BMV were analysed. All the patients prior to the procedure had detailed clinical and echocardiographic evaluation. The data collected included NYHA class and heart rhythm. Mitral valve structural pathology was assessed using Wilkins[25] score. Commissural calcification was assessed for the suitability of BMV. Mitral valve area was determined by 2D echo planimetry and doppler pressure half time method. Because of the difference in body surface area between the young and adult populations, mitral valve area index was considered for comparison. LA diameter measured in parasternal long axis (PLAX) view were taken and indexed to body surface area for comparison

between the groups. Mitral regurgitation was assessed by color Doppler according to the degree of jet extension into the left atrium using Helmcke classification[26]. Maximum regurgitant jet area/ left atrial area from three orthogonal planes < 20% was defined as mild, 20-40% as moderate and > 40% as severe. Transmitral gradient was measured in apical four chamber view by continuous wave Doppler. Pulmonary artery hypertension was assessed by the right ventricular systolic pressure with peak tricuspid regurgitation jet velocity using modified Bernoulli's equation ($4v^2$ + Estimated right atrial pressure). Prior to the procedure, transesophageal echocardiography was performed for every patient to rule out any clots in the left atrial body or the left atrial appendage. In addition transesophageal echocardiography provided additional information on the mitral valve structure and the severity of mitral regurgitation. The contraindications to the procedure were MR assessed by echocardiography of more than mild degree and left atrial (LA) thrombus on TEE performed prior to PTMC. Patients who were found to have LA clot were anticoagulated for 3-6 months and then re-assessed for disappearance of the clot. Echocardiography was repeated within 24 hours after the procedure to evaluate mitral valve area, to assess the severity of mitral regurgitation and to detect the presence of iatrogenic atrial septal defect.

Hemodynamic data was obtained from the cardiac catheterization at the time of BMV. Right and left heart catheterization was performed and transseptal puncture was done using Brockenbrough needle. Mean left atrial pressure, left ventricular end diastolic pressure, pulmonary artery pressure, transmitral gradient, mitral valve area indexed to body surface area and the cardiac index were obtained and compared between the two groups. The procedure was done using Accura, Inoue balloons and Cribier metallic commisurotome. BMV was performed using standard technique as described [27]. Maximum balloon size was chosen using the formula[28]

Balloon size (mm) = Patient's height (cm)/10 + 10

Percutaneous metallic mitral commissurotomy was done as reported previously[16]. The metallic commissurotome (Medicorp, Villers-les-Nancy, Cedex, France) consists of a distal metallic head (5 cm long, 5 mm in diameter) comprising two 15-mm long hemicylindrical bars. It is fixed at the tip of a 12-Fr catheter and connected by an internal cable to a proximal hand-operated device, which can open the arms gradually to 33, 35, and 37 mms, up to a maximum of 40 mm. Extent of bar opening was based on the body surface area and the mitral valve morphology. The initial bar opening was set at 37 or 40 mm if the patients had a BSA of more than or equal to 1.5 m^2 and if they had no significant calcium in the mitral valve. If the valve had significant calcium, we preferred lower extent of bar opening. Patients with smaller body frames had bar opening set to 33 or 35 mm and increased to 35, 37, or 40 mm, according to the result after initial dilatations.

BMV using Accura balloon was done in 111 (71.1%) patients of juvenile group and 111 (71.1%) patients of adult group whereas Inoue balloon was utilized in 21 (13.4%) patients of juvenile group and 16 (10.2%) of adults and Cribier device was used in 24 (15.3%) of juvenile group and 29 (18.5%) patients of adult group. Table 1. shows various devices used among the two groups.

Procedural success was defined as increase in mitral valve area of at least 50% from the basal or a final valve area of >1.04cm^2/m^2 with no major complications[29]. Major complications included cardiac tamponade, systemic embolism, or death, increase in MR grade ≥3 or shunt across the iatrogenic septal defect ≥2. The threshold of 1.04 is derived from the usual threshold of valve area in adults of 1.5 cm^2 divided by the mean body surface area among our adult population which was 1.43 m^2.

Table 1: Devices used between the two groups

Device	**Juvenile, n (%)**	**Adult, n (%)**
Accura	111 (71.1)	111 (71.1)
Inoue	21 (13.4)	16 (10.2)
Cribier	24 (15.3)	29 (18.5)

Follow up evaluation

After discharge, patients were followed up 6 monthly for 1 year, yearly for first few years and then 2-3 yearly depending upon their symptoms. Clinically by NHYA class and rhythm and echocardiographic parameters were analysed at 6 months, 1-3 years, 5 years, and the last follow up whichever available was analysed. The mean follow up among the juvenile group was 10.09 ± 6.71 years and the adult group was 11.58± 5.12 years (Range- 0.25-23.6 years). 92.3% follow up data was available in the juvenile group and 94.8% was available in the adult group.

Mitral valve restenosis was defined as mitral valve area index < 1.04cm^2/m^2 or >50% loss of initial gain in the valve area[29]. A clinical event was defined as: (1) death from any cause, (2) mitral valve replacement, (3) repeat balloon mitral commissurotomy, or (4) Worsening of symptom class to NYHA class III or IV. All the patients were taking penicillin prophylaxis upto 40 years of age or lifelong.

Statistical analysis

Data are expressed as mean ± standard deviation. Continuous variables were analysed using unpaired Student's t test and categorical variables using Chi-square and Fisher exact test. Comparison of variables before and after the procedure was carried out using paired t test. P value <0.05 was considered to be significant.

Kaplan–Meier analysis was used to determine the freedom from restenosis. Differences in restenosis free survival rates between the two groups were analysed by the Log-rank test. To identify predictors of restenosis multivariate analysis was performed. All analyses were performed using SPSS 25.

RESULTS

RESULTS

156 juvenile mitral stenosis patients were compared with 156 adult mitral stenosis. The mean age in the juvenile group was 15.87 ± 2.97 (range- 8-19 years) and in adult group was 32.32 ± 7.65 (range-21-50 years). 52 patients (33.3%) were males in the juvenile group whereas 26 (16.6%) of the adult patients were males. There were significantly higher number of males in the juvenile group compared to adults. 14 (8.9%) and 13 (8.3%) of them had prior CMV in juvenile and adult groups, respectively. 11 (7%) in juvenile group and 3 (1.9%) in adult group had prior BMV. History of rheumatic fever was present in 34 (21.7%) and 32 (20.5%) patients with juvenile and adult groups respectively (P= 0.88). There was one patient in the adult group with Lutembacher's syndrome who had undergone OMV with ASD surgical closure previously. Mean body surface area was 1.30 ± 0.21 in the juvenile group and 1.43 ± 0.16 in the adult group.

Among the juvenile group, 108 (69.2%) were in NYHA II and 48 (30.7%) were in NYHA III and in the adult group 99 (63.4%) were in NYHA II and 57 (36.5%) were in NYHA III (P=0.33). 5(3.2%) and 22(14.1%) were in atrial fibrillation in the juvenile and adult group, respectively (P = <0.05). Wilkin's score was 6.25 ± 1.73 and 6.91 ± 1.94 in the juvenile and adult groups, respectively (p = <0.05). There was no difference in the history of LA clot and ESR, TLC between the groups. Baseline characteristics between the two groups are shown in Table 2.

Table 2: Baseline charcteristics

Parameter	**Juvenile (n=156)**	**Adult (n=156)**	**P value**
Age (in years), mean ± SD	15.87 ± 2.97	32.32 ± 7.65	<0.0001
Male sex, n(%)	52 (33.33)	26 (16.66)	0.001
Prior CMV, n (%)	14 (8.9)	13 (8.3)	1
Pre BMV, n(%)	11 (7.05)	3 (1.9)	0.051
H/o Rheumatic fever, n(%)	34 (21.7)	32 (20.51)	0.88
Lutembacher's syndrome, n	0	1	1
BSA(m^2), mean± SD	1.30 ± 0.21	1.43 ± 0.16	<0.0001
NYHA class, n(%)	II - 108 (69.23) III- 48 (30.76)	II- 99 (63.46) III- 57 (36.53)	0.33
Heart failure, n(%)	23 (14.74)	33 (21.15)	0.18
Rhythm (AF) , n(%)	5 (3.2)	22 (14.1)	0.0009
MR, n (%)	0- 45 (28.8)	0 - 54 (34.6)	

	1- 57 (36.5)	1 – 53 (33.9)	
	2- 54 (34.6)	2 – 49 (31.4)	
AR, n (%)	0 - 105 (67.3)	0 - 92 (58.9)	
	1 – 16 (10.2)	1 - 12 (7.69)	
	2 – 29 (18.5)	2 - 45 (28.8)	
	3 – 6 (3.8)	3 - 7 (4.48)	
AS (Mild) , n (%)	5 (3.2)	17 (10.8)	
TR, n (%)	1 – 22 (14.1)	1 – 15 (9.6)	
	2 – 35 (22.4)	2 – 49 (31.4)	
	3 – 19 (12.17)	3 – 15 (9.6)	
	4 – 6 (3.8)	4 – 3 (1.9)	
Wilkin's score, mean ± SD	6.25 ± 1.73	6.91 ± 1.94	0.002
H/o LA clot, n (%)	3 (1.9)	9 (5.76)	0.13
SEC, n (%)	14 (8.97)	20 (12.8)	0.36
ESR, mean ± SD	17.08 ± 13.29	18.39 ± 14.14	0.43
TLC, mean ± SD	9716 ± 2548	9479 ± 2670	0.46

Immediate results

Echocardiographic and hemodynamic parameters pre and post BMV are shown in Table 3. LA size was 41.74 ± 6.5 and 43.99 ± 7.78mm in the juvenile and adult group, respectively ($p = <0.05$), but the indexed LA size was 32.96 ± 7.24 and 30.96± 6.23mm/m^2 ($p= <0.05$), respectively. Though the adults had larger LA size which was similar to other studies, indexed left atrial size was higher in the juvenile group. Post procedure LA size was 38.65 ± 6.58 and 42.64 ± 6.59mm ($p = <0.05$) and indexed LA size was 30.49 ± 5.95 and 29.8 ± 4.89mm/m^2 (p= NS) in the juvenile and adult group, respectively suggesting the decrease in the left atrial size was slightly higher in the juvenile group.

2D mitral valve area was 0.78 ± 0.19 and 0.85 ± 0.2cm^2 ($p= <0.05$) and indexed mitral valve area was 0.61 ± 0.15 and 0.60 ± 0.14cm^2/m^2 (p= NS) in the juvenile and adult group, respectively. Mitral valve area by Doppler PHT was 0.82 ± 0.19 and 0.85 ± 0.19cm^2 (p= NS) and indexed mitral valve area was 0.66 ± 0.21 and 0.60 ± 0.15cm^2/m^2 ($p= <0.05$)) in the juvenile and adult group, respectively. Post procedure 2D mitral valve area was 1.52 ± 0.35 and 1.64 ± 0.37cm^2 ($p= <0.05$) and indexed mitral valve area was 1.18± 0.27 and 1.15 ± 0.28cm^2/m^2 (p= NS) in the juvenile and adult group, respectively. Post procedure mitral valve area PHT was 1.54 ± 0.33 and 1.53 ± 0.36cm^2 (p= NS) and indexed mitral valve area was 1.24 ± 0.38 and 1.08± 0.28cm^2/m^2 ($p= <0.05$) in the juvenile and adult group, respectively.

Mean transmitral gradient was higher in the juvenile group prior procedure with 19.07 ± 6.91 and 16.39 ± 7.28mmHg (p= 0.001) and post procedure 6.19 ± 3.02 and 6.54 ± 5.01mmHg (p=NS) in the juvenile and adult group, respectively. RV systolic pressure was 55.51± 23.86 and 53.89 ± 22.8mmHg prior (p= NS) and 37.18 ± 14.29 and 38.25 ± 12.07mmHg post (p =NS) in the juvenile and adult group, respectively.

Table 3: Echocardiographic and hemodynamic parameters pre and post BMV

Echocardiographic parameters	**Juvenile** (mean ± SD)	**Adult** (mean ± SD)	**P value**
EF (%)	66.31 ± 7.34	66.46 ± 7.66	0.88
LA size (mm)	Pre 41.74 ± 6.5	43.99 ± 7.78	0.007
	Post 38.65 ± 6.58	42.64 ± 6.59	<0.0001
Indexed LA size (mm/m^2)	Pre 32.96 ± 7.24	30.96± 6.23	0.011
	Post 30.49 ± 5.95	29.8 ± 4.89	0.40
MVA (2D) (cm^2)	Pre 0.78 ± 0.19	0.85 ± 0.2	0.001
	Post 1.52 ± 0.35	1.64 ± 0.37	0.005
MVAI (2D) (cm^2/mm^2)	Pre 0.61 ± 0.15	0.60 ± 0.14	0.60
	Post 1.18± 0.27	1.15 ± 0.28	0.49
MVA PHT (cm^2)	Pre 0.82 ± 0.19	0.85 ± 0.19	0.30
	Post 1.54 ± 0.33	1.53 ± 0.36	0.85
MVAI (PHT) (cm^2/mm^2)	Pre 0.66 ± 0.21	0.60 ± 0.15	0.012
	Post 1.24 ± 0.38	1.08± 0.28	0.0005
TMG mean (mmHg)	Pre 19.07 ± 6.91	16.39 ± 7.28	0.001
	Post 6.19 ± 3.02	6.54 ± 5.01	0.489
RVSP (mmHg)	Pre 55.51± 23.86	53.89 ± 22.8	0.57
	Post 37.18 ± 14.29	38.25 ± 12.07	0.61

Hemodynamic parameters	**Juvenile** (mean ± SD)	**Adult** (mean ± SD)	**P value**
PASP (mmHg)	Pre 56.04 ± 21.8	52.96 ± 20.84	0.22
	Post 41.33 ± 14.4	41.03 ± 15.87	0.87
PA mean (mmHg)	Pre 37.06 ± 14.56	34.26 ± 14.17	0.10
	Post 26.85 ± 10.22	25.92 ± 10.11	0.47
LA mean (mmHg)	Pre 24.43 ± 6.64	22.78 ± 6.62	0.029
	Post 14.13 ± 4.86	13.77 ± 5.36	0.542
LV ed (mmHg)	Pre 8.77 ± 3.06	9.51 ± 3.80	0.065
	Post 11.64 ± 3.91	11.87 ± 4.8	0.65
TMG (mmHg)	Pre 16.82 ± 5.86	15.63 ± 5.894	0.088
	Post 6.33 ± 2.98	6.06 ± 3.60	0.506
MVA (cm^2)	Pre 0.75 ± 0.21	0.77 ± 0.23	0.388
	Post 1.49 ± 0.50	1.51 ± 0.53	0.69
MVAI (cm^2/m^2)	Pre 0.58 ± 0.17	0.54 ± 0.15	0.022
	Post 1.16 ± 0.40	1.05 ± 0.37	0.033
CO (l/min)	Pre 3.55 ± 0.82	3.47± 0.84	0.43
	Post 4.22 ± 3.59	3.73 ± 0.91	0.13
CI ($l/min/m^{2)}$	Pre 2.79 ± 0.64	2.41 ± 0.50	<0.0001
	Post 3.28 ± 2.58	2.61 ± 0.58	0.0058

Hemodynamic parameters

PASP was 56.04 ± 21.8 and 52.96 ± 20.84mmHg pre BMV (p=NS) and 41.33 ± 14.4 and 41.03 ± 15.87mmHg post BMV (p =NS) in the juvenile and adult group, respectively. Mean LA pressure was 24.43 ± 6.64 and 22.78 ± 6.62mmHg (p= 0.029) prior procedure and 14.13 ± 4.86 and

13.77 ± 5.36mmHg post procedure (p =NS) in the juvenile and adult group, respectively. Juvenile group had higher LA pressure and significant fall in the LA pressure immediately after the procedure. Transmitral gradient was 16.82 ± 5.86 and 15.63 ± 5.894mmHg before procedure (p=0.08) and 6.33 ± 2.98 and 6.06 ± 3.60mmHg after procedure (p=0.5) in the juvenile and adult group, respectively.

MVA was 0.75 ± 0.21 and 0.77 ± 0.23cm^2 pre (p=NS) and 1.49 ± 0.50 and 1.51 ± 0.53cm^2 post (p= NS) and the indexed mitral valve area 0.58 ± 0.17 and 0.54 ± 0.15cm^2/m^2 pre (p=0.022) and 1.16 ± 0.40 and 1.05 ± 0.37cm^2/m^2 post (p=0.03) in the juvenile and adult group, respectively. Though the mitral valve area did not vary between the groups, indexed mitral valve area was higher in the juvenile group both pre and post procedure. Cardiac index was 2.79 ± 0.64 and 2.41 ± 0.50$l/min/m^2$ pre procedure (p = <0.0001) and 3.28 ± 2.58 and 2.61 ± 0.58$l/min/m^2$ post procedure (p= 0.005) in the juvenile and adult group, respectively.

Procedural aspects

Table 4. shows comparison of maximum dilatation with various balloons and devices between the two groups. Maximum mean dilatation combining both Inoue and Accura balloon is 23.75 ± 1.46mm in the juvenile group as compared to 24.24 ± 1.09mm in adults (p=0.0027). Maximum dilatation was significantly lower in the juvenile group when compared to the adults.

Table 4: Maximum dilatation between the groups

Device	**Juvenile (mean ± SD)**	**Adult (mean ± SD)**	**p value**	
Accura (mm)	23.63 ± 1.5	24.16 ± 1.1	0.0032	0.0027
Inoue (mm)	24.35 ± 1.13	24.78 ± 0.87	0.2225	
Cribier (mm)	38.87 ± 1.48	39.79 ± 0.77	0.0056	

Table 5. shows peri-procedural complications. Post procedure 31 (19.8%) juveniles and 25 (16.02%) adults developed ASD detected on colour flow Doppler (P=0.46). 1 patient (0.64%) in the juvenile group developed SVT and 2 patients (1.28%) in the juvenile group had transient AF, all of which terminated spontaneously and there were no peri-procedural arrhythmias in the adult group. 5 (3.2%) in juvenile group and 4 (2.5%) in adult group had AML tear (p=1) and 1 (0.64%) in adult group and none of the juveniles had PML tear (p=1). 2 patients (1.28%) in the adult group and none in the juvenile group developed severe commissural MR (p=0.49). All the leaflet tears in the juvenile group had moderate MR and did not progress to severe MR over the course and were kept on medical follow up. One leaflet tear and two commissural MR in the adult group underwent emergency MVR, whereas others had moderate MR and kept on medical follow up.

Table 5: Complications following BMV

	Juvenile, n (%)	Adult, n (%)	p value
SVT	1 (0.64)	0	1
Transient AF	2 (1.28)	0	0.49
ASD	31 (19.8)	25 (16.02)	0.46
Mechanism of MR			
AML tear	5 (3.2)	4 (2.5)	1
PML tear	0	1 (0.64)	1
Avulsion of papillary muscle	1 (0.64)	0	1
Commissural MR	0	2 (1.28)	0.49
MR severity			
Moderate MR	17 (10.89)	14 (8.97)	0.70
Severe MR	0	3 (1.92)	0.24
Emergency MVR	0	3 (1.92)	0.24
Systemic embolism			
Peripheral artery occlusion	4 (2.5)	2 (1.28)	0.68
TIA	1 (0.64)	0	1
Stroke	0	1 (0.64)	1
Seizure	0	1 (0.64)	1

17 (10.89%) in the juvenile group and 14 (8.97%) in the adult group (p=0.7) developed moderate MR and 3 (1.92%) adults and none of the juveniles developed severe MR (p=0.24). All the 3 adult patients who developed severe MR underwent emergency MVR with no perioperative complications. 4 (2.5%) of juveniles and 2 (1.28%) of adults developed peripheral arterial occlusion. 1 (0.64%) juvenile developed TIA and in the adult group 1 patient developed seizure and one patient developed stroke.

Follow up results

Echocardiographic parameters at 6 months between the two groups are shown in Table 6. LA size was 38.69 ± 6.18 and 41.05 ± 6.39mm in the juvenile and adult group, respectively (p = 0.043), but the indexed LA size was 31.17 ± 6.99 and 28.99 ± 5.66mm/m^2 (p = 0.065), respectively. 2D mitral valve area was 1.49 ± 0.39 and 1.66 ± 0.32cm^2 (p= <0.05) and indexed mitral valve area was 1.16 ± 0.27 and 1.17 ± 0.26 cm^2/m^2(p= NS) in the juvenile and adult group, respectively. Mitral valve area PHT was 1.44 ± 0.34 and 1.64 ± 0.39cm^2 (p= 0.002) and indexed mitral valve area was 1.14 ± 0.28 and 1.16 ± 0.32cm^2/m^2 (p= NS)) in the juvenile and adult group, respectively. Mean transmitral gradient was 7 .72 ± 4.77 and 6.03 ± 2.92mmHg (p= 0.01) in the juvenile and adult group, respectively. Right ventricular systolic pressure was 36.38 ± 13.39 and 31.68 ± 13.00mmHg (p= 0.1) in the juvenile and adult group, respectively.

Table 6: Echocardiographic parameters at 6 months

	Juvenile (mean ± SD)	**Adult** (mean ± SD)	**P value**
LA size (mm)	38.69 ± 6.18	41.05 ± 6.39	0.043
Indexed LA size (mm/m^2)	31.17 ± 6.99	28.99 ± 5.66	0.065
MVA (2D) (cm^2)	1.49 ± 0.39	1.66 ± 0.32	0.005
MVAI (2D) (cm^2/mm^2)	1.16 ± 0.27	1.16 ± 0.27	0.874
MVA PHT (cm^2)	1.44 ± 0.34	1.64 ± 0.39	0.002
MVAI (PHT) (cm^2/mm^2)	1.14 ± 0.28	1.16 ± 0.32	0.75
TMG mean (mmHg)	7 .72 ± 4.77	6.03 ± 2.92	0.01
RVSP (mmHg)	36.38 ± 13.39	31.68 ± 13.00	0.1

Echocardiographic parameters at 1-3 years of follow-up are shown in Table 7. LA size was 40.68 ± 6.86 and 42.57 ± 7.22mm in the juvenile and adult group, respectively (p = 0.07) and the indexed LA size was 31.96 ± 6.75 and 29.77 ± 5.52mm/m^2 (p = 0.017), respectively. 2D mitral valve area was 1.35 ± 0.42 and 1.51 ± 0.40cm^2 (p= 0.007) and indexed mitral valve area was 1.01 ± 0.29 and 1.03 ± 0.28cm^2/m^2 (p= NS) in the juvenile and adult group, respectively. Mitral valve area PHT was 1.36 ± 0.38 and 1.48 ± 0.36cm^2 (p= 0.02) and indexed mitral valve area was 1.07 ± 0.29 and 1.04 ± 0.29cm^2/m^2 (p= NS)) in the juvenile and adult group, respectively. Mean transmitral gradient was 10.05 ± 6.57 and 7.51 ± 5.21mmHg (p= 0.0027) in the juvenile and adult group, respectively. RV systolic pressure was 38.15 ± 18.35 and 33.78 ± 14.55mmHg (p= 0.134) in the juvenile and adult group, respectively.

Table 7: Echocardiographic parameters at 1-3 years

	Juvenile (mean ± SD)	**Adult** (mean ± SD)	**P value**
LA size (mm)	40.68 ± 6.86	42.57 ± 7.22	0.07
Indexed LA size (mm/m^2)	31.96 ± 6.75	29.77 ± 5.52	0.017
MVA (2D) (cm^2)	1.35 ± 0.42	1.51 ± 0.40	0.007
MVAI (2D) (cm^2/mm^2)	1.01 ± 0.29	1.03 ± 0.28	0.649
MVA PHT (cm^2)	1.36 ± 0.38	1.48 ± 0.36	0.02
MVAI (PHT) (cm^2/mm^2)	1.07 ± 0.29	1.04 ± 0.29	0.49
TMG mean (mmHg)	10.05 ± 6.57	7.51 ± 5.21	0.0027
RVSP (mmHg)	38.15 ± 18.35	33.78 ± 14.55	0.134

Echocardiographic parameters at 5 years are shown in Table 8. LA size was 42.42 ± 7.47 and 42.88 ± 7.19mm in the juvenile and adult group, respectively (p = 0.68) and the indexed LA size was 33.83 ± 8.59 and 30.52 ± 5.27mm/m^2(p = 0.0025), respectively. 2D mitral valve area was 1.19 ± 0.44 and 1.35 ± 0.32cm^2 (p= 0.0087) and the indexed mitral valve area was 0.95 ± 0.37and 0.95 ± 0.23cm^2/m^2 (p= NS) in the juvenile and adult group, respectively. Mitral valve area PHT was 1.19 ±

0.4 and 1.39 ± 0.37cm^2 (p= 0.002) and the indexed mitral valve area was 0.96 ± 0.36 and 0.98 ± 0.27cm^2/m^2 (p= NS)) in the juvenile and adult group, respectively. Mean transmitral gradient was 13.35 ± 8.42 and 8.71 ± 5.73mmHg (p= <0.0001) in the juvenile and adult group, respectively. RV systolic pressure was 46.97 ± 23.35 and 37.40 ± 15.90mmHg (p= 0.0086) in the juvenile and adult group, respectively.

Table 8: Echocardiographic parameters at 5 years

	Juvenile (mean ± SD)	**Adult** (mean ± SD)	**P value**
LA size (mm)	42.42 ± 7.47	42.88 ± 7.19	0.683
Indexed LA size (mm/m^2)	33.83 ± 8.59	30.52 ± 5.27	0.0025
MVA (2D) (cm^2)	1.19 ± 0.44	1.35 ± 0.32	0.0087
MVAI (2D) (cm^2/mm^2)	0.95 ± 0.37	0.95 ± 0.23	0.919
MVA PHT (cm^2)	1.19 ± 0.4	1.39 ± 0.37	0.002
MVAI (PHT) (cm^2/mm^2)	0.96 ± 0.36	0.98 ± 0.27	0.641
TMG mean (mmHg)	13.35 ± 8.42	8.71 ± 5.73	<0.0001
RVSP (mmHg)	46.97 ± 23.35	37.40 ± 15.90	0.0086

Echocardiographic parameters at the last mean follow up of 10.83 ± 6 years are shown in Table 9. LA size was 44.29 ± 8.06 and 43.90 ± 8mm in the juvenile and adult group, respectively (p = 0.805), and the indexed LA size was 35.80 ± 8.72 and 30.99 ± 6.29mm/m^2 (p = 0.0019), respectively. 2D mitral valve area was 1.26 ± 0.39 and 1.33 ± 0.35cm^2 (p= 0.36) and indexed mitral valve area was 1.03 ± 0.38 and 0.95 ± 0.24cm^2/m^2 (p= 0.18) in the juvenile and adult group, respectively. Mitral valve area PHT was 1.30 ± 0.36 and 1.34 ± 0.35cm^2 (p= 0.61) and the indexed mitral valve area was 1.09 ± 0.38 and 0.95 ± 0.25cm^2/m^2 (p= 0.045) in the juvenile and adult group, respectively. Mean transmitral gradient was 11.67 ± 6.23 and 8.11 ± 3.7mmHg (p= 0.0005) in the juvenile and adult group, respectively. RV systolic pressure was 42.11 ± 17.31 and 36.05 ± 14.71mmHg (p= 0.097) in the juvenile and adult group, respectively.

Table 9: Echocardiographic parameters at Last follow up (mean 10.83 ± 6 years)

	Juvenile (mean ± SD)	**Adult** (mean ± SD)	**P value**
LA size (mm)	44.29 ± 8.06	43.90 ± 8	0.805
Indexed LA size (mm/m^2)	35.80 ± 8.72	30.99 ± 6.29	0.0019
MVA (2D) (cm^2)	1.26 ± 0.39	1.33 ± 0.35	0.36
MVAI (2D) (cm^2/mm^2)	1.03 ± 0.38	0.95 ± 0.24	0.18
MVA PHT (cm^2)	1.30 ± 0.36	1.34 ± 0.35	0.61
MVAI (PHT) (cm^2/mm^2)	1.09 ± 0.38	0.95 ± 0.25	0.045
TMG mean (mmHg)	11.67 ± 6.23	8.11 ± 3.7	0.0005
RVSP (mmHg)	42.11 ± 17.31	36.05 ± 14.71	0.097

Figures 1-8 show the linear trends of echocardiographic parameters between the two groups over the mean follow up of 10.83± 6 years.

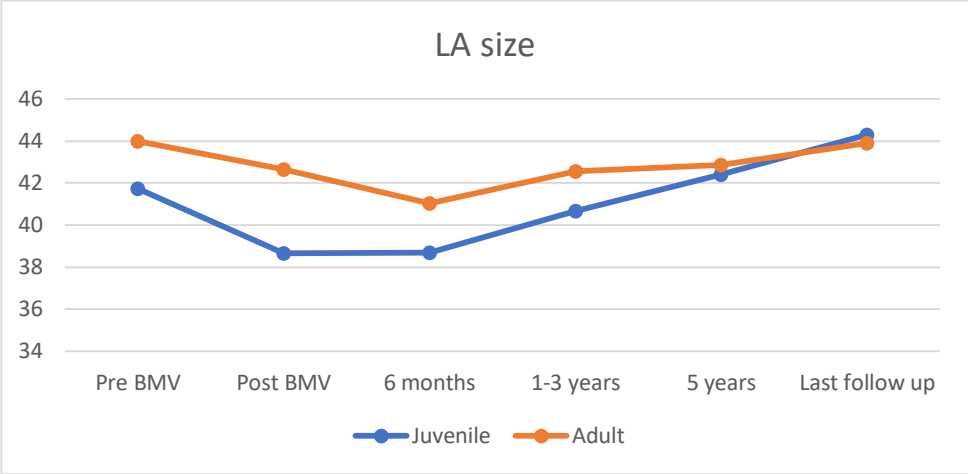


Fig 1: shows the comparison of LA size between the juvenile and adult group over the long term follow up (mean follow up- 10.83 ± 6 years)

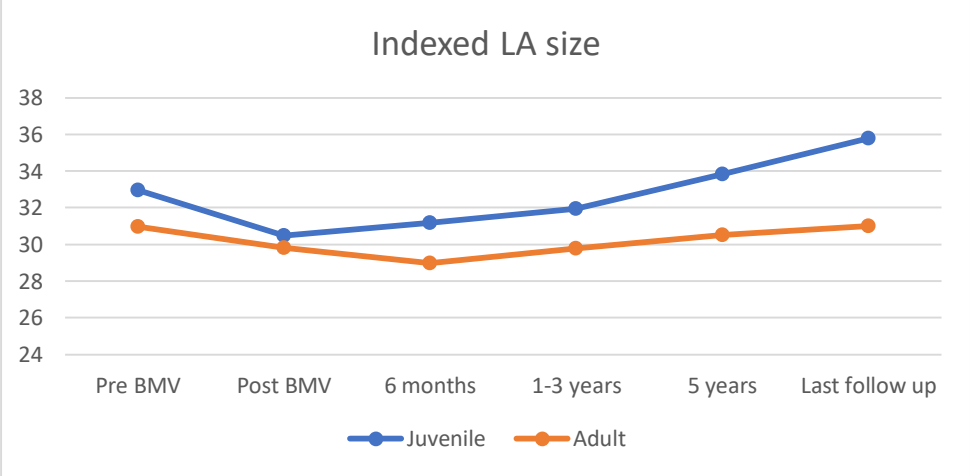


Fig 2: shows the comparison of indexed LA size between the juvenile and adult group over the follow up

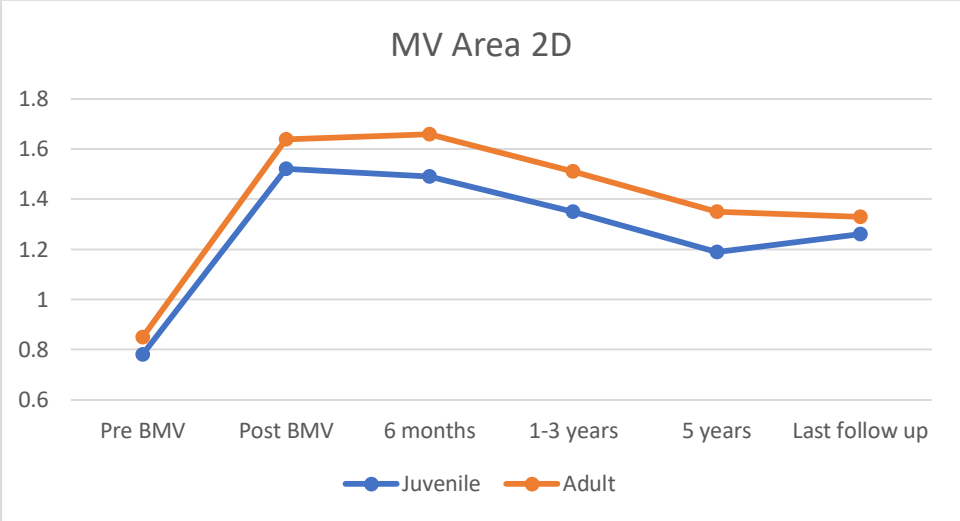


Fig 3: shows the comparison of 2D Mitral valve area between the juvenile and adult group over the follow up

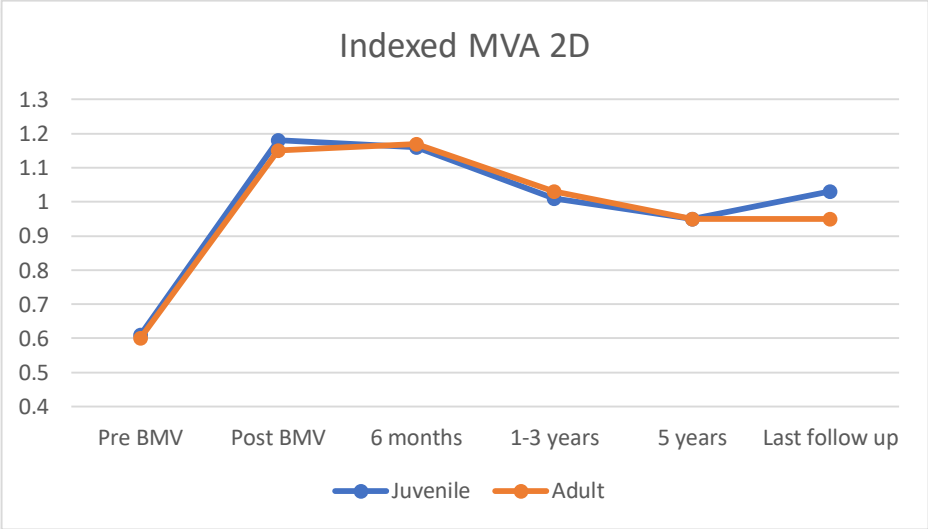


Fig 4: shows the comparison of indexed 2D Mitral valve area between the juvenile and adult group over the follow up

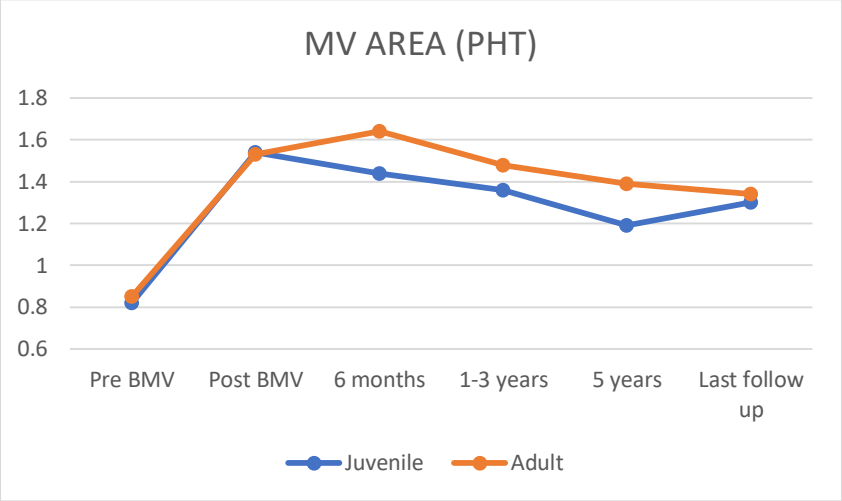


Fig 5: shows the comparison of Mitral valve area PHT between the juvenile and adult group over the follow up

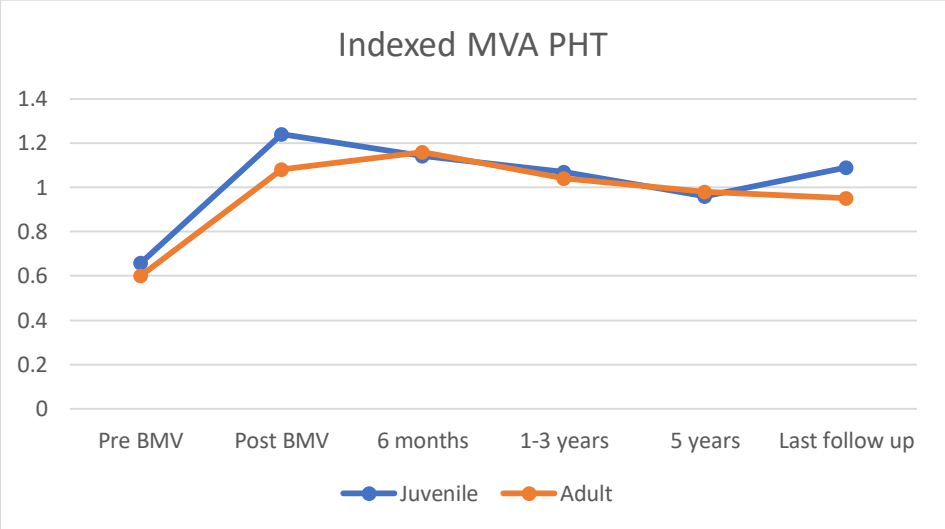


Fig 6: shows the comparison of indexed Mitral valve area PHT between the juvenile and adult group over the follow up

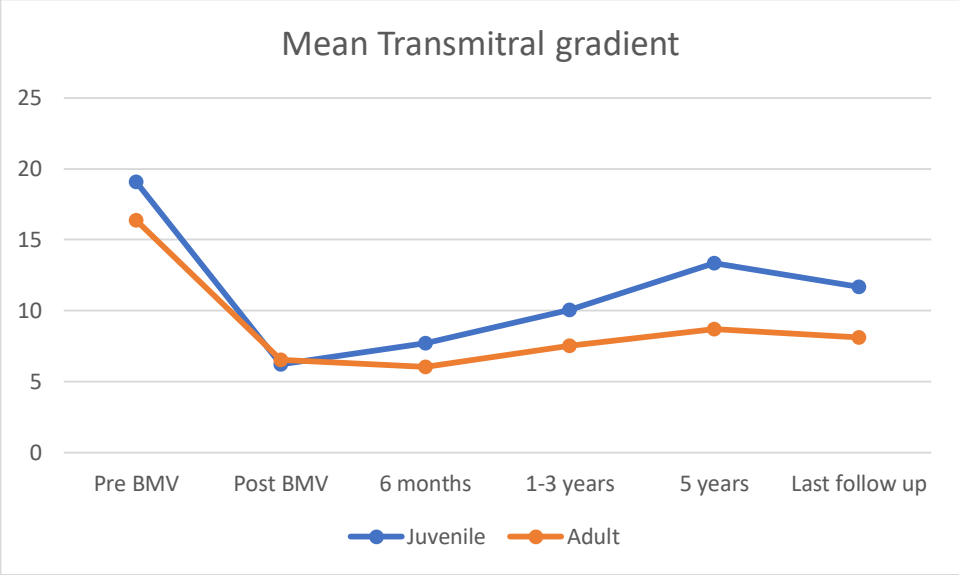


Fig 7: shows the comparison of mean transmitral gradient between the juvenile and adult group over the follow up

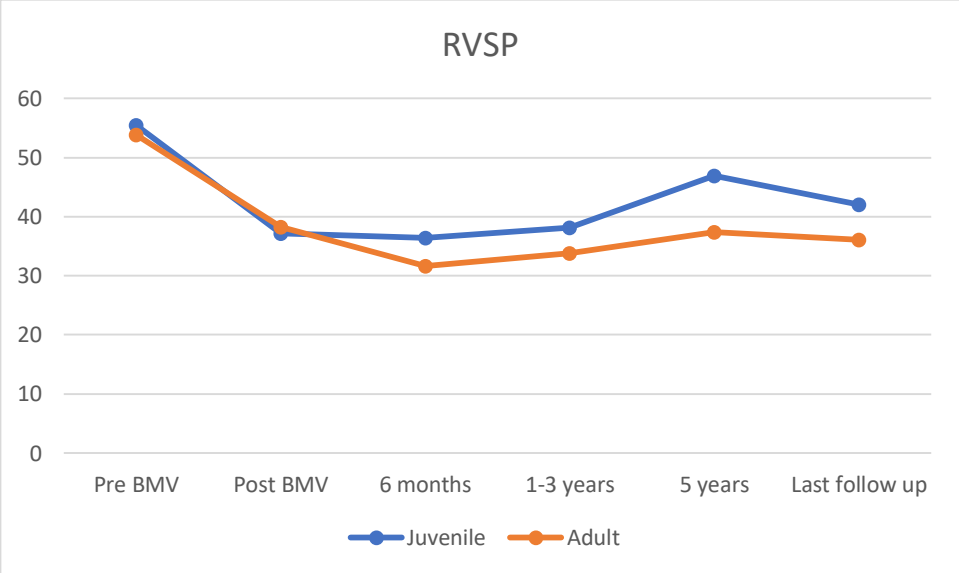


Fig 8: shows the comparison of RV systolic pressure between the juvenile and adult group over the follow up

Restenosis

79 (50.64%) patients in the juvenile group and 60 (37.82%) in the adult group had restenosis (p=0.04). Time to 1st restenosis in the juvenile group was 6.46 ± 4.23 years and in the adult group was

10.32 ± 6.21 years. 32 of the patients (20.51%) had 2nd restenosis over 6.23 ± 4.05 years in the juvenile group and in the adult group 13 (8.33%) of them had 2nd restenosis over 7.92 ± 3.2 years. 12 (7.69%) in juvenile group and 2(1.28%) in adult group had 3rd restenosis; juveniles developed it over the mean period of 7 ± 4.04 years. 2 patients (1.28%) in the juvenile group had restenosis for the 4th time over a period of 5.5 ± 4.94 years. Table 10. shows the rate of restenosis and the time to restenosis between the two groups.

Table 10: Number of restenosis and time to restenosis between the two groups

	Juvenile	**Adult**	**P value**
No. of restenosis (%)	79 (50.64)	60 (37.82)	0.04
Times of restenosis (mean±SD)	1.59 ± 0.82	1.25 ± 0.48	
1 restenosis, n (%)	79 (50.64)	60 (37.82)	
2 restenosis, n (%)	32 (20.51)	13 (8.33)	
3 restenosis, n (%)	12 (7.69)	2 (1.28)	
4 restenosis, n (%)	2 (1.28)		
Time to 1st restenosis, years (n)	6.46 ± 4.23 (79)	10.32 ± 6.21(60)	
Time to 2nd restenosis, years (n)	6.23 ± 4.05 (32)	7.92 ± 3.2 (13)	
Time to 3rd restenosis, years (n)	7 ± 4.04 (12)	0.9 ± 0.14 (2)	
Time to 4th restenosis, years (n)	5.5 ± 4.94 (2)		

Analysing the freedom from restenosis with the Kaplan Meir survival curve (figure 9), adults had higher freedom from restenosis at 5 years, 10 years upto 23 years when compared to juvenile group with log rank of 15.53 (p =0.000). Freedom from restenosis in the juvenile group was 64% at 5 years, 16% at 10 years and 5% at 15 and 20 years whereas in the adult group it was 82% at 5 years, 38% at 10 years and 19% at 15 years and 10% at 20 years.

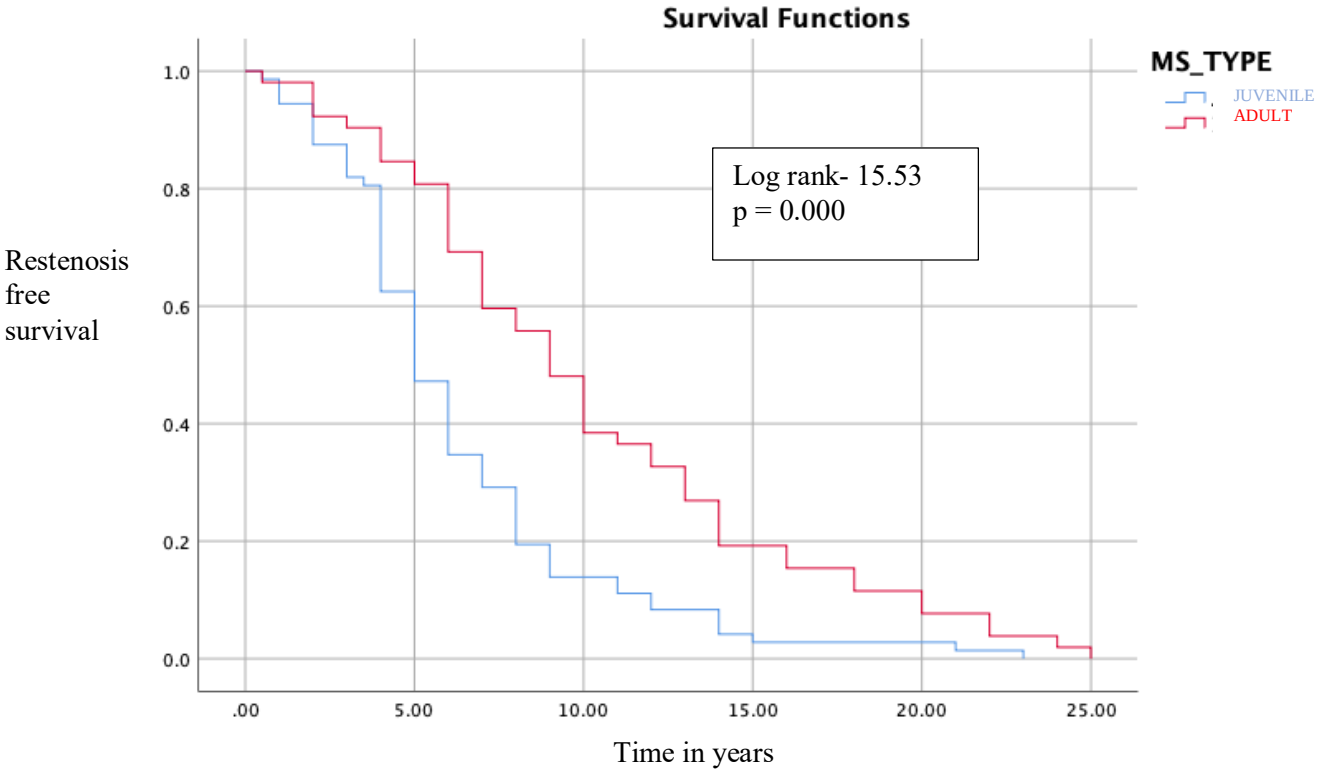


Figure 9: Kaplan Meir curve showing the freedom from restenosis between the two groups

Long term Complications

Over the long term mean follow up of 10.83± 6 years (range- 0.25-23.6 years) 15 (9.6%) of juvenile patients and 35 (22.4%) of adult patients were in atrial fibrillation (p = 0.0031). 10 of the juveniles and 13 of the adults had developed new onset AF during the course. Left ventricular dysfunction was seen in 3 (1.9%) of the juveniles and 6 (3.8%) of the adults (p = 0.5). 21 (13.4%) of juveniles and 20 (12.8%) of adults underwent Mitral valve replacement (p=1). None of the juveniles had progression of aortic valve disease whereas 7 (4.4%) adults underwent DVR (p=0.014). 8 (5.1%) juveniles and 13 (8.3%) adults developed stroke (p=0.36). 4 (2.5%) adults had documented seizures which could be possible TIA or seizure disorder whereas none of the juveniles had (p=0.12). 3 adults (1.9%) expired all of them due to massive stroke and there was no mortality in the juvenile group, among the patients who were followed up. Table 11. shows long term complications between the two groups.

Table 11: Long term complications

	Juvenile, n (%)	**Adult, n (%)**	**P value**
AF	15 (9.6)	35 (22.4)	0.0031
LV dysfunction	3 (1.9)	6 (3.8)	0.5
MVR	21 (13.4)	20 (12.8)	1

DVR	0	7 (4.4)	0.014
Stroke	8 (5.1)	13 (8.3)	0.36
Seizure	0	4 (2.5)	0.12
Mortality	0	3 (1.9)	0.24

Predictors of restenosis

Table 12. shows the predictors of restenosis using multivariate analysis. Age, H/o prior CMV, H/o prior BMV were related to restenosis. MR by echocardiography, PA pressure and cardiac output prior to the BMV as estimated by catheterization predicted the restenosis. Post procedure indexed LA size by echocardiography; mean PA pressure, Mitral valve area and indexed mitral valve area by catheterization predicted restenosis. Mitral valve area by Doppler, mean transmitral gradient and RV systolic pressures at 6 months are also early predictors of restenosis by echocardiography. Whereas H/o rheumatic fever, higher inflammatory markers, Wilkin's score, sex, rhythm did not predict the restenosis.

Table 12: Predictors of restenosis using multivariate analysis

Variable	P value
History and Clinical parameters	
Age	0.008
Sex	0.13
BSA	0.018
H/o rheumatic fever	0.54
Prior CMV	0.000
Prior BMV	0.005
NYHA class	0.31
Heart failure	0.52
Rhythm	0.805
ESR	0.538
TLC	0.597
Echocardiographic parameters prior BMV	
LA size	0.928
Indexed LA size	0.638
MVA 2D	0.799
MVAI 2D	0.859
MVA PHT	0.290
MVAI PHT	0.390
Mean transmitral gradient	0.64
Wilkin's	0.484
RVSP	0.437
MR	0.005
Hemodynamic parameters prior BMV	
PA systolic pressure	0.012
PA mean pressure	0.007
LA pressure	0.075
LV ed	0.021
Transmitral gradient	0.647
MVA	0.053

MVAI	0.353
Cardiac output	0.012
Cardiac index	0.202
Echocardiographic parameters post BMV	
LA size	0.244
Indexed LA size	0.024
MVA 2D	0.219
MVAI 2D	0.519
MVA PHT	0.751
MVAI PHT	0.707
Mean transmitral gradient	0.469
RVSP	0.225
MR	0.205
Hemodynamic parameters post BMV	
PA systolic pressure	0.052
PA mean pressure	0.042
LA pressure	0.249
LV ed	0.799
Transmitral gradient	0.375
MVA	0.000
MVAI	0.012
Cardiac output	0.091
Cardiac index	0.185
MR severity	0.613
Procedural aspects	
Maximum balloon dialatation	0.085
Procedural success	0.211
Echocardiographic parameters at 6 months post BMV	
LA size	0.065
Indexed LA size	0.337
MVA 2D	0.113
MVA 2D indexed	0.098
MVA PHT	0.01
MVA PHT indexed	0.034
Mean transmitral gradient	0.001
RVSP	0.003

DISCUSSION

DISCUSSION

We studied 156 juvenile mitral stenosis patients who underwent BMV from 1995 to 2017 and followed them upto July 2020. These patients were compared to 156 adult mitral stenosis patients who underwent BMV within two or three days of the procedure of the juvenile mitral stenosis patients. Till date, there are reports of immediate results[22, 14] and intermediate[19,17] follow up of juvenile mitral stenosis following balloon valvotomy. Long term results[12,23] till date with the maximum follow-up has been reported by Fawzy et al[13] with a mean follow up of 8.5 ± 4.8 years (range 1.5-18 years). Except for Sinha et al[19] who reported 193 patients with juvenile mitral stenosis, to the best of our knowledge ours is the largest study followed up for the longest period with a mean follow up of 10.83 ± 6 years (range- 0.25 - 23.6 years)

33.3% were males in the juvenile group whereas 16.6% of adult patients were males. Unlike as reported by Roy et al[7] our juvenile group had higher number of females when compared to males, though there were relatively higher number of males in the juvenile group compared to adults. Gamra et al.[12] did not find any male predominance in the juvenile group. History of rheumatic fever was present in 34 (21.7%) and 32 (20.5%)of patients with juvenile and adult groups respectively (P= 0.88). There was no difference in the history of rheumatic fever, reactivation of rheumatic fever or any evidence of infection or inflammation as noted by ESR and TLC between the two groups and thus could not explain our hypothesis of more restenosis due to recurrent rheumatic activity[30,31]. This was similar to the other study of mitral valve restenosis which did not show any association with hs-CRP[32].

NYHA functional class was similar between the two groups as demonstrated by Gamra et al[12] and other studies[14] whereas Bahl et al[22] reported 75% to be in NYHA III and 25% in NYHA IV. Our study also showed higher atrial fibrillation in adults as shown by all other previous studies. Wilkin's echo score was lower in juveniles when compared to adults supporting more pliable mitral valve in young as demonstrated by other studies[12].

Immediate results

Adults had larger LA size, but the indexed left atrial size was higher in the juvenile group. Post procedure the decrease in the left atrial size was relatively higher in the juvenile group. Left atrial size was significantly higher in the adult group compared to the juvenile patients in all other studies though none reported left atrial size indexed to the body surface area.

2D mitral valve area and indexed mitral valve area 2D did not vary much between the groups similar to Gamra et al[12]. Though mitral valve area PHT was similar, indexed mitral valve area by PHT was higher in the juvenile group. Fawzy et al.[13], though had a smaller Doppler derived mitral valve area prior to procedure in juvenile group, they did not index with body surface area which must have

led to significant difference. As noted by Gamra et al[12] and Bahl et al[22], we did not notice acute gain in the mitral valve area much larger when compared to adults. We did not find any difference after indexing the 2D MVA but there was significant gain in the MVA index derived by Doppler method. As Doppler derived MVA is not reliable in the acute setting of BMV[33] it was not given due consideration. Even at catheterization, though the mitral valve area did not vary between the groups, indexed mitral valve area was higher in juvenile group both pre and post procedure.

Mean transmitral gradient by Doppler was higher in the juvenile group prior procedure with no difference post procedure indicating higher fall in the LA pressures immediately in the juvenile group. Adding on, juvenile group had higher mean LA pressure on catheterization whereas as no significant difference in LA pressures post procedure highlighting the greater fall in LA pressure immediately after the procedure. However there was no difference in transmitral gradient on catheterization.

Juvenile mitral stenosis patients are reported to have higher PA pressures and higher fall in PA immediately post BMV[19]. we did not find difference in PA pressures as measured by RV systolic pressure by echocardiography and during catheterization in both the groups prior and post procedure and significant fall off pressure was noted in both the groups post BMV as shown similarly by Fawzy et al[13].

Procedural aspects

Maximum balloon dilatation diameter was significantly lower in the juvenile group when compared to the adults. Procedural success was seen in 89.1% in juvenile group and 87.8% in adult group. Neither the maximum balloon dilatation nor the procedural success predicted restenosis on follow up. Immediate complications were similar between both the groups. Moderate MR was similar between the groups whereas three adults developed severe MR who underwent emergency MVR.

Follow up results

On follow up 96.1%, 85.9%, 73%in the juvenile group and 96.1%, 83.3%, 73.7% in the adult group were < NYHA class II at 6 months, 1-3 year and 5 year follow up suggesting similar results between the two groups over 5 year follow up similar to other studies with good intermediate results[23].

Comparing the echocardiographic parameters between the groups transmitral gradient started to rise significantly in the juvenile group at 6 months. MVA began to fall in the juvenile group from 6th month of follow up though there was no difference in the indexed mitral valve area. Indexed LA size was found to be higher in the juvenile group from 1-3 year of follow up. Though the difference in RV

systolic pressures were noted only at 5 year follow up indicating the progression to restenosis from then.

Restenosis

50.64% patients in the juvenile group and 37.82% in the adult group had restenosis. Time to 1st restenosis in the juvenile group was 6.46 ± 4.23 years and in the adult group was 10.32 ± 6.21 years. 32 of the patients (20.51%) had 2nd restenosis over 6.23 ± 4.05 years in the juvenile group and in the adult group 13 (8.33%) of them had 2nd restenosis over 7.92 ± 3.2 years. 12 (7.69%) in juvenile group and 2(1.28%) in adult group had 3rd restenosis; juveniles developing it over the mean period of 7 ± 4.04 years. 2 patients (1.28%) in the juvenile group had restenosis for the 4th time over a period of 5.5 ± 4.94 years.

Analysing the freedom from restenosis with the Kaplan Meir survival curve, adults had higher freedom from restenosis at 5 years, 10 years upto 23 years when compared to juvenile group with log rank of 15.53 (p =0.000). Contradicting to other long term studies[12], which showed there was no significant difference in the freedom from restenosis and event free survival between the two groups. Fawzy et al.[13] showed actuarial freedom from restenosis at 10, 15, and 18 years for juvenile and adult groups were 78% ± 7%, 64% ± 9%, and 18% ± 14% and 77% ± 2%, 43% ± 4%, and 17% ± 4%, respectively (P = 0.26).

Since ours is a longer term follow up it may depict the natural course of juvenile mitral stenosis patients post balloon mitral valvotomy and the rate of restenosis much better.

Reintervention

53 patients in juvenile group and 28 patients in the adult group had repeat PMV done with the procedural success of 84.9% in juveniles and 82.14% in adults. Among them 16 juveniles and 2 adults underwent PMV thrice with procedural success of 87.5% in juveniles and both of the adults. 2 juveniles had the procedure 4 times with optimal results.

Long term Complications

Over the long term mean follow up of 10.83± 6 years (range- 0.25-23.6 years), 9.6% of juvenile patients and much higher about 22.4% of adult patients were in atrial fibrillation. 10 of the juveniles and 13 of the adults had developed new AF during the course. No difference in mitral valve replacement among the groups. None of the juveniles had progression of aortic valve disease whereas 7 (4.4%) adults underwent DVR . No much difference in stroke and seizure in both groups. 3 adults (1.9%) expired all of them due to massive stroke and there was no expiry in the juvenile group among the followed individuals.

Predictors of restenosis

Age, prior CMV, prior BMV were related to restenosis. MR, PA pressure and cardiac output were the factors prior to BMV that predicted the restenosis. Post procedure indexed LA size by echocardiography; mean PA pressure, Mitral valve area and indexed mitral valve area by catheterization predicted restenosis. Mitral valve area by Doppler, mean transmitral gradient and RV systolic pressures at 6 months are also early predictors of restenosis by echocardiography. Whereas history of rheumatic fever, higher inflammatory markers, Wilkin's score, sex, rhythm did not predict the restenosis in our study.

LIMITATIONS

LIMITATIONS

1. Ours is a retrospective study and all the procedures were done before the start of data collection. Echo score depended on the data documented which would have been a subject of variation. This might have accounted for our Wilkin's echo score not predicting the restenosis.
2. Body surface area was taken at the time of the procedure which was used over the entire follow up course. Indexed values may not be depicting the true figures.
3. We have used 3 different gadgets (Accura balloon, Inoue balloon and Cribier devices) for the procedure, which may be one of the factor for our long term results varying with other studies with single device.
4. Attrition in our study group was 6.5% over a mean follow up of 10.83± 6 years (range- 0.25 - 23.6 years) which would have led to bias in the calculated freedom from restenosis.

CONCLUSIONS

CONCLUSION

1. BMV is safe and effective in juvenile mitral stenosis with immediate results similar to adults.
2. Atrial fibrillation is more common in adults. Male preponderance is noted in the juvenile group as compared to adults.
3. Juvenile mitral stenosis have a higher transmitral gradient and higher LA pressures with a rapid fall in LA pressures immediately after BMV. No significant difference in indexed mitral valve area and PA pressures were noted between the groups.
4. Freedom from restenosis was much higher in the adult group as compared to juveniles.
5. Age, previous commissurotomy; MR, PA pressure prior to BMV; PA pressure and mitral valve area by catheterization post BMV predicted the restenosis. Post procedure indexed LA size; mitral valve area by doppler, mean transmitral gradient and RV systolic pressures at 6 months are also early predictors of restenosis by echocardiography.
6. BMV is also safe and effective in juvenile patients with previous commissurotomy.

REFERENCES

REFERENCES

1. Zaky Adib, Nasser William K., Feigenbaum Harvey. A Study of Mitral Valve Action Recorded by Reflected Ultrasound and Its Application in the Diagnosis of Mitral Stenosis. Circulation. 1968 May 1;37(5):789–99.

2. Cutler EC, Levine SA. Cardiotomy and valvulotomy for mitral stenosis. Boston Med Surg J 1923; 188: 1023. - Google Search [Internet]. [cited 2020 Aug 2].

3. Inoue K, Owaki T, Nakamura T, Kitamura F, Miyamoto N. Clinical application of transvenous mitral commissurotomy by a new balloon catheter. J Thorac Cardiovasc Surg. 1984 Mar;87(3):394–402.

4. S Padmavati. Rheumatic fever and rheumatic heart disease in India at the turn of the century. Indian Heart J. 53:35–7.

5. Jose VJ, Gomathi M. Declining prevalence of rheumatic heart disease in rural schoolchildren in India: 2001-2002. Indian Heart J. 2003 Apr;55(2):158–60.

6. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. Lancet Lond Engl. 2006 Sep 16;368(9540):1005–11.

7. Sb R, Ml B, Ej L, V R. JUVENILE MITRAL STENOSIS IN INDIA. Lancet Lond Engl. 1963 Dec 1;2(7319):1193–5.

8. Mishra TK, Rath PK, Mohanty NK et al. Juvenile chronic RHD, our decade long experience (Abstr.).Indian Heart J 1999;51:653. - Google Search [Internet]. [cited 2020 Aug 2].

9. Inoue K, Hung JS. Percutaneous transvenous mitral commisurotomy (PTMC): the Far East Experience. In Topol EJ (ed): ''Test book of Interventional Cardiology," 2nd Edition, Philadelphia: WB Saunders, 1994, PP 1226-1242. - Google Search [Internet]. [cited 2020 Aug 2].

10. Arora R, Karla GS, Murty GSR, Trehan V. Jolly N, Mohan JC, Sethi KK, Nigam M, Khalilullah M. Percutaneous transatrial mitral commissurotomy: immedi ate and intermediate results. J Am Coll Cardiol 1994, 23: 1327- 1332. - Google Search [Internet]. [cited 2020 Aug 2].

11. Shaw TRD, Sutaria N, Prendergast B. Clinical and haemodynamic profiles of young, middle aged, and elderly patients with mitral stenosis undergoing mitral balloon valvotomy. Heart. 2003 Dec;89(12):1430–6.

12. Gamra H. Balloon mitral commissurotomy in juvenile rheumatic mitral stenosis: a ten-year clinical and echocardiographic actuarial results. Eur Heart J. 2003 Jul;24(14):1349–56.

13. Fawzy ME, Stefadouros M, Amraoui SE, Osman A, Ibrahim I, Nowayhed O, et al. Long-Term (Up to 18 Years) Clinical and Echocardiographic Results of Mitral Balloon

Valvuloplasty in Children in Comparison with Adult Population. J Intervent Cardiol. 2008 Jun;21(3):252–9.

14. Karur S, Veerappa V, Nanjappa MC. Balloon Mitral Valvotomy in Juvenile Rheumatic Mitral Stenosis: Comparison of Immediate Results with Adults. Heart Lung Circ. 2014 Dec;23(12):1165–8.

15. Shrivastava S, Chandra YV, Krishnamoorthy KM, Radhakrishnan S. Mitral valvotomy with the Inoue balloon in juvenile rheumatic mitral stenosis. Am J Cardiol. 1995 Aug 15;76(5):404–6.

16. Harikrishnan S, Nair K, Tharakan JM, Titus T, Kumar VKA, Sivasankaran S. Percutaneous transmitral commissurotomy in juvenile mitral stenosis—comparison of long term results of Inoue balloon technique and metallic commissurotomy. Catheter Cardiovasc Interv. 2006 Mar;67(3):453–9.

17. Joseph PK, Bhat A, Francis B, Sivasankaran S, Kumar A, Pillai VR, et al. Percutaneous transvenous mitral commissurotomy using an Inoue balloon in children with rheumatic mitral stenosis. Int J Cardiol. 1997 Oct;62(1):19–22.

18. NDLI Presents: Immediate and intermediate term results of percutaneous transmitral commissurotomy in juvenile mitral stenosis(1).Clinical, hemodynamic, andiographic study of patients with pulmonary atresia and intact ventricular septum(2) [Internet]. [cited 2020 Aug 7]. Available from: https://www.ndl.gov.in/document/UWJHNStScHFJZGpnMlZTeGJLTittM0Nya0tOMEZqRldpRjNaa3oyOHQvdz0

19. Immediate and follow up results of Inoue balloon mitral valvotomy in juvenile rheumatic mitral stenosis. - Abstract - Europe PMC [Internet]. [cited 2020 Aug 25]. Available from: https://europepmc.org/article/med/9427127

20. Gupta S, Vora A, Lokhandwalla Y, Kerkar P, Gupta S, Kulkarni H, et al. Percutaneous balloon mitral valvotomy in mitral restenosis. Eur Heart J. 1996 Oct 2;17(10):1560–4.

21. Rafla S, Bishay T. Does Mitral Valve Commissural Calcification Predicts Restenosis at Long-Term Follow-up After Percutaneous Balloon Mitral Valvuloplasty? Cardiol Cardiovasc Med [Internet]. 2020 [cited 2020 Aug 6];04(01). Available from: http://www.fortunejournals.com/articles/does-mitral-valve-commissural-calcification-predicts-restenosis-at-longterm-followup-after-percutaneous-balloon-mitral-valvuloplas.html

22. Bahl VK, Chandra S, Kothari SS, Talwar KK, Sharma S, Kaul U, et al. Percutaneous transvenous mitral commissurotomy using Inoue catheter in juvenile rheumatic mitral stenosis. Cathet Cardiovasc Diagn. 1994;Suppl 2:82–6.

23. Zaki A, Salama M, El Masry M, Elhendy A. Five-year follow-up after percutaneous balloon mitral valvuloplasty in children and adolescents. Am J Cardiol. 1999 Mar;83(5):735–9.

24. Kothari SS, Kamath P, Juneja R, Bahl VK, Airan B. Percutaneous transvenous mitral commissurotomy using Inoue balloon in children less than 12 years. Cathet Cardiovasc Diagn. 1998 Apr;43(4):408–11.

25. Wilkins GT, Weyman AE, Abascal VM, Block PC, Palacios IF. Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism of dilatation. Br Heart J. 1988 Oct;60(4):299–308.

26. Helmcke F, Nanda NC, Hsiung MC, Soto B, Adey CK, Goyal RG, et al. Color Doppler assessment of mitral regurgitation with orthogonal planes. Circulation. 1987 Jan;75(1):175–83.

27. Feldman T, Herrmann HC, Inoue K. Technique of percutaneous transvenous mitral commissurotomy using the Inoue balloon catheter. Cathet Cardiovasc Diagn. 1994;Suppl 2:26–34.

28. Lau K-W, Hung J-S. A simple balloon-sizing method in Inoue-balloon percutaneous transvenous mitral commissurotomy. Cathet Cardiovasc Diagn. 1994;33(2):120–9.

29. Herrmann HC, Ramaswamy K, Isner JM, Feldman TE, Carroll JD, Pichard AD, et al. Factors influencing immediate results, complications, and short-term follow-up status after Inoue balloon mitral valvotomy: a North American multicenter study. Am Heart J. 1992 Jul;124(1):160–6.

30. Rifaie O, Abdel–Rahman MA, Desoky A, Omar AMS. Does a Chronic Inflammatory State Have a Role in Predicting Mitral Restenosis After Balloon Mitral Valvuloplasty? J Am Coll Cardiol. 2013 Mar 12;61(10 Supplement):E2014.

31. Harikrishnan S, Rajeev E, Tharakan JA, Thomas T, Ajith K, Sivasankaran S, et al. Acute phase reactants predict mitral regurgitation following mitral valvuloplasty. Int J Cardiol. 2006 Sep;112(1):127–9.

32. Ostovan M, Aslani A, Abounajmi S, Razazi V. Mitral valve restenosis after percutaneous transmitral valvuloplasty, role of continuous inflammation. J Cardiovasc Thorac Res. 2014;6(3):191–5.

33. Thomas JD, Wilkins GT, Choong CY, Abascal VM, Palacios IF, Block PC, et al. Inaccuracy of mitral pressure half-time immediately after percutaneous mitral valvotomy. Dependence on transmitral gradient and left atrial and ventricular compliance. Circulation. 1988 Oct;78(4):980–93.

APPENDIX

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

Institutional Ethics Committee

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

SCT/IEC/1301/OCTOBER-2018

27.11.2018

Dr. Shrusthi Walad
Senior Resident
Department of Cardiology
SCTIMST, Thiruvananthapuram

Dear Dr. Shrusthi Walad,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "IMMEDIATE AND LONG TERM OUTCOMES OF BALLOON MITRAL VALVOTOMY IN JUVENILE MITRAL STENOSIS IN COMPARISION WITH ADULT MITRAL STENOSIS (IEC/1301)" on 26th October, 2018.

The following documents were reviewed:

Original submission

1. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 26.09.2018 with check list*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Forwarding Letter from the HOD*
7. *Letter regarding the consent waiver*
8. *CV of Principal Investigator and Co-Principal Investigators*

Revised submission

1. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 23.11.2018 with check list*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Forwarding Letter from the HOD*
7. *CV of Principal Investigator and Co-Principal Investigators*

The following members of the Ethics Committee were present at the meeting held on 26th October, 2018 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

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

IEC Decision

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

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

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

Sincerely,

Mala Ramanathan
Member Secretary, IEC

PROFORMA

Immediate and long term outcomes of Balloon mitral valvotomy in Juvenile mitral stenosis in comparision with adult mitral stenosis

Name:
Age :
Sex:
Cat: Hos No:
BMV Date: Re BMV Date:
Duration of follow up: Ht /Wt / BSA:

Parameters	Pre BMV	Post BMV	6 Months	1-3 Years	5 year	Last
Clin & lab						
FC						
Rhythm						
ECHO data						
LA Sixe						
MVA (2D)						
MVA(PHT)						
Indexed MVA						
MS Grad						
Wilkins						
Mobility						
Calcification						
Thickening						
SVP						
MC						
LC						
MR(0-4)						
AR(0-4)						
AS Grade						
OTVD						
RVSP						
CATH Data						
PAP						
LA						
LV						
TMG						
MVA						
Indexed MVA						
CO						
CI						

1st BMV

Dilator /Balloon Used :

Size :

No. of dilatations :

MR Severity :

Acute complications:

Length of Hospital Stay:

Re BMV

Dilator /Balloon Used :

Size :

No. of dilatations :

MR Severity :

Acute complications:

Length of Hospital Stay:

CONSENT WAIVER FORM

From,
Dr. SHRUSTHI WALAD
Senior Resident,
Cardiology,
SCTIMST

4/8/2018

To,
Technical Advisory Committee
SCTIMST

Dear Sir/ Madam,

I am proposing for a study "**Immediate and long term outcomes of Balloon mitral valvotomy in Juvenile mitral stenosis in comparision with adult mitral stenosis".** It is an observational model study with retrospective data collection and prospective follow up of patient data from medical records. There is no need for consent as it is retrospective study and data will be taken only from medical records. Kindly acknowledge the study and do the needful .

Thanking you

Yours faithfully,

Dr. SHRUSTHI WALAD
SR, Cardiology

Date- 4/8/2018
PLACE- SCTIMST

URKUND

Document Information

Analyzed document	Srushti edited HKS.docx (D78380337)
Submitted	8/31/2020 7:57:00 AM
Submitted by	Dr Harikrishnan S
Submitter email	drhari@sctimst.ac.in
Similarity	10%
Analysis address	drhari.sctims@analysis.urkund.com

W	
W	
W	
W	
W	
J	
W	
W	
W	
W	
W	
SA	

URKUND

W

SA

W

W

SA

W