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Early and Mid-Term Outcomes of Mitral Valve Repair in the Pediatric Age Group

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ABSTRACT

Background: *Mitral valve (MV) disease in children remains a tough challenge because of the varied pathology, heterogeneous lesions and coexisting cardiac anomalies. Surgical management of mitral regurgitation (MR) in the pediatric population remains a challenge because of the heterogeneity of the lesions, requirement for growth potential, and necessity of avoiding mitral valve (MV) replacement. Various non-standardized repair techniques have been reported in children with congenital MV disease. Evaluation the early and midterm results of surgical repair of mitral valve in the pediatric age and the impact of the type of the pathology, the method of repair used on the outcome.* ***Methods:*** *a total of sixty children -all are human- with mitral valve diseases were operated upon by mitral valve repair and followed-up during the period from August 2014 and April 2018 at Al-Housein University hospital and Atfal Masr insurance hospital.* ***Results*** *(59 cases excluding one case of immediate postoperative mortality) and midterm postoperatively at 6 months (57 cases excluding 1 early mortality and one early reoperation revision by replacement. In early postoperative follow up EF%, FS, LVED, LVES, LA, PASP their improvement statistically, non-significant when compared with the preoperative data, on the contrary follow up 6 months later there were statistically significant improvement when compared with the preoperative data.* ***Conclusions:*** *Mitral valve repair in children is a safe procedure with early and midterm acceptable results and low mortality rates. Long-term follow up is needed to detect long-term durability of mitral valve repair in children.*

Introduction

Mitral valve (MV) disease in children remains a tough challenge because of the varied pathology, heterogeneous lesions and coexisting cardiac anomalies [(1)].

Surgical management of mitral regurgitation (MR) in the pediatric population remains a challenge because of the heterogeneity of the lesions, requirement for growth potential, and necessity of avoiding mitral valve (MV) replacement [(2)]. MV repair is desirable and should be attempted because it conserves the subvalvar apparatus and ventricular geometry, preserving left ventricular function [(3)]. With all these recent evolutions in mitral valve repair, we planned to study and to assess the results of mitral valve repair in different etiological pathologies in children, and to assess its morbidity and mortality, with its effect on left ventricular function in the midterm period after surgery.

Patients and methods

Our study designed as a prospective observational study. After passed the Ethical approval of the Ethical Committee of the Faculty and took the consent of the patients' parents, 60 patients (26 males (44%) and 34 females (56%)) (all are human) with mitral valve diseases of different aetiologies, underwent mitral valve repair at Al-Houssein University Hospital and Atfal Misr Hospital from August 2014 to April 2018. The age of the patients ranged from 1 year to 18 years old.

Inclusion criteria: (1) children 1-18 years old. **(2)** Elective cases of mitral valve diseases. **(3)** Patients with concomitant intra cardiac pathologies beside mitral valve disease.

Exclusion criteria: **(1)** Patients for mitral valve repair beyond this age group. **(2)** Patents with unbalanced ventricles not suitable for biventricular repair. **(3)** Patients with mitral valve disease who are not suitable for repair but replacement.

Primary endpoint: the need for replacement due to failed repair and failure of going off bypass.

Secondary endpoint: improvement of clinical findings, mitral valve condition, echocardiographic measurements.

Statistical analysis: Data will be presented as mean ± SD and numbers (percentages); as indicated. Quantitative data will be analyzed by the use of Student's test or analysis of variance as indicated. The distribution of qualitative variance will be analyzed by compared Chi square test (Fisher's exact test); as indicated. Hazard ratios (HR) and 95% confidence intervals (CIs)were calculated during the multivariate analysis.

Table 1. Preoperative NYHA classification

Aim of the work: To evaluate the early and midterm results of surgical repair of mitral valve in the pediatric age group from age of 6 month to age of 18 years old and the impact of **(A)** The type of the pathology**. (B)** The method of repair used on the outcome.

Limitations of the study: (1) Collection of data of 60 consecutive patients of mitral valve disease. **(2)** Availability of transesophageal echo (TEE) qualified operator. **(3)** Availability of suitable TEE probe.

Preoperative evaluation:

The decisions to attempt mitral repair were made after preoperative evaluation and assessment of the patients was done, NYHA Functional Classification was used as shown in (table 1), Electrocardiogram (ECG), Chest X-ray

NYHA preoperative	Frequency	Percentage%
I	0	0
II	3	5
III	48	76
IV	9	19
Total	60	100

Transthoracic echocardiographic evaluation was the cornerstone in patient's evaluation. To evaluate: **(A)** Degree of mitral valve regurgitation or stenosis, two children had Grade II MR (2 children, 3.33%), two children had Grade III MR (2 children, 3.33%), fifty-four children had Grade IV MR (54 children, 90.01%), two children had severe mitral stenosis (2 children, 3.33%). **(B)** MV pathology, (table 2) demonstrates a wide variety of MV pathologies that were demonstrated by preoperative transthoracic echocardiography. **(C)** Data and measurements, EF (%) Mean ± SD (range) 58.72 ± 5.71 (35-77), FS (%) Mean ± SD (range) 30.85 ± 4.76 (24-53), LVED (cm) Mean ± SD (range) 4.59 ± 0.85 (2.7-6.8), LVES (cm) Mean ± SD (range) 2.95 ± 0.72 (1.3-5.0), LA (cm) 3.67 ± 0.94 (1.9-6), PASP (mmHg) 42.98 ± 14.58 (18-85mmhg). (D) Contractility, Good (EF ≥ 55%) in (50 children, 83%), Fair (EF 45-30%) in (9 children, 14.6%), Impaired (EF ≤ 30%) in (1 child, 2.4%). **(E)** pulmonary hypertension, (5 children, 8.4% have no pulmonary hypertention), (33 children, 55% with mild degree), (10 children, 16.6% with moderate degree), (12 children, 20% with sever degree).

Table 2: Mitral valve pathology by preoperative transthoracic echocardiography

	Mitral regurgitation	**Frequency**	**Percent**
Type I	Annular Dilatation	47	78.86%
	Cleft AML	12	19.51%
	Under Developed Leaflet	7	12.3%
Type II	AML Elongated Chordae	16	27.64%
	Prolapse Rupture Chordae	4	6.5%
	PML Elongated Chordae	2	2.44%
	Prolapse Rupture Chordae	1	1.6%
	Bileaflet prolapsed (Elongated Chordae)	2	2.44%
	Abnormal Chordae Attachment	2	2.44%
Type III	PML retraction (Short Chordae)	11	18.7%
	Commissural Fusion	1	1.6%
	Double orifice mitral valve	1	1.6%
	Mitral stenosis	**Frequency**	**% %**
Type A	Papillary Muscle & Commissural Fusion	1	1.6%
Type B	Parachute MV	1	1.6%
	Mitral regurgitation & Mitral stenosis	**Frequency**	**%**
	Papillary Muscle & Commissural Fusion	2	2.44%

AML: anterior mitral leaflet, **PML**: posterior mitral leaflet

Intraoperative management:
Every patient was undergoing to general anesthesia then monitored and only 3 cases underwent to TEE. Standard midline sternotomy was used for all cases, Standard CPB, myocardial protection was made.

Surgical techniques:
For all cases of rheumatic mitral disease and isolated mitral of any aetiology exposure of the mitral valve was generally achieved by Superior-transeptal, transeptal, superior left atrial, transeptal plus aortotomy approach as shown in table 3.

MV repair was performed through median sternotomy then Cardiopulmonary bypass was established by ascending aortic and bicaval cannulation with moderate systemic hypothermia, antegrade intermittent cold hyperkalemic blood and crystalloid cardioplegia was used for myocardial protection.

Table 3: Surgical approaches used during mitral valve repair

Surgical Approach	Surgical Approach	Percent (%)
Superior Transeptal	41	68.3
Transeptal	16	26.7
Superior left atrial	1	1.6
Transeptal plus aortotomy	2	3.4
Total	60	100

There were different operative procedures used, according to pathology, technique may be: Ring Annuloplasty to 38 patient (63.4 %), Cleft Repair (interrupted sutures) 11 patient (18.7%), Commissural Plication & Obliteration 6 patient (10.57%), Chordal transfer & fixation to 6 patient (10.57%), chordal second-order cutting to 3 patient (5.7%), Shortening to 1 patient (1.63%), Plication suture annuloplasty 2 patient (2.44%), Segmental suture annuloplasty 1 patient (1.63%), PTFE band 1 patient (1.63%), Pericardial strip 1 patient (1.63%), Alfieri Stitches 3 patient (5.7%), Papillary Muscle Splitting 3 patient (5.7%), Commissurotomy 3 patient (5.7%), Leaflet plication 2 patient (2.44%), Obliteration of additionary orifice of Double orifice mitral valve 1 patient (1.63%). Then Intraoperative mitral valve repair assessment was done either by Injection of cold saline with 50cc syringe through valve orifice was done in all patients and revealed trivial mitral regurgitation in 15 children (25%) and valve was completely competent and looks smiling in 45 children (75%) or Intraoperative trans-esophageal echocardiography was done for only 3 patients after weaning from cardiopulmonary bypass and before decannulation because of lack of operator sometimes and lack of suitable probe other times.

Early and Midterm postoperative follow-up: All patients were followed clinically and by transthoracic echocardiography which is the tool of postoperative midterm follow up in our study

Statistical methods: The early and late mortality and the rate of reoperation were analyzed bivariately for age, type of intracardiac pathologic condition, concomitant procedures, preoperative degree of MR, and technique of repair (annuloplasty, anterior leaflet, posterior leaflet, shortening of chords, and suture of cleft valve). A bivariate analysis of the impact of annuloplasty with anterior leaflet repair versus annuloplasty with posterior repair, with age and severity of MR held constant as controls, was done by logistic regression.

Results
Survival:
We had one early mortality in our study; this one was one-year old child of severe congenital mitral regurgitation who died 6 hours postoperative in ICU with low cardiac output. We had two cases of mortality midterm postoperative (2 children,3.33%) one of them was a male 18 years old of rheumatic mitral valve repair for severe mitral regurgitation, he came back with severe mitral regurgitation and severe aortic regurgitation so he had double valve replacement. He died three days postoperative with low cardiac output, low blood pressure on high inotropic support, anuria on peritoneal dialysis then heart failure and cardiopulmonary arrest. The second case was a female 10 years old died at hospital with acute infective endocarditis, she was admitted with high grade fever and manifestations of heart failure she suffered low cardiac output with inotropic support and antifailure measures, she went to be bradycardic then she arrested with no response to CPR. This means we had a mortality rate of 3 (5%) postoperative either early or midterm (Table 4).

Table 4: Postoperative mortality rates

Mortality	Frequency (%)	Freedom from mortality
Early	1(1.66%)	59(98.33%)
Midterm	2(3.33%)	57(95%)
Total mortality rate	3 (5%)	

Follow up:
Early postoperative :
Clinically: There was a significant improvement in NYHA classification early postoperative compared with preoperative functional classification as; 14 children were in NYHA class I (14 children, 23.3%), 36 children were in NYHA class II (36 children, 60 %) and 9 children were in NYHA class III (9 children, 15%), none was in NYHA class IV.
Echocardiography: MV regurge grades early postoperative; there were 12 patients with 0 MR grade (20.04 %), 31 patient I MR grade (51.86%), 14 patients II MR (23.27%), one patient IV MR (1.69%), one patient Mild MS

(1.69%). The following table demonstrate Echocardiographic data early postoperatively.

Table 5: Echocardiographic data early postoperatively

Echocardiographic data	Early postoperative	P value
EF%	64.15 ± 9.23 (34 - 77)	>0.05
FS%	34.72 ± 5.51 (19 - 48)	
LVED (cm)	4.32 ± 0.9 (2.7 - 6.8)	
LVES (cm)	2.88 ± 0.85 (1.6 - 5.6)	
LA (cm)	3.44 ± .88 (1.50 - 5.80)	
PASP (mmHg)	37.25 ± 13.38 (17- 83)	

EF: ejection fraction, FS:

Midterm 6 months postoperative follow-up data:

Clinical follow-up: NYHA functional classification; there was a highly significant clinical improvement in all children. There were 47 patients in NYHA class I (80%), 12 patients were in NYHA class II (18.3 %), none were in NYHA class III or NYHA class IV.

Echocardiographic follow up: MR grades; complete postoperative MV incompetence or stenosis were evaluated in all children (57 children, 98.3%), 5 patients were 0 MR grade (8.94%), 33 patients were I MR grade (55.28%),16 patients were II MR grade (26.33%), 3 patients were III MR (4.38%), one \patient was IV MR grade (1.69%), one patient was Mild MS (1.69%), no patients with Moderate MS or Severe MS (Table 6)

Table 6: Echocardiographic data 6 months midterm postoperative

Echocardiographic data	6 months midterm postoperative	P- Value
EF%	64.66 ± 4.01 (34 - 77)	<0.05
FS%	34.87 ± 4.02 (19 - 48)	<0.05
LVED (cm)	3.75 ± 0.82 (2.7 - 6.8)	<0.05
LVES (cm)	2.28 ± 0.73 (1.6 - 5.6)	<0.05
LA (cm)	2.76 ± 0.87 (1.50 - 5.80)	<0.05
PASP (mmHg)	29.87 ± 9.76 (17-83mmHg)	<0.05

Discussion

Numerous studies have reported results of mitral valve (MV) repair in children interestingly; MV repair has evolved with the introduction of standardized and reproducible techniques. In our study, the mean ± SD age of the patients was (8 ± 4.9) in the range of 1 months to 18 years. While in a study conducted by Sungkyu Cho and colleagues. The median age was 10.3 months (ranging from 22 days to 9.1 years) [5]. As regards sex, female gender was predominant in our study; 34 (56%) to 26 (44%) with female to male ratio of 5:4. According to a study performed by Shinichiro Oda and colleagues. there were 34 males and 44 females 6. This tells us that in all studies, female sex was predominant but it was non-significant predominance which means that mitral valve diseases have no direct relation to gender [6].

As regards aetiology of mitral valve pathology, in our study they were chronic rheumatic 23 children (38.8%), congenital 32 children (52.8%), and degenerative 4 children (7.3%). This is the difference between our study and other studies regarding aetiology of the mitral valve pathology as in developed countries most of patients had degenerative mitral valve. In study performed by Silva and his colleagues [7]; it was to analyze the outcomes of surgical mitral repair in children with rheumatic lesions.

As regards New York Heart Association (NYHA) functional status in our study, preoperatively there were; none was in NYHA class I (0 child, 0%), three children were in NYHA class II (3 child, 4.9%), forty-eight children were in NYHA class III (48 children, 79.7%) and nine children in NYHA class IV (9 children, 18.7%). In study performed by Silva and his colleagues [7]; the preoperative NYHA functional class ranged from II to IV: functional class II in (7 children, 17.5%), functional class III in (17 children, 42.5%), and functional class IV in (16 children, 40.0%) that is, 33 patients (80.5%) were in functional class III and IV in the preoperative period.

In our study, there were associated pathologies beside MV disease especially with cases of congenital MV disease. There was tricuspid valve regurgitation more than moderate (6 children, 9.7%), ventricular septal defect (8 children, 13.8%), atrial septal defect (3 children, 4.9%), subaortic membrane (2 children, 4%), and moderate aortic valve regurgitation (2 children, 4%).

As regards surgical approach, in our study exposure of the mitral valve was done by: superior transeptal approach in (41 children, 68.3%), right atriotomy with transeptal approach in (16 children, 26.7%) for other associated anomalies beside MV disease, superior approach to left atrium in (1 child, 1.6%) and transeptal approach plus aortotomy in (2 children,3.4%). In a

study performed by Mohd. Azhari Yakub and his colleagues [1], the mitral valve was exposed with a left atriotomy through the Waterston groove in case of isolated mitral repair and through the interatrial septum for associated right-sided heart procedure. In our study, various techniques were used for mitral valve repair in all our patients; ring annuloplasty with Carpentier-Edwards Physio Annuloplasty Ring was used in (38 children, 63.4%). Mean ring size ranged between 26 and 34; with mean ± SD of 29 ± 2.31. Cleft Repair with interrupted sutures was made in (11 children, 18.7%). Commissural plication & obliteration was made in (6 children, 10.57%). Chordal transfer and fixation were made in (6 children, 10.57%). Secondary chordae resection was made in (3 children, 5.7%). Chordal shortening was made in (1 child, 1.63%). Posterior mitral leaflet annuloplasty was made in (5 children, 8.1%); plication suture annuloplasty in (2 children, 2.44%), segmental suture annuloplasty in (1 chil, 1.63%), with PTFE band divided at P2 in (1 child, 1.63%) and with pericardial strip in (1 child, 1.63%). Alfieri stitches were made in (3 children, 5.7%). Leaflet plication was made in (2 children, 2.44%). Papillary muscle splitting was made in (3 children, 5.7%). Obliteration of additionary mitral orifice in DOMV was made in (1 child, 1.63%). Commissurotomy was made in (3 children, 3.7). In our study, Carpentier-Edwards ring was used for annuloplasty repair in (38 cases, 62.5%); in almost all cases of rheumatic MV (31 cases, 52%), only (3 cases, 4%) of congenital MV disease were repaired with ring, all cases of degenerative MV disease were repaired using ring (4 cases, 7%). In a study conducted by Sungkyu Cho and colleagues, A supravalvular mitral ring was resected in 8 patients, of whom 4 did not need any other procedures. A single or dominant papillary muscle was split in 7 patients. Fused or shortened chordae were mobilized or resected in 6 patients. Commissurotomy was performed in 5 patients [5]. This makes it obvious that repair with Carpentier-Edwards Physio Annuloplasty Ring was the predominant repair technique in our study and (Silva et al., 2008) study especially for rheumatic cases and interrupted sutures technique for cleft MV in congenital cleft cases. No intraoperative mortality was found in our study, as regards early mortality we had one case (1 child, 1.63%). In a study conducted by Sungkyu Cho and colleagues, there was 1 hospital death in a 2.9-kg neonatal patient died 3 months after the operation from postoperative septic shock that was suspiciously related to a peritoneal catheter infection [5].

In our study, regarding early morbidity: 2 children had re-exploration for bleeding day 0 postoperatively (3.39%), one of them was a female 9 years old with rheumatic MV disease and the other was a male 3 years old with VSD and congenital cleft MV. Mohd. Azhari Yakub and his colleagues in their study there were nonfatal complications include 1 patient who was brought back to the operating room for management of postoperative bleeding. Two patients required drainage of large pericardial effusions. One patient required a permanent pacemaker for complete heart block. Two patients required prolonged pleural drainage for chylothorax [1]. In our study there was a significant improvement of MV grade early postoperatively by transthoracic echocardiography, regarding MR; (12children, 20.04 %) had grade 0 MR, (31 children, 51.86%) had grade I MR, (14 children, 23.27%) had grade II MR, (0 child, 0%) had grade III MR and (1 child, 1.69%) had grade IV MR. Regarding mitral stenosis only (1 child, 1.69%) had mild MS. In a study conducted by Sungkyu Cho and colleagues, Postoperative echocardiography at discharge showed that the mean mitral inflow pressure gradient significantly improved from 10.4 ± 3.9 to 3.4 ± 1.7mmHg (n = 18, P = 0.001) 5. In our study, there was a significant improvement of NYHA functional classification of most of our patients at midterm follow-up as compared with preoperative functional classification as for 6 months midterm follow up group it was a highly significant improvement as there were 47 patients in NYHA class I (80%), 12 patients were in NYHA class II (18.3 %), none were in NYHA class III or NYHA class IV. According to study performed by C. Lee and his colleagues8 all 122 survivors (122 survivors with MR, 14 survivors with MS) remained in the NYHA class I or II (Figure 1).

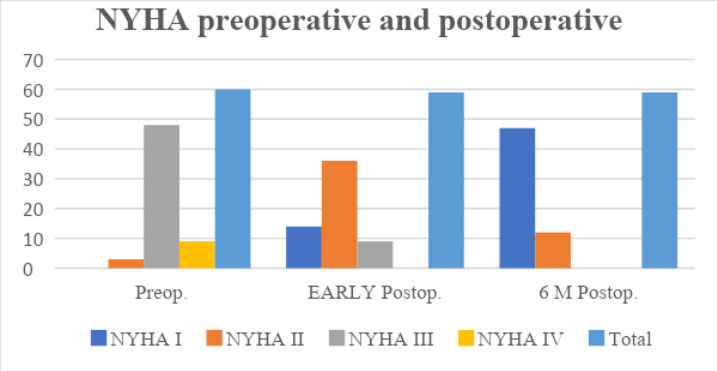

Fig 1: NYHA classification preoperative and postoperative

In our study, there was a significant improvement of MR grade midterm postoperatively by transthoracic echocardiography, regarding MR; as for 6 months midterm follow up group (5 children, 8.94 %) had grade 0 MR, (33 children, 55.28%) had grade I MR, (16 children, 26.33%) had grade II MR, (3 children, 4.38%) had grade III MR and (1 child, 1.6%) had grade IV MR. Regarding mitral stenosis only (1 child, 1.63%) had mild MS. According to study performed by C. Lee and his colleagues; 122 survivors with MR, 102 patients (84%) underwent echocardiography during follow-up. Significant improvement in degree of MR was noted as it was none in 42 patients, grade 1 in 36, grade 2 in 19 and grade 3 in five. 14 survivors with MS, 8 patients (57%) underwent echocardiography during follow up. The degree of MS decreased significantly and median MS gradient was 2.8 mmHg (0-10 mmHg). MV condition showed a significant improvement in all grades of MV postoperatively, either early or 6 months' midterm postoperative as shown in following table.

Table 7 : Follow up early and midterm postoperative

MV Grade	Preoper.	Early Postop.	6 Months Postop.	P value
0 MR	0	12	5	
I MR	0	31	33	<0.05
II MR	2	14	16	
III MR	2	0	3	
IV MR	54	1	1	
Mild MS	0	1	1	
Moderate MS	0	0	0	
Severe MS	2	0	0	
Total	60	59	59	

In our study with transthoracic echocardiography midterm postoperatively follow-up showed a statistically significant improvement compared to preoperative results as; for 6 months' midterm follow up group; LA diameter decreased in range of 1.50 - 5.80cm; with mean ±SD of 2.76 ± 0.87. LVESD decreased in range of 1.6- 5.6 cm; with mean ± SD 2.28 ± 0.73. LVEDD decreased in range of 2.7 - 6.8 cm; with mean ± SD 3.75 ± 0.82. EF% increase in range of 34 – 77% with mean ± SD 64.66 ± 4.01 %. FS% increased in range of 19-48% with mean ± SD 34.87 ± 4.02 %. PASP decreased in the range of 17 and 83mmHg with mean ± SD 29.87 ± 9.76 mmHg. In a study conducted by Sungkyu Cho and colleagues, postoperative echocardiography at discharge showed that the mean mitral inflow pressure gradient significantly improved from 10.4 ± 3.9 to 3.4 ± 1.7mmHg (n = 18, P = 0.001) 5. At the last follow up, the mean mitral inflow pressure gradient was 4.5 ± 3.1mmHg for all patients who did not have reoperation for MV and moderate or greater MI was detected in 3 patients [(5)].

Conclusion

Mitral valve repair in children is established as the procedure of choice for the surgical correction of mitral regurgitation of all aetiologies. It has good midterm results and should be attempted as possible especially with cases of rheumatic MV regurgitation which are endemic in Egypt. Mitral valve repair using classic open rigid ring is safe, with acceptable early and midterm results and mortality rates. The surgeon should repair the mitral valve perfectly and not accept varying degrees of regurgitation or stenosis otherwise the patient will be submitted for another surgery few years later. The surgeon should repair the mitral valve perfectly and not accept varying degrees of regurgitation or stenosis otherwise the patient will be submitted for another surgery few years later.

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