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Early Results and Fate of Moderate Mitral Regurgitation in Patients Undergoing Surgical Aortic Valve Replacement

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ABSTRACT
Background: The management of studied cases with moderate mitral regurgitation (MR) undergoing surgical aortic valve replacement (SAVR) remains debatable.
Objective: The aim of the current study to investigate the early results and fate of moderate MR after AVR.
Patients and methods: This study was both prospective and retrospective, conducted in the Cardiothoracic Surgery Department in the Faculty of Medicine at Cairo University, from March 2020 to October 2021. A total 200 studied cases undergoing AVR with moderate functional MR were screened. The fate of residual MR was evaluated by transthoracic echocardiography 6 months post-operative, and the prognosis of studied cases with residual MR.
Results: Up to 76% of the studied cases with moderate functional MR after isolated AVR enhanced mitral valve function, while 18% did not show a significant change, and 6% showed deterioration in mitral valve function over the short-term follow-up period. The decrease in MR is associated with the degree of LV acute reverse remodeling, which can be demonstrated by the decrease in LV end-diastolic volume. Perioperative morbidity did not find any significant variation among studied cases. The clinical outcomes showed significantly improved symptoms during the follow-up period for all patients. **Conclusion:** Patients with aortic valve disease and moderate functional MR should undergo AVR alone. The degree of MR will remain stable or may improve.
Keywords: Aortic valve disease, Mitral regurge, Aortic valve replacement, Follow up study, Cairo University.

INTRODUCTION
Aortic valve replacement (AVR) is the most common valve surgery to be performed worldwide. In many cases, these patients have an associated mitral valve (MV) disease. If the degree of mitral disease is severe, concomitant MV surgery with AVR is indicated. With lower degrees of mitral regurge (MR), the decision to attack the mitral valve in the same sitting is debatable [(1)]. This research aimed to evaluate the early clinical results in studied cases with moderate MR undergoing isolated surgical aortic valve replacement (SAVR) for aortic disease and evaluate the degree of residual MR postoperatively.

PATIENTS AND METHODS
This study is an observational research aimed to determine the fate and short-term prognostic implications of moderate MR in studied cases undergoing SAVR identified from the database of Cairo University Medical School Hospital, between January 2020 and August 2021.

Study population: Data of 200 studied cases, who underwent isolated SAVR for aortic stenosis or regurge with MR before surgery, are reviewed and data analyzed regarding fate and short-term prognostic problems of moderate MR.
Inclusion criteria: Studied cases undergoing isolated SAVR for aortic stenosis and/or regurge with moderate MR.
Exclusion criteria: Studied cases with concomitant valve lesions (pulmonary valve disease, tricuspid valve disease) or, concomitant CABG, any patient with more than moderate MR, and redo cases.

Preoperative data: Patients were subjected on admission to the following history taking regarding age, gender, NYHA class, and underlying conditions (hypertension, DM, COPD, preoperative atrial fibrillation, pulmonary artery pressure, renal functions, and aortic valve lesion).

Investigations: Echocardiography was performed to all patients to establish LV Function [EF LA size, ESV, EDV, EF, MR (effective regurgitant orifice, regurgitant volume)].

Intra Operative data: Median sternotomy, opening and suspension of pericardium followed cannulation. Cardiopulmonary bypass is initiated using ascending aorta and right atrial appendage as arterial and venous access respectively. The aorta is cross clamped.
Antegrade Cardioplegia is delivered proximal to the clamp. Aortotomy is performed above the valve. The aortic valve is inspected, debrided, and valve replacement is performed in the normal fashion. After weaning from the bypass and removing all cannulae, temporary dual pacing is inserted, and the sternum is re-approximated with stainless steel wires.
A record was made of the following: Ischemic time, bypass time (in minutes) and type of valve (mechanical, tissue valve).

Postoperative data: Patients were transferred to the ICU while being mechanically ventilated with monitoring of the blood pressure, central venous pressure, pulse (rate, rhythm), blood loss, and urine output. Need for inotropic support in different

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concentrations. Weaning from mechanical ventilation was done when the criteria of weaning were met.
The following data were recorded: Period of mechanical ventilation, duration of hospital and ICU stay and incidence of postoperative problems (ventricular arrhythmia, atrial arrhythmia, and stroke).
Studied cases were discharged from the hospital when they had good post-operative recovery, and satisfactory echocardiographic results.
Follow up echocardiography after 6 months included LA size, ESV, EDV, EF, and MR (effective regurgitant orifice, regurgitant volume)
Follow up using NYHA class was done after 6 months of the surgical intervention.

Ethical Approval:
This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Cairo University. Written informed consent was obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical Analysis
The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (SPSS) version 20 for windows. Qualitative data were defined as numbers and percentages. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as means and SD, and ANOVA test was used for comparison between groups. P value ≤0.05 was considered to be statistically significant.

RESULTS
Regarding associated diseases in our study, there were 46 diabetic patients, 129 hypertensive patients, 54 COPD, 20 AF and 18 chronic kidney diseases, as shown in **Figure 1**.

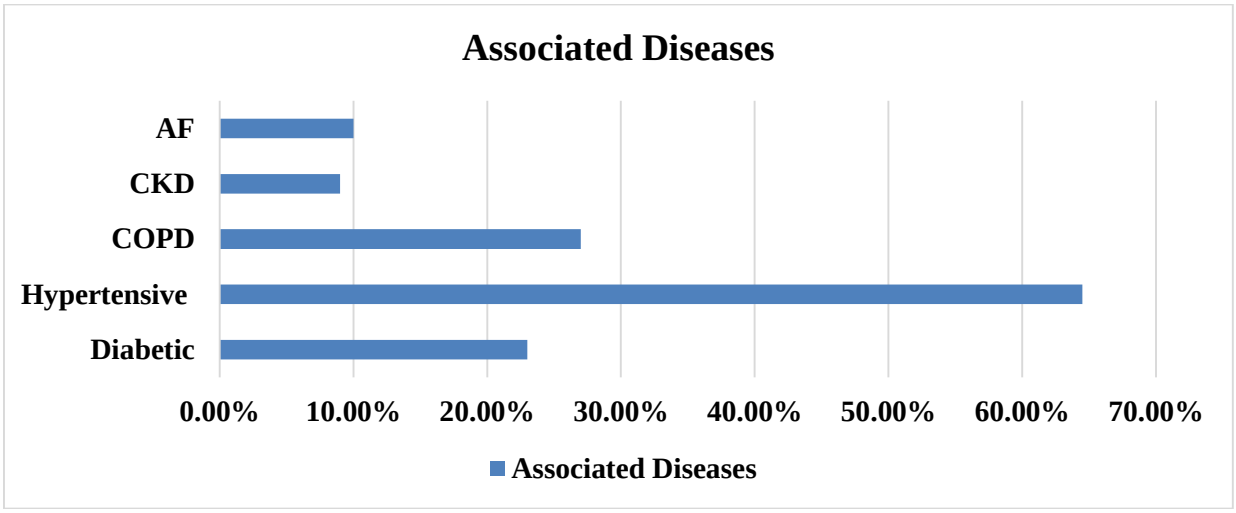

Figure 1: Frequency of associated disease among the studied patients.

Considering the Functional NYHA class, there was 79 patients in class 2, 82 patients in class 3 and 39 patient in class 1, as shown in **Figure 2**.

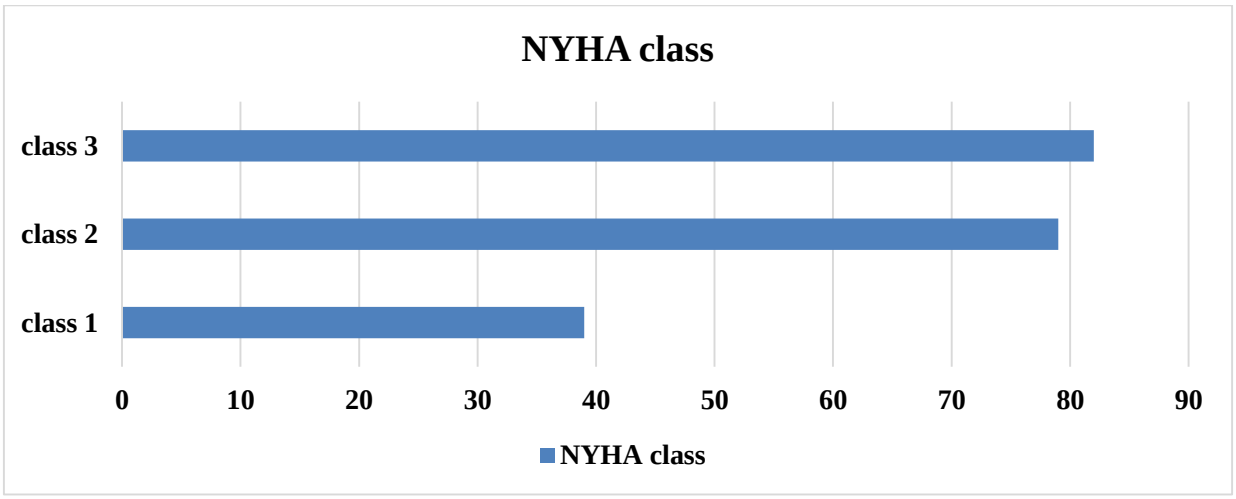

Figure 2: Distribution of the studied patients according to NYHA class.

In our study 179 patients received mechanical valves and 21 patients received tissue valves (**Table 1)**.

Table 1: Type of aortic valve used in patients participating in the current study.

Variable		Count	%
Valve	**Tissue**	21	10.5%
	Mechanical	179	89.5%

Table 2 summarizes mean ischemia (cross-clamp) time and mean Bypass time of the participants in our study.

Table 2: Operative data of the studied patients.

Variable	Mean	Standard Deviation	Minimum	Maximum
Cardiopulmonary bypass time	83.16	9.69	65	100
Cross-clamp time	52.44	6.32	45	65

The mean duration of mechanical ventilation, intensive care unit stay and hospital stay were recorded from ICU data and summarized in **Table 3**.

Table 3: ICU data of the studied patients.

Variable	Mean	Standard Deviation	Minimum	Maximum
Duration of mechanic ventilation (hours)	8.25	2.12	5	12
Intensive care unit stay(days)	2.68	0.54	2	4
Hospital stay(days)	6.57	0.85	5	8

Table 4 summarizes the number of patients who had postoperative ventricular arrhythmia, atrial arrhythmia and stroke.

Table 4: Postoperative data of studied patients.

Variable	Number of patients	Percentage
Ventricular arrhythmia (post-operative)	5	2.5%
Atrial arrhythmia (post-operative)	27	13.5%
Stroke (post-operative)	5	2.5%

Data of patients who underwent echocardiography 6 months after the operation are shown in **Table 5**.

Table 5: Postoperative echocardiography of studied patients.

Variable	Mean	Standard Deviation	Minimum	Maximum
EDV cm	4.62	0.53	3.5	6.3
ESV (post-operative) cm	3.34	0.63	2.3	4.3
EF (post-operative) %	55.9	8.50	41	70
Mitral effective regurgitant orifice (post-operative) cm^2	0.2	0.03	0.12	0.29
Mitral regurgitant volume (post-operative) ml	29.35	4.60	20	41

MV function over the short-term follow-up period is shown in **Table 6**.

Table 6: Mitral valve function **changes after 6 months of the studied patients.**

Variable		Count	%
MR	**Unchanged**	36	18%
	Improved	152	76%
	Worsened	12	6%

Comparisons between the 3 studied groups regarding the age showed no statistical significance (**Table 7**).

Table 7: Association between MR changes and age in the 3 studied groups.

Variable	MR						
	Group B		Group A		Group C		P-value
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	
Age	63.83	8.24	63.69	7.30	65.17	7.54	0.806

Table 8 summarizes the associations between MR changes post-operative echocardiography. The left ventricular end-diastolic dimension across groups was statistically significant (P-value <0.001). Also, there was statistical significance regarding mitral regurgitant volume across groups (P-value <0.001).

Table 8: Associations between MR changes post-operative echocardiography.

Variable	MR						P-value
	Unchanged		Improved		Worsened		
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	
LA size cm	4.02	0.42	3.79	0.37	4.62	0.09	<0.001
EDV cm	4.66	0.63	4.55	0.48	5.30	0.17	<0.001
ESV cm	3.53	0.57	3.25	0.63	3.95	0.22	<0.001
EF %	51.06	10.36	57.73	7.38	47.25	3.72	<0.001
Mitral effective regurgitant orifice cm^2	0.22	0.03	0.20	0.03	0.27	0.01	<0.001
Mitral regurgitant volume ml	33.22	3.66	27.76	3.46	38.00	3.22	<0.001

DISCUSSION

AVR is the most common valve surgery to be performed worldwide. In many cases, these patients have an associated MV disease. If the degree of mitral disease is severe, concomitant MV surgery with AVR is indicated. With lower degrees of MR, the decision to attack MV in the same sitting is debatable [(2)].

Guidelines do not give a clear evidence-based strategy regarding the management of concomitant MV pathology due to the lack of randomized control studies on the subject. The natural course of non-surgically treated mild to moderate MR in studied cases undergoing SAVR remains to be elucidated [(3)].

Studies have reported a worse prognosis in patients with a residual MR after isolated SAVR but have failed to identify the actual risk factors leading to this residual regurgitation. Our study aims to determine the fate and early prognostic problems of moderate mitral regurgitation in studied cases undergoing SAVR [(4)].

The mean age in our study was 63.80 (SD 7.46) years with no statistical difference between the three groups.

Wang *et al.* [(5)] evaluated the variations in MV geometry and the degree of MR in studied cases undergoing AVR and reported a mean age of 52.6 (SD 12) years and had no significance with MV changes.

In a study by **Absil *et al.*** [(6)] the impact of moderate MR on early or mid-term clinical findings in studied cases undergoing isolated AVR for aortic stenosis was studied with a reported mean age of 52.6 (SD 12) years.

In our study, there were 124 (62%) patients with aortic stenosis and 76 (38%) patients with aortic regurge with moderate functional mitral regurge. In our research, organic MR and studied cases with coronary artery diseases were also excluded because ischemic heart diseases could also cause functional MR.

Takeda *et al.* [(7)] reported the effect of untreated mild to moderate mitral regurgitation at the period of isolated AVR on late adverse results and compared two groups: group 1(73 AS, 47 AR, mixed 14) and group 2(26 AS, 21 AR, 12 mixed)

In our study, the mean cardiopulmonary bypass time was 83.16 (SD 9.69), mean cross-clamp time was 52.44 (SD 6.32), with no statistically significant difference between groups.

Similarly in a study by **Wang *et al.*** [(5)], the mean operation time was 208.2 (SD 31.2) minutes, the mean cardiopulmonary bypass time was 32.5 (SD 7.3) minutes and cross-clamp time was 24.3 (SD 3.4) minutes, with no statistically significant difference between groups.

In our study, we used 179 mechanical valves and 21 tissue valves, with no statistically significant between groups.

In a study by **Wang *et al.*** [(5)] they used 37 mechanical valves and 12 tissue valves, with no statistical significance.

Similarly, in a study by **Kim *et al.*** [(2)], they used 163 mechanical valves and 129 tissue valves, with no statistical significance.

In our study the mean duration of mechanical ventilation was 8.25 (SD 2.12) hours, the mean ICU stay

was 2.68 (SD 0.54) days, and the mean hospital stay was 6.57 (SD 0.85) days, with statistical significance between the three groups.

In our study, 27 (13.5%) patients had postoperative atrial arrhythmia, and 5 (2.5%) patients had a stroke.

Similarly, a study by **Wang *et al.*** [5] showed the mean mechanic ventilation time was 7.5 (SD 2.2) hours, the mean intensive care unit stay was 2.77 (SD 0.60) days, the mean hospital stay was 6.74 (SD 0.90) days, 6 (12.2%) patients had postoperative atrial arrhythmia with not statistically significance.

Earlier studies like the study by **Absil *et al.*** [(6)] studied 58 cases with MR grades zero–one and 58 studied cases with MR grades two–three. Regression of MR occurred in most cases even in patients with grade 2-3 MR preoperatively with no effect on early morbidity and mortality. The study concluded that these cases should be treated conservatively, especially in the older more fragile subgroup of aortic stenosis patients.

Also, **Kim *et al.*** [(2)] found that not attacking MV in studied cases with mild to moderate MR during SAVR resulted in excellent postoperative results noting that in the case of rheumatic etiology of mitral valve disease the degree of MR was more likely to progress. A recent study by **Witberg *et al.*** [(8)] from 16 TAVR centres and including 7303 cases compared patients with moderate or greater MR versus those with less MR. Regression of MR occurred in 44.1% of cases in the first group. The 4-year mortality was higher in patients with MR persistence. They concluded that patients with the expected persistence of MR can be identified as patients at a higher risk of mortality post-TAVR.

CONCLUSION

In patients undergoing SAVR, concomitant moderate MR should be treated conservatively performing only the aortic valve surgery. MR will remain stable or improve in most cases.

DECLARATIONS

- **Consent for Publication:** I verify that all authors have agreed to submit the manuscript.
- **Availability of data and material:** Available
- **Competing interests:** None
- **Funding:** Self-funding
- **Conflicts of Interest:** No conflicts of interest about the publication of this paper.

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