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Outcome stratification of patients with impaired renal functions after isolated prosthetic mitral valve replacement

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Abstract

Objectives: Patients with impaired renal functions have a variable risk of morbidity and mortality in cardiovascular surgery. Poor outcome was reported among patients who underwent valve surgery. Current study is presumed to compare the early outcomes of patients having different degrees of impaired renal functions and undergoing mitral valve replacement surgery.

Methods: 135 patients were admitted into the three highly specialized centers in Cairo and Ismailia–Egypt between Dec.2018 and Jan.2020 Preoperative, intraoperative and early post-operative data were recorded. Impairment may present as one of these strata: early reversible (G1-2 included strata 1 & 2 kidney disease patients), moderate G3-4 included strata 3 & 4 kidney disease patients) or advanced irreversible renal damage. (The 5th stratum or G5-KD included end stage renal disease patients undergoing 4-hour hemodialysis sessions, three times a week, with bicarbonate dialysate). We correlated outcome among each stratum with cardiac and renal functions in that stratum.

Results: The more is the impairment of renal functions at any peri- operative stage, the longer is the need for prolonged mechanical ventilation and the longer is the hospital stay. We found that levels of serum creatinine were significantly increased postoperatively Also, the more is the reversibility of the renal impairment, even by renal dialysis, the much better is the outcome (P=.0019). We also found insignificant difference between different strata of irreversible renal impairment in the early outcome of the prosthetic mitral valve replacement surgery. The early reversible damage can be repaired peri-operatively.

Conclusions: Prosthetic mitral valve replacement among patients with different degrees of impaired renal functions is not only feasible but also it does not seem to add any more deterioration into renal function. Prolonged mechanical ventilation and hospital stay are the only drawbacks of irreversibly impaired renal damage by dialysis or renal transplant.

Keywords: Mitral Valve Replacement; Chronic kidney disease; Hemodialysis.

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1. Introduction

Glomerular Filtration Rate {GFR}: values are normalized to an average body- surface area of 1.73 m^2. Description of different strata of impaired renal functions (table 1):

Table 1 Strata of Chronic Kidney Disease [17]

Stratum	GFR	Description	Management
Stage I	≥90	Normal renal function (but urinalysis, structural abnormalities or genetic factors indicate renal disease).	Observation and control of blood pressure.
Stage II	60-89	Mildly reduced renal function (Stage 2 CKD should not be diagnosed on GFR alone - but urinalysis, structural abnormalities or genetic factors indicate renal disease.)	Observation, control of blood pressure and cardiovascular risk factors.
Stage IIIa	45-59	Moderate decrease in renal function, with or without other evidence of kidney damage.	Observation, control of blood pressure and cardiovascular risk factors.
Stage IIIb	30-44	Moderate decrease in renal function, with or without other evidence of kidney damage.	Observation, control of blood pressure and cardiovascular risk factors.
Stage IV	15-29	Severely reduced renal function.	Planning for end-stage kidney disease.
Stage V	<15	Very severe (end-stage) kidney disease.	Transplant or dialysis
Use the suffix (p) to denote the presence of proteinuria when staging chronic kidney disease			

Chronic kidney disease (CKD) has significantly associated with development of cardiovascular disease. The most common cause of high mortality in renal disease-patients is associating cardiovascular disease, if any [1]. A large previous study demonstrated that CKD is associated with worse echocardiographic characteristics and that left-sided valve disease is highly prevalent. The latter is associated with a higher mortality rate among CKD-patients [2].

In cardiac surgical settings, CKD-patients are reported to have short life expectancy with renal dysfunction severity and are often associated with other medical problems compared to those without CKD [3, 4]. Cardiac, pulmonary, metabolic, and hematological complications have a major effect on outcome after cardiac surgery [5, 6]

Our main aim was to investigate the association between stratum of renal impairment with the outcome of morbidity and mortality during peri-operative period of isolated mitral valve replacement; and to identify further the degree of renal failure at time of prosthetic mitral valve replacement going to affect the outcomes of surgery.

2. Patients and Methods

This study is a comparative prospective study. Patients included in this study were undergoing mitral valve replacement at Suez Canal University Hospitals or Zagazig university Hospitals from December 2018 to January 2020. Current study included 135 patients undergoing mitral valve replacement with previous medical history of chronic renal disease or renal dialysis. Patients were divided into three groups according to renal function stage at the time of operation (according to The Kidney Disease; Improving Global Outcomes Clinical Practice Guideline) [7]: G1-2 included strata 1 & 2 kidney disease patients; G3-4 included strata 3 & 4 kidney disease patients. The 5th stratum or G5-KD included end stage renal disease patients undergoing 4-hour hemodialysis sessions, three times a week, with bicarbonate dialysate.

We excluded patients undergoing Redo mitral valve replacement, undergoing emergency valve replacement, patients with other system failure as hepatic failure, Stroke, etc.., and patients requiring other cardiac procedures as Coronary artery bypass grafting (CABG) or Aortic valve replacement.

Patients were subjected to detailed history taking include name, age, sex, special habits and risk factors such as obesity, smoking, associated comorbid diseases e.g., diabetes mellitus and hypertension, history of previous surgeries including cardiac surgery and history of renal disease and renal dialysis. Clinical examination carried out regarding arterial blood pressure, pulse examination, respiratory rate, body mass index (BMI) and blood samples were drawn from all patients to assess the following: complete blood count, urea, creatinine, alanine transaminase, aspartate aminotransferase, albumin and bilirubin (total and direct), random blood sugar, bleeding profile and C-reactive protein (CRP). Radiological investigations were performed with the same specialists to all patients; Rest 12 leads ECG, P-A view Plain chest- X-ray, Trans-thoracic Echocardiography, dobutamine stress echocardiography done to assess viability if needed, coronary angiography to define affected vessels if the age is above 40 years and history of typical chest pain for determination of extent and location of each lesion, and Pelvis-abdominal Ultrasound.

2.1. Preoperative assessment

All patients received their morning dose of cardiac medications. Intramuscular 10-mg morphine sulphate was given to all patients before transfer to the operating theater. Sedation was optimized using 0.03-0.07 mg/kg midazolam. Monitoring started preoperatively using five leads Electrocardiogram, direct arterial blood pressure and pulse oximetry.

2.2. Intraoperative assessment

Operative time and Ischemic time, inotropic drugs use, use of intra-aortic balloon, and blood products given to the patient were recorded.

2.3. Surgical technique

Cardiopulmonary Bypass (CPB): The membrane oxygenators were used. Hematocrit was kept around 28% during CPB.

Technique of mitral valve replacement: Operation entails secure fixation of valve prosthesis to the annulus by reliable suture techniques without damage to adjacent structures or myocardium and without tissue interference with valve function.

2.4. Postoperative assessment

We assessed the following criteria in the first days postoperative: Kidney function tests, monitor urine output, monitor cardiac output and hemodynamics, Blood gases.

2.5. Statistical analysis

All data were collected, tabulated and statistically analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Chi square test ($\chi 2$) and Fisher exact was used to calculate difference between qualitative variables as indicated. One-way ANOVA test supplemented with LSD post hoc test was used to compare between more than two dependent groups of normally distributed variables while Friedman's test ranks test was used for non-normally distributed variables. Pearson's correlation coefficient was used for correlating normal and non-parametric variables respectively. All statistical comparisons were two tailed with significance Level of P-value ≤ 0.05 indicates significant, p <0.001 indicates highly significant difference while, P> 0.05 indicates Non-significant difference

3. Results

Regarding the demographic data such as sex, age, hypertension, diabetes, and smoking comparison between the three strata were found to be insignificant difference groups (table 2). However, baseline creatinine was significantly higher in (G5) group 5, while LVEF was significantly lower or within the normal range. In current study, we found that levels of serum creatinine were significantly increased postoperatively but there was an improvement in LVEF in overall patients with a significant difference between the groups. ICU stay in days was significantly longer in G5 groups. No significant difference was found in mortality (Table 3). Postoperative complications were comparable in the three groups, varied between CNS, pulmonary complication and / or wound infection.

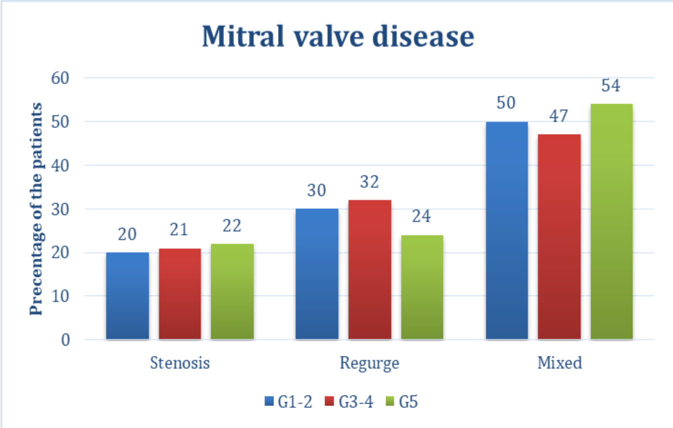

Figure 1 Types of lesions of mitral valve disease among the three strata of renal impairment

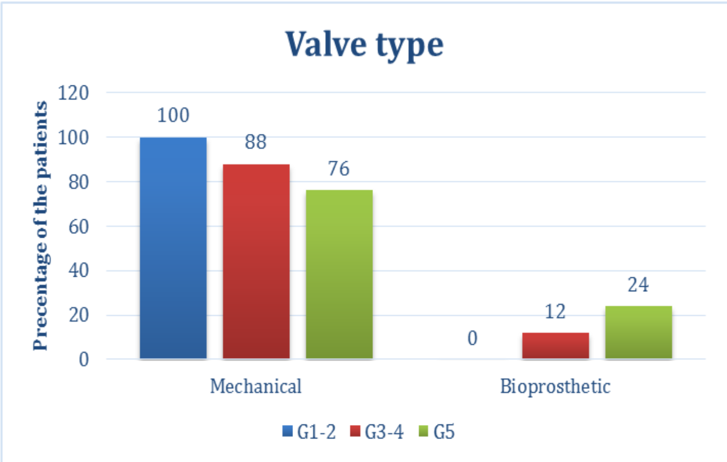

Figure 2 Types of prosthetic valves used for replacement

Table 2 Demographic and clinical preoperative characteristics between the groups

Variables	G1-2(N=50)	G3-4(N=40)	G5-HD(N=45)	P
Age *(years)*	48.32 ± 5.2	47.28 ± 4.9	52.4 ± 3.7	.677
Male, *n (%)*	22 (44)	16 (40)	21 (46.7)	.850
BMI *(kg/m²)*	25.63 ± 1.2	24.82 ± 3.1	25.12 ± 3.6	.753
Smoking, *n (%)*	15 (30)	13 (32.5)	19 (42.2)	.650
DM, *n (%)*	25 (50)	25 (62.5)	28 (62.2)	.802
HTN, *n (%)*	20 (40)	21 (52.5)	30 (66.7)	.370
Hemoglobin *(g/dl)*	13.34 ± 1.2	11.15 ± 3.4	9.42 ± 2.7	.001
Baseline creatinine *(mg/dl)*	0.91 ± 0.6	2.15 ± 0.1	6.89 ± 1.3	<0.001
CRP *(U/L)*	2.48 ± 2.3	5.2 ± 3.7	8.13 ± 5.1	<0.001
LVEF *(%)*	64.4 ± 6.1	60.89 ± 5.7	57.6 ± 8.5	.049
LVEDP *(mmHg)*	19.6 ± 3.1	19.02 ± 2.9	18.1 ± 2.6	.236
LVEDD *(mm)*	51.4 ± 3.6	52.7 ± 4.1	54.3 ± 5.9	.271

BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; CRP, C-reactive protein; LVEF, left ventricular ejection fraction; LVEDP, left ventricular end diastolic pressure; LVEDD, left ventricular end- diastolic diameter. Data are presented as mean ±SD

Table 3 Operative and Postoperative data between the groups.

Variables	G1-2(N=50)	G3-4(N=40)	G5-HD(N=45)	P
Ischemic time *(min)*	44.6 ± 6.1	45.4 ± 6.3	46.1 ± 7.1	.181
Ventilation time *(min)*	5.91 ± 1.13	7.66 ± 1.2	9.01 ± 1.19	.003
Inotropic drugs use, *n (%)*	21 (42)	23 (57.5)	30 (66.7)	.173
Postop. Hemoglobin *(g/dl)*	11.79 ± 2.1	10.03 ± 1.9	8.22 ± 2.7	<0.001
Postop. creatinine *(mg/dl)*	1.21 ± 0.2	4.34 ± 0.8	9.57 ± 2.1	<0.001
Blood loss volume *(ml)*	2.48 ± 2.3	5.2 ± 3.7	8.13 ± 5.1	.063
UOP *(ml/24h)*	2300 ± 416	1700 ± 289	40 ± 29	<0.001
ICU stay *(days)*	1.7 ± 0.6	4.3 ± 0.7	8.2 ± 1.1	<0.001
LVEF *(%)*	65.5 ± 3.9	62.3 ± 5.2	59 ± 9.8	.04
Reopening, *n (%)*	5 (10)	7 (18)	11 (24.4)	.392
Mortality, *n (%)*	0	2 (5)	0	.794

UOP, urine output; ICU: intensive care unit; LVEF, left ventricular ejection fraction; LVEDP, left ventricular end-diastolic pressure; LVEDD, left ventricular diastolic diameter. Data are presented as mean ±SD

4. Discussion

With this rising incidence of ESRD and an increasingly aging population, it is expected that the number of chronic dialysis patients requiring open-heart surgery will likely continue to increase. However, the heterogeneity among these patients will be wide, because the comorbidities, such as diabetes, baseline cardiac function, and symptoms, will vary. Providing individual patients with specific prognostic data and evaluating their suitability for surgery is often a challenge. Patients with advanced kidney disease often request information on whether the surgery will precipitate a requirement for permanent dialysis [8].

In the present study, we studied the early outcomes of patients having chronic renal disease at the time of cardiac valve replacement operations and those with different stages of renal disease.

Chang et al. [9] investigated 196 adult patients and divided them into two group according to develop renal deterioration or not; there were 76 patient developed renal deterioration with a mean age of 65 ± 1.0 years, 53.9% of whom (n = 41) were male while 120 patient had normal renal function with a mean age of 52 ± 1.0 years, 49.2% of whom (number = 59) were male. Compared with the patients without normal renal function, those with postoperative renal deterioration were older and more likely to have diabetes mellitus (DM), hypertension, and function class III or IV heart failure.

Like our finding Brinkman et al., [10] who noted that no differences in preoperative rates of systemic hypertension, smoking history, diabetes mellitus, endocarditis, or cardiac arrhythmias.

In our study, we found that preoperative factors such as the mitral valve disease or the NYHA classification have a non-significant relation to the chronic renal failure. We also found that mechanical valves were higher in preserved renal function group but bio-prosthetic valves were higher in advanced renal disease, and the bleeding rate and blood transfusion increases highly in patients with advanced renal disease comparing to those with grade I renal disease. Similarly, Christiansen et al., [11] reported that ten patients were in New York Heart Association class III (NYHA class III) and seven in class IV preoperatively, but they disagree with the left ventricular ejection fraction that it was measured in eight patients and the range was 25-74% (47% mean) this may be due to the low number of patients they measured.

Chang et al. [9] finding who reported that regurgitation severity did not differ significantly between the postoperative renal deterioration and normal renal function groups. Of the patients in Brinkman et al. [10], at least 69% were in congestive heart failure (New York Heart Association class III or IV) before operation, and 24% reported a previous myocardial infarction. Significant cardiac arrhythmias had occurred in at least 18% and a previous stroke in 15%. They also documented that twenty-one patients required valve replacement for rheumatic disease, four for degenerative disease, three for infective endocarditis, and one for reoperation (stuck prosthetic valve). Similar thirty mechanical valves and one bio-prosthetic valve were applied to those 29 patients. None of the patients were re-operated in the follow-up period except one patient who was re-operated for progression of I/IV aortic insufficiency to III/IV after the first operation. Eleven patients were in the NYHA Functional Class III, and 19 patients were in Class II preoperatively. Nine of the survivors were Class I, and four of them were Class II at their last control. Ko et al., [12] found that the urgency for an operative intervention and NYHA class IV are independent factors for an increased operative risk.

We also found that LVEF has a significant difference between those with renal impairment and those with good renal function preoperatively and postoperatively. In line with our finding, Chang et al. [9] documented that compared with normal renal function group; the postoperative renal deterioration group had more patients diagnosed with dilated cardiomyopathy. Furthermore, the echograms of the patients with renal deterioration exhibited lower ejection fractions (EFs), but in disagree with us they reported that higher left ventricular end-systolic diameters (LVESDs), and greater left ventricular end-systolic volumes (LVESVs), indicating long-term left ventricular overload.

Tribouilloy et al. [13] demonstrated that patients with LVESD ≥40 had unfavorable outcomes and that LVESD is a powerful predictor of survival in patients with organic mitral regurgitation. Regarding preoperative serum creatinine, we found that there was a significant difference between the groups as others authors reported [9, 11]. Chang et al., [9] finding agree with our finding that they observed that the patients with postoperative renal deterioration had longer ICU stays and ventilator time. Of the patients with postoperative renal deterioration, 45 were stage 1, 18 were stage 2, and 13 were stage 3. Overall, 6 patients received dialysis within 7 days after surgery. Also, Christiansen et al. [11] reported that the average duration of artificial ventilation was 10 hours to 3 days, the average length of stay in the intensive care unit 1-12 days, and the average hospital stay of the 14 patients who survived the operation 15 to 39 days.

On the contrary, Brinkman et al. [10] documented that length of stay in the intensive care unit ranged between 1 and 29 days (mean 4.26 ± 4.86 days), whereas length of hospital stay was between 6 and 29 days (mean 10.00 ± 4.51 days). Christiansen et al. [11] documented that only five patients underwent their cardiac surgical interventions electively. This may indicate that patients with end stage renal failure are not being referred early enough. Some initial reluctance to refer these patients seems understandable, but it needs to be emphasized that the operative risk will increase when patients become more symptomatic.

We found that levels of serum creatinine were significantly increased postoperatively. In agreement with ours, Chang et al. [9] found that the patients had higher levels of serum creatinine postoperatively compared with basal ones. We also noticed that no significant change in the NYHA class in the early postoperative outcome of groups. Kaul et al. [14] noted that in addition to NYHA class age is also a risk factor. Because of the high risk of concomitant cardiovascular disease so, all candidates are screened for coronary artery disease.

Critically, Chang et al. [9] data revealed that compared with the normal renal function group, the postoperative renal deterioration group exhibited higher rates of DM and hypertension, which are risk factors for occult renal disease. The postoperative renal deterioration group also exhibited lower albumin and hemoglobin levels, suggesting the presence of malnutrition because of heart failure. They found that the patients with postoperative renal deterioration had larger LVESD and LVESV in echocardiograms.

Regarding the surgical details and postoperative outcomes:

Chang and others [9] reported that patients who had postoperative renal deterioration were those who had a longer bypass time and /or a longer aortic clamp time than did the patients with normal renal function. Although no publication has discussed the association between LVESD and renal dysfunction Taniguchi et al. [15] suspected that it may be reasonable to report that chronic left ventricular dysfunction indicated by larger LVESD might affect the kidney Functions. Furthermore, the ESRD group, in their study, exhibited longer bypass time and more frequent tricuspid valve repair.

Nevertheless, we reported two cases of mortality due to brain hemorrhage in G3-4 group can be the result of hypertension and raised INR level while on Warfarin (Marivan®) maintained dose. Owen et al. [16] reported a rate of a high operative mortality. Christiansen et al. [11] documented that postoperative complications occurred in seven patients, Brinkman et al. [10] reported that infectious complications are more common in patients with ESRD, this can be due to one or more of the following: decreased chemotaxis, decreased bone marrow reserve; lymphopenia, decreased cell mediated immunity, decreased interferon levels, and decreased monocyte and macrophage function. In our series, no bacterial endocarditis was detected.

However, Ando et al. [18] demonstrated that major postoperative complications or mortality share similar risk factors that may contribute to renal disease, such as decreased left ventricular EF and increased serum creatinine level, as we indicated in this study. Collectively, these data confirm the value of using current mortality risk scores to predict complications of ESRD following mitral valve replacement.

Carefully selected patients with advanced renal disease and severe cardiac symptoms can undergo cardiac surgical intervention with acceptable morbidity and mortality.

5. Conclusion

Valve replacement in patients with ESRD on hemodialysis is not only feasible but also does not seem to decrease life expectancy. Surgical intervention not only brings reasonable expectation of symptomatic improvement and improved quality of life but also creates an opportunity for renal transplantation.

This study concluded that the higher is the stratum of renal impairment, the higher is the rate of morbidity. The more is the impairment of renal functions, the longer is the need for prolonged mechanical ventilation and hospital stay.

The more is the reversibility of the renal impairment, the much better is the outcome. More studies are needed to evaluate long term relationship.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of informed consent

Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Suez Canal University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

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