Comparison between percutaneous coronary intervention versus coronary artery bypass graft with mitral valve replacement in patients with single-vessel and mitral valve disease

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Background

We compared staged percutaneous coronary intervention (PCI) versus coronary artery bypass graft (CABG) with mitral valve replacement (MVR) in patients with combined single-vessel and rheumatic mitral valve (MV) disease.

Patients and methods

We prospectively evaluated 80 patients with combined single coronary artery (requiring revascularization in non-left anterior descending artery territory) and rheumatic MV disease, who were divided into two groups: group I consisted of 40 patients who underwent staged PCI and MVR 3 months later, and group II consisted of 40 patients who underwent combined CABG (using saphenous venous graft) and MVR. We compared between both groups.

Results

The median aortic cross-clamp and cardiopulmonary bypass times were 44 and 62 min, respectively, for group I versus 60.5 and 82 min, respectively, for group II; the difference between groups was statistically significant. A total of eight (20%) patients in group I needed inotropic support versus 12 (30%) patients in group II, which was not statistically significant. No patients in both groups needed any mechanical support in the form of intra-aortic balloon pump. None of the patients in both groups had intraoperative ECG changes in the form of ischemia or arrhythmias. The median ICU length of stay (h) and hospital length of stay (days) were 39 h and 5.5 days, respectively, for group I versus 56.5 h and 8.5 days, respectively, for group II; the difference between groups was statistically significant. The median blood loss (ml) postoperatively was 925 in group I versus 1075 in group II, which was statistically significant. However, the rate of re-exploration for bleeding did not differ significantly between both groups, with 1one (2.5%) case only in group I versus two (5%) cases in group II, and no postoperative delayed cardiac tamponade was noted in any of the two groups. The postoperative complications for groups I and II were as follows: 0 versus three (7.5%), respectively, regarding prolonged mechanical ventilation (>24 h); 0 versus one (2.5%), respectively, regarding respiratory complications; 0 versus two (5%), respectively, regarding wound infection; 0 versus one (2.5%), respectively, regarding cerebrovascular accidents; and two (5%) versus one (2.5%), respectively, regarding acute kidney injury. There was no statistically significant difference between both groups regarding these previous postoperative complications. None of the patients in both groups died within the first 30 days after surgery. None of the patients in both groups had major cardiac events or Cardiac Care Unit admission. Regional wall motion abnormalities were noted in 15 (37.5%) patients of group I versus 17 (42.5%) patients of group II; all underwent stress ECG, and of them, nine (22.5%) patients in group I versus 11 (27.5%) patients in group II showed positive results and were qualified for diagnostic coronary angiography, which confirmed the need for reoperation for myocardial ischemia/infarction within the first year of follow-up postoperatively in four (10%) patients of group I versus eight (20%) patients of group II. All of these follow-up outcomes showed no significant difference between both groups.

Conclusion

A staged approach of PCI followed by MVR is an alternative to the conventional combined CABG and MVR, can be performed safely in some patients with single coronary artery and MV disease, and is associated with good short-term and follow-up outcomes.

Keywords:
CABG, MVR, PCI

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Background

Combined coronary artery mitral valve (MV) disease is a major cause of morbidity and mortality in the adult patient population. Traditional treatment involves combined MV and coronary artery bypass graft (CABG) surgery using a median sternotomy. However, this combined surgical approach confers a higher risk when compared with isolated MV surgery; the risks of such a combined surgical procedure may outweigh the benefits. Thus, the concept of parsing the total risk of a single major procedure to the lesser individual and summed risks of two smaller procedures – percutaneous coronary intervention (PCI) plus the MV operation – has been applied in clinical practice and reported by various groups.

Interest in hybrid procedures, defined for the purpose of this thesis as MV surgery and PCI, has intensified with improved coronary stent technology, increased collaboration between cardiac surgeons and interventional cardiologists, and the introduction of hybrid operating suites. The complementary goals of minimizing the morbidity of surgical procedures and optimizing resource utilization have driven development of new solutions for concurrent valvular and coronary heart disease [1].

Patients and methods

The study was a prospective comparative review, of 2-year duration, of 80 patients with combined single coronary artery [requiring revascularization in non-left anterior descending artery (LAD) territory] and rheumatic MV disease, who were divided into two groups: group I consisting of 40 patients who underwent staged PCI and MV replacement (MVR) 3 months later, and group II consisting of 40 patients who underwent combined CABG [using saphenous venous graft (SVG)] and MVR. The study centers were Cardiothoracic Surgery Department of Ain Shams University Hospitals and National Heart Institute (NHI). PCI was done at Cardiology Department of Ain Shams University Hospitals and National Heart Institute (NHI).

Included were patients with combined single vessel and MV disease, of age between 35 and 60 years old. Excluded were patients with ejection fraction (EF) less than 45%, concomitant aortic or tricuspid valve disease requiring surgery, concomitant congenital heart disease requiring surgical correction, redo-cardiac surgery, acute coronary syndrome requiring primary PCI together with MV disease, renal/hepatic failure, chronic obstructive pulmonary disease or other respiratory disease, any neurological deficit or previous cerebrovascular event, or hematological disorders.

In all patients, the coronary and valvular lesions were documented by diagnostic catheterization and echocardiography, respectively. Patients were selected to undergo a hybrid approach after a comprehensive heart team evaluation. Baseline variables, operative characteristics and outcomes, and major adverse cardiovascular events during the follow-up period were analyzed using our institutional medical records, outpatient surgical and cardiology office visits, and a follow-up survey at 3-month intervals within the first postoperative year.

All patients were clinically stable for both PCI and the operation. Preoperative medication regimens were similar. Once the treatment plan was established, the interventional cardiologist proceeded with PCI of the significant lesion in the native vessel. Drug-eluting stents (DES) were placed in all of group I patients. A loading dose of 600-mg clopidogrel and 325-mg aspirin was administered at the time of stent placement, followed by clopidogrel 75 mg daily and aspirin 81–325 mg daily thereafter (dual antiplatelet therapy). Management of antiplatelet therapy between the PCI and the operation was at the discretion of the interventional cardiologist. The patients had their antiplatelet agents stopped 5 days before surgery. All patients resumed their antithrombotic regimen within 24–48 h after surgery, which comprised of single antiplatelet (clopidogrel 75 mg daily) and an oral anticoagulant dose adjusted according to the target international normalized ratio, because of the mechanical MV prosthesis inserted in all patients.

In all patients, standard median sternotomy was performed, followed by inverted T-shaped pericardiotomy, aorto-bicaval cannulation, conduction of cardiopulmonary bypass, and application of aortic cross-clamp. Warm blood antegrade cardioplegia was given. MV was accessed through left atriotomy via Sondergaard's groove, preservation of the posterior leaflet was done, and the mechanical mitral prosthesis was inserted using 2-0 interrupted Ethibond sutures with pledgets sitting on the atrial surface of the MV. Closure of left atrium, deairing through aortic root vent, and removal of aortic cross-clamp were done. Weaning off bypass, hemostasis, and anatomical closure in layers were done. In group II patients, the distal and proximal anastomoses using 7-0 and 6-0 prolene sutures, respectively, were done in addition to the previous steps of MVR, using the SVG harvested simultaneously with the median sternotomy at the start of the operation.

The intraoperative variables prospectively assessed as per our study included total cardiopulmonary bypass time, total cross-clamp time, the need for inotropic support, and ECG changes in the form of ischemia or arrhythmias. The postoperative outcomes included bleeding, cerebrovascular accidents, renal failure, respiratory complications, duration of mechanical ventilation, duration of ICU stay, wound infection, duration of hospital stay, and 30-day mortality. All patients underwent postoperative routine trans-thoracic echo (TTE) follow-up upon discharge, after 3 months, 6 months, and 1 year; postoperative stress ECG; and/or coronary angiography if needed. The follow-up outcomes included major cardiac events or Cardiac Care Unit (CCU) admission within first year and the need for reoperation for myocardial infarction or ischemia within the first year.

Statistical analysis

The community, Environmental, and Occupational Medicine Department of Ain Shams University suggested a minimum sample size of 36 patients in each group to get reliable results. The collected data were revised, coded, tabulated, and introduced to a PC using the Statistical Package for the Social Sciences (SPSS 15.0.1 for Windows, 2001; SPSS Inc., Chicago, Illinois, USA). The variables are reported as mean±SD, median, and interquartile range (IQR), or number and percentage. Suitable analysis was done according to the type of data obtained. An independent *t* test, χ^2 test, and Mann–Whitney *U* test are used to analyze data accordingly. *P* value less than 0.05 was considered statistically significant.

Results

Baseline demographic, clinical, angiographic, and echocardiographic information was prospectively collected for all patients. The baseline characteristics were more or less similar between both groups. There were 23 (57.5%) men in the staged PCI+MVR group (group I) and 25 (62.5%) in the CABG+MVR group (group II) (*P*=0.648), with a mean age of 51.1 ± 3.2 and 52.1 ± 4.6 years, respectively (*P*=1.000) and BMI of 27.2 ± 1.7 and 27.3 ± 2.1, respectively (*P*=0.819). The incidence of hypertension, diabetes mellitus, and dyslipidemia for both groups was 82.5 versus 87.5% (*P*=0.531), 37.5 versus 42.5% (*P*=0.648), and 77.5 versus 82.5% (*P*=0.576), respectively. There was no statistically significant difference between both groups in the baseline characteristics, including age, sex, BMI, hypertension, diabetes mellitus, and dyslipidemia (Table 1).

The median preoperative creatinine in groups I and II was 1.2 versus 1.1, respectively (*P*=0.299), which was not statistically significant. None of the patients in both groups had cerebrovascular disease, peripheral vascular disease, prior myocardial infarction, congestive heart failure, liver disease, chronic lung disease, prior cardiac surgery or PCI, preoperative aspirin administration, preoperative clopidogrel administration, or preoperative dual-antiplatelet administration (Table 2).

The median left ventricular EF was 56% (IQR, 54–60%) in group I and 55% (IQR, 52–60%) in group II (*P*=0.579). A total of nine (22.5%) patients in group I had atrial fibrillation (AF) versus 11 (27.5%) in group II (*P*=0.606). Median pulmonary artery pressure (PAP) was 25 in both groups (*P*=0.330). There was no statistically significant difference between both groups regarding EF, AF, and median PAP (Table 3). No left ventricular dilatation or right ventricular dysfunction was noted in both groups preoperatively.

The most commonly treated coronary arteries were the right coronary in 24 (60%) patients of group I versus 20 (50%) patients of group II (*P*=0.369), and the left circumflex in 16 (40%) patients of group I versus 20 (50%) patients of group II (*P*=0.369). None of the patients in both groups had left anterior descending or ramus intermedius artery lesions. Regarding the MV lesions, mitral stenosis was found in 24 (60%)

Table 1 Baseline characteristics of the study patients

	Group I (*N*=40)	Group II (*N*=40)	Significance	*P*
Age			*t*	
Mean±SD	51.1 ± 3.2	52.1 ± 4.6	0.001	1.000
Range	45.0–56.0	45.0–59.0		
Sex	*n* (%)	*n* (%)	χ^2	
Males	23 (57.5)	25 (62.5)		
Females	17 (42.5)	15 (37.5)	0.208	0.648
BMI				
Mean±SD	27.2 ± 1.7	27.3 ± 2.1		
Range	24.0–30.0	24.0–31.0	−0.230	0.819
Hypertension	33 (82.5)	35 (87.5)	0.392	0.531
Diabetes mellitus	15 (37.5)	17 (42.5)	0.208	0.648
Dyslipidemia	31 (77.5)	33 (82.5)	0.313	0.576

χ^2, χ^2 test; *t*, independent samples *t* test.

patients of group I versus 16 (40%) patients of group II (P=0.074), mitral regurgitation was found in eight (20%) patients of group I versus four (10%) patients of group II (P=0.210), and mixed mitral lesions (stenosis+regurgitation) were found in eight (20%) patients of group I versus 20 (50%) patients of group II (P=0.005). There was a statistically significant association between groups regarding mixed MV lesions only. However, the association was not statistically significant regarding left circumflex artery lesions, right coronary artery lesions, MV stenosis, and MV regurgitation. The median time interval between PCI and MV surgery in group I was 93 days (IQR, 91–95) (Table 4).

The median aortic cross-clamp and cardiopulmonary bypass times were 44 (IQR, 39–48) and 62 min (IQR, 59–68), respectively, in group I versus 60.5 (IQR, 55–65) and 82 min (IQR, 75–88), respectively, in group II (P=0.001); the difference between groups

Table 2 Baseline characteristics of the study patients 'continued'

	Group I (*N*=40)	Group II (*N*=40)	Significance	*P*
Preoperative creatinine				*t*
Median	1.2	1.1	1.046	0.299
IQR	1.0–1.3	1.0–1.2		
	n (%)	*n* (%)		
Cerebrovascular disease	0	0	–	–
Peripheral vascular disease	0	0	–	–
Prior MI	0	0	–	–
Congestive heart failure	0	0	–	–
Liver disease	0	0	–	–
Chronic lung disease	0	0	–	–
Prior cardiac surgery	0	0	–	–
Prior PCI	0	0	–	–
Preoperative aspirin administration	0	0	–	–
Preoperative clopidogrel administration	0	0	–	–
Preoperative dual-antiplatelet therapy	0	0	–	–

IQR, interquartile range; MI, myocardial infarction; PCI, percutaneous coronary intervention; *t*, independent samples *t* test.

Table 3 Baseline characteristics of the study patients 'continued'

	Group I (*N*=40)	Group II (*N*=40)	Significance	*P*
Ejection fraction %			*t*	
Median	56.0	55.5	0.557	0.579
IQR	54.0–60.0	52.0–60.0		
Atrial fibrillation			χ^2	
n (%)	9 (22.5)	11 (27.5)	0.267	0.606
Median PAP			*t*	
Median	25.0	25.0		
IQR	23.0–30.0	22.0–30.0	0.909	0.330

χ^2, χ^2 test; IQR, interquartile range; PAP, pulmonary artery pressure; *t*, independent samples *t* test.

Table 4 Baseline characteristics of the study patients 'continued'

	Group I (*N*=40) [*n* (%)]	Group II (*N*=40) [*n* (%)]	χ^2	*P*
Coronary artery lesions				
Left circumflex artery lesions	16 (40.0)	20 (50.0)	0.808	0.369
Right coronary artery lesion	24 (60.0)	20 (50.0)	0.808	0.369
Left anterior descending lesions	0	0	–	–
Ramus intermedius lesions	0	0.0	–	–
Mitral valve lesions				
Mitral valve stenosis	24 (60.0)	16 (40.0)	3.200	0.074
Mitral valve regurgitation	8 (20.0)	4 (10.0)	1.569	0.210
Mixed mitral valve lesions	8 (20.0)	20 (50.0)	7.912	0.005*
Time of PCI to valve surgery (days)				
Median	93.0	–	–	–
IQR	91.0–95.0	–		

χ^2, χ^2 test; IQR, interquartile range; PCI, percutaneous coronary intervention.
*Statistically significant.

was statistically significant. A total of eight (20%) patients in group I needed inotropic support versus 12 (30%) patients in group II (*P*=0.302), which was not statistically significant. No patients in both groups did need any mechanical support in the form of intra-aortic balloon pump. None of the patients in both groups had intraoperative ECG changes in the form of ischemia or arrhythmias (Table 5). The AF patients preoperatively in both groups went through several changes in the rhythm and rate intraoperatively before returning back to baseline AF again.

The median ICU length of stay (h) and hospital length of stay (days) were 39 h (IQR, 32–45) and 5.5 days (IQR, 5–6), respectively, in group I versus 56.5 h (IQR, 49–69) and 8.5 days (IQR, 7–13), respectively, in group II (*P*=0.001); the difference between groups was statistically significant. The median bleeding loss (ml) postoperatively was 925 (IQR, 650–1200) in group I versus 1075 (IQR, 900–1400) in group II (*P*=0.021), which was statistically significant, with a median of 2 U of packed red blood cells (RBCs) transfused (IQR, 1–2) in group I compared with a median of two packed RBC units transfused (IQR, 2–3) in group II (*P*=0.002), which was statistically significant also. However, the rate of re-exploration for bleeding did not differ significantly between both groups, with one (2.5%) case only in group I versus two (5%) cases in group II (*P*=0.556) (Table 6), and no postoperative delayed cardiac tamponade was noted in any of the two groups.

The postoperative complications for groups I and II included the following: 0 versus three (7.5%), respectively, regarding prolonged mechanical ventilation (>24 h) (*P*=0.077); 0 versus one (2.5%), respectively, regarding respiratory complications (*P*=0.314); 0 versus 2 (5%), respectively, regarding wound infection (*P*=0.152); 0 versus one (2.5%), respectively, regarding cerebrovascular accidents (*P*=0.314); and two (5%) versus one (2.5%), respectively, regarding acute kidney injury (*P*=0.556). There was no statistically significant difference between both groups regarding these previous postoperative complications. None of the patients in both groups died within the first 30 days after surgery (Table 6).

After 1 year of follow-up, none of the patients in both groups had major cardiac events or CCU admission. Postoperative routine TTE follow-ups upon discharge, after 3 months, 6 months, and 1 year were done for all patients in both groups. Regional wall motion abnormalities were noted in 15 (37.5%) patients in group I versus 17 (42.5%) patients in group II (*P*=0.648); they all underwent stress ECG, and of them, nine (22.5%) patients in group I versus 11 (27.5%) patients in group II showed positive results (*P*=0.606) and were qualified for diagnostic coronary angiography, which confirmed the need for reoperation for myocardial ischemia/infarction within the first year of follow up postoperatively in four (10%) patients of group I versus eight (20%)v of group II (*P*=0.210). All of these follow-up outcomes showed no significant difference between both groups (Table 7, Figs 1–7).

Discussion

The Society of Thoracic Surgeons (STS) adult cardiac surgery database cites the operative mortality of isolated MV replacement at 4.7%. When performing concomitant CABG, the operative mortality increases to 9.8%, with a significantly greater occurrence of postoperative complications and major morbidity occurring in 7.0–11.6% [1]. Thus, it is hypothesized that the operative risk of combined CABG and MV surgery may be reduced by partitioning the operation into the two lower-risk, less invasive procedures of PCI+MVR. The present study demonstrated a low morbidity and mortality with staged PCI+MVR for significant single coronary artery and MV disease, compared with combined CABG and MVR.

Table 5 Operative characteristics of the study patients

	Group I (*N*=40)	Group II (*N*=40)	Significance	*P*
Aortic cross-clamp time (min)			*t*	
Median	44.0	60.5	–10.433	0.001*
IQR	39.0–48.0	55.0–65.0		
Cardiopulmonary bypass time (min)				
Median	62.0	82.0	–9.752	0.001*
IQR	59.0–68.0	75.0–88.0		
Operative need for inotropic support			χ^2	
Yes [*n* (%)]	8 (20.0)	12 (30.0)	1.067	0.302
No [*n* (%)]	32 (80.0)	28 (70.0)		
ECG changes in the form of ischemia or arrhythmias	0	0	–	–

χ^2, χ^2 test; IQR, interquartile range; *t*, independent samples *t* test.
*Statistically significant.

Table 6 Postoperative outcomes of the study patients

	Group I (*N*=40)	Group II (*N*=40)	Significance	*P*
ICU length of stay (h)			*U*	
Median	39.0	56.5		
IQR	32.0–45.0	49.0–69.0	–8.379	0.001*
Blood loss (ml)				
Median	925.0	1075.0	–2.316	0.021*
IQR	650.0–1200.0	900.0–1400.0		
Packed RBCs units transferred				
Median	2.0	2.0	–3.091	0.002*
IQR	1.0–2.0	2.0–3.0		
Hospital length of stay (days)				
Median	5.5	8.5	–6.571	0.001*
IQR	5.0–6.0	7.0–13.0		
Prolonged mechanical ventilation (>24 h)	0	3 (7.5)	χ^2=3.117	0.077
Respiratory complications	0	1 (2.5)	1.013	0.314
Wound infection	0	2 (5.0)	2.051	0.152
Cerebrovascular accidents	0	1 (2.5)	1.013	0.314
Re-operation for bleeding	1 (2.5)	2 (5.0)	0.346	0.556
Acute kidney injury	2 (5.0)	1 (2.5)	0.346	0.556
30-day mortality	0	0	–	–

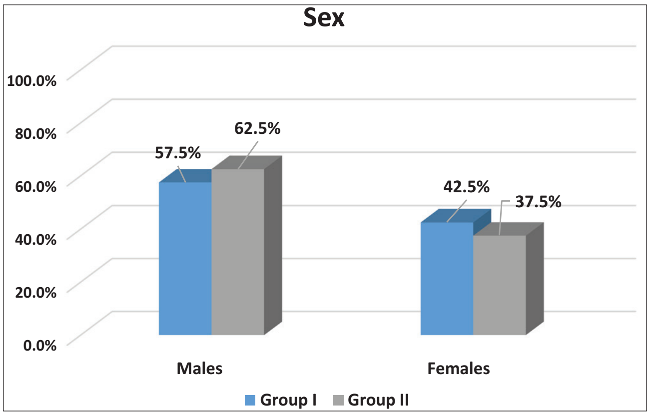
χ^2, χ^2 test; IQR, interquartile range; RBC, red blood cell; *U*, Mann–Whitney *U* test.
*Statistically significant.

Table 7 Follow up outcomes within first year of the study patients

	Group I (*N*=40)	Group II (*N*=40)	χ^2	*P*
Major cardiac events or CCU admission	0	0	–	–
Echo regional wall motion abnormalities	15 (37.5)	17 (42.5)	0.208	0.648
Positive stress ECG	9 (22.5)	11 (27.5)	0.267	0.606
Need for reoperation for myocardial infarction or ischemia	4 (10.0)	8 (20.0)	1.569	0.210

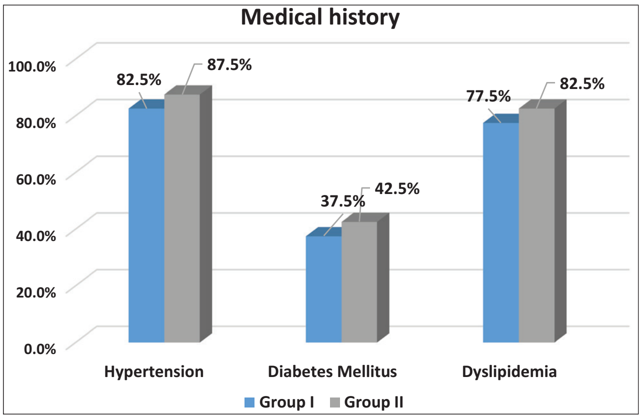
CCU, Cardiac Care Unit.

Figure 1



Sex distribution among study groups.

Figure 2

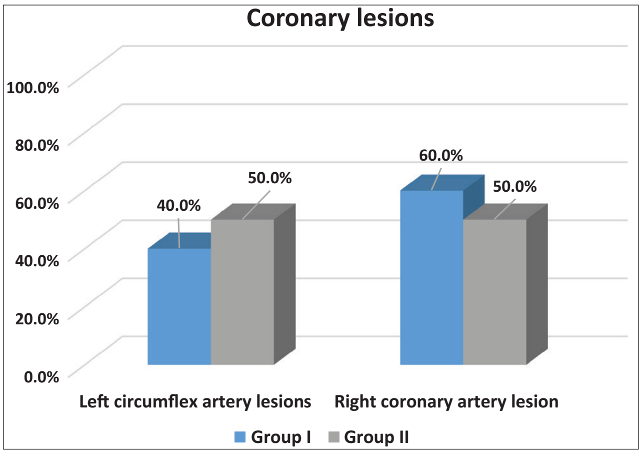


Medical history among study groups.

Given the trends toward increases in minimally invasive cardiac surgery, the broad applicability of the hybrid approach described here may be particularly appealing. Gammie *et al*. [2] reported that from 2004 to 2008, the percentage of MV operations that were done via a minimally invasive approach increased from 11.9 to 20.1% (P<0.0001). With this progression, it is most likely that a hybrid approach will increase as well. On the contrary, the short-term benefits of a hybrid approach are not without potential long-term hazards.

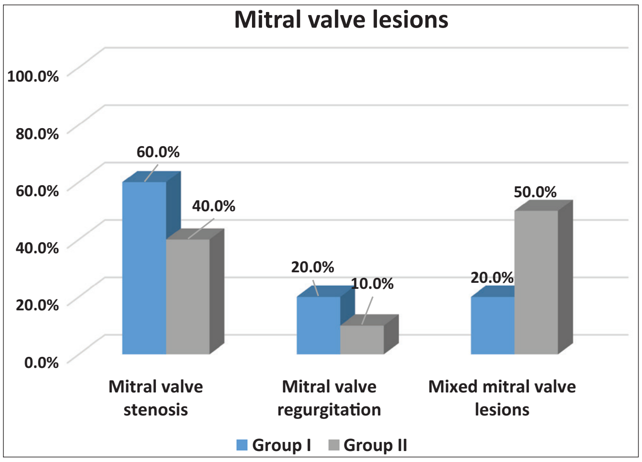
Fortunately, in-stent restenosis, one of the major limitations of percutaneous revascularization, has decreased with each new generation of coronary stent [3]. PCI, however, has yet to match CABG regarding long-term benefits [4]. Multiple studies have consistently demonstrated that for patients with multivessel disease and/or left main disease, regardless of the presence of diabetes, CABG yields better outcomes than PCI in terms of mortality, myocardial infarction, and need for repeat coronary

Figure 3



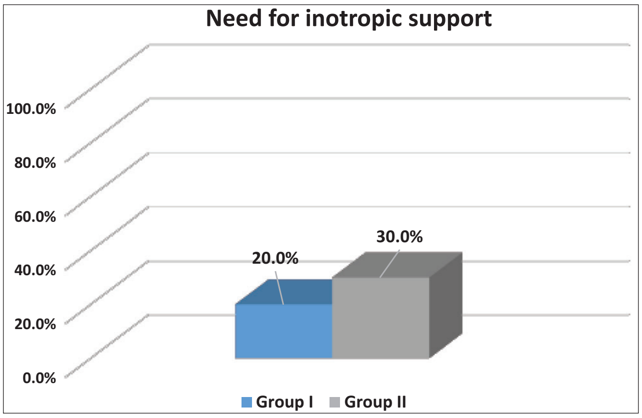
Coronary lesions among study groups.

Figure 4



Mitral valve lesions among study groups.

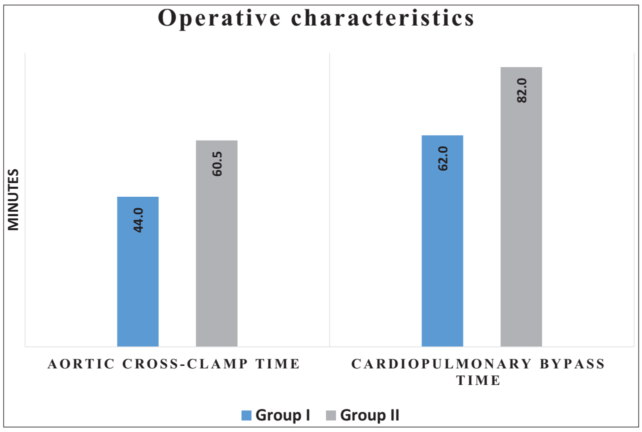
Figure 5



Need for inotropic support intraoperatively.

revascularization [5]. Even when comparing CABG versus PCI for patients with proximal LAD disease, Hannan *et al.* [6] showed that CABG patients had lower rates of repeat revascularization. The benefit of CABG over PCI involves the long-term effects of

Figure 6



Operative characteristics among study groups.

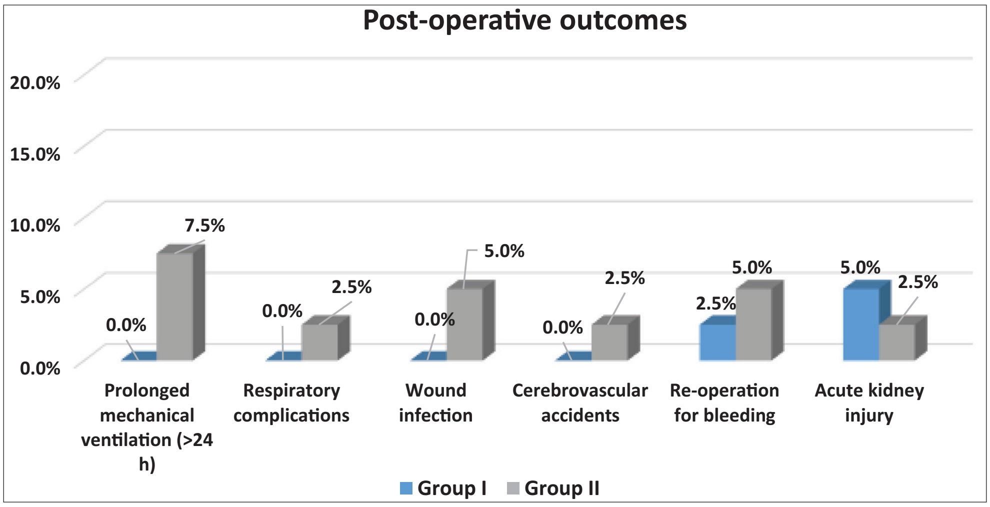
internal mammary artery (IMA) to LAD anastomosis, the potential ability of bypass grafts to 'treat' lesions that subsequently develop, and resultant downstream effects of cytokines on arterial disease [7]. On the contrary, PCI offers lower rates of morbidity and shorter hospital stay.

The primary purpose of a hybrid valve/PCI is to substitute PCI for bypass grafting with SVGs, particularly for lesions not in the LAD coronary artery [8]. With the current excellent performance of DES, restenosis and thrombosis rates of DES may be less than the estimated rate of SVG failure of 20% at 12 months [9]. The two most common clinical objectives of hybrid procedures are to reduce overall operative morbidity and mortality by transforming a single, high-risk surgery into two less risky procedures, and to facilitate minimally invasive surgery [8].

Hybrid procedures offer a reasonable alternative to traditional surgery for patients who meet the following basic criteria: non-LAD coronary lesions, not amenable to internal mammary bypass grafting; PCI that is technically feasible and likely durable from a procedural standpoint; and ability to tolerate the required antiplatelet and anticoagulation regimens.

Our study was a prospective comparative review, of 2-year duration, of 80 patients with combined single coronary artery (requiring revascularization in non-LAD territory) and rheumatic MV disease, who were divided into two groups: group I consisted of 40 patients who underwent staged PCI, and MVR 3 months later, and group II consisted of 40 patients who underwent combined CABG (using SVG) and MVR. Our aim was to compare intraoperative, postoperative, and follow-up outcomes of staged PCI versus CABG with MVR in patients with combined single-vessel and MV disease.

Figure 7



Postoperative outcomes among study groups.

Reoperative coronary bypass grafting in a patient with valvular disease poses a particular challenge in cardiac surgery. The hybrid approach is of particular benefit in reoperative patients who have had prior CABG with patent grafts. The technical difficulty of accessing lateral wall targets, safely dissecting patent bypass grafts, and obtaining exposure often precludes safe surgery, and these risks are not reflected in traditional scoring systems. Hybrid valve/PCI may be particularly useful in this regard and can dramatically simplify a challenging open valve and CABG surgery by substituting PCI for reoperative bypass grafting in lesions amenable to PCI [9]. However, we excluded redo patients from our study, as this cohort is extremely high risk and would have affected the results in a different way.

Although DESs have shown excellent results in clinical trials, their effectiveness in clinical practice with more complex patients and complex lesions (high SYNTAX score, totally occluded coronary vessels, bifurcated lesions, small vessels, long lesions requiring multiple stents, ostial stenosis, and calcified vessels) remains to be seen. Patients with diabetes, who comprise 30% of the surgical population and 37.5% of group I in our study, have higher restenosis rates with DES [10]. Late stent restenosis and thrombosis is another concern.

The most recent data from STS demonstrate that in those undergoing isolated MV surgery, the rate of MV repair was 57.4%, and MV replacement was 42.6% [1]. In the cases where MV pathology and etiology were documented, 56.6% were identified as having mitral regurgitation due to annular or degenerative disease, without stenosis, of which repair was performed in 75.0% of patients. In the present study, regarding the MV lesions, mitral stenosis was found in most of the patients: 24 (60%) patients of group I versus 16 (40%) patients of group II (P=0.074); mixed mitral lesions (stenosis+regurgitation) come in the second place, with eight (20%) patients of group I versus 20 (50%) patients of group II (P=0.005) (statistically significant association between groups regarding mixed MV lesions only); and mitral regurgitation was found in the minority of study groups, with eight (20%) patients of group I versus four (10%) patients of group II (P=0.210). This means that mitral repair could have been feasible in a minority of patients with pure mitral regurgitation, as the reparability of other pathologies varies markedly. This encouraged us to exclude mitral repair and standardize mitral replacement as the uniform approach for MV surgery in this study.

Although one needs to be cautious when making direct comparison with other studies, reductions in the parameters of morbidity were noted when compared with data from the most recent STS adult cardiac surgery database outcomes. In patients undergoing CABG plus MV replacement, the most common complication is new-onset AF, which occurs in 44.2% and increases perioperative morbidity and hospital length of stay [11]. This figure is higher than the 16.1% noted in the present cohort of PCI+minimally invasive mitral valve surgery (MIMVS) and is consistent with prior studies suggesting a reduced incidence of postoperative AF when utilizing a minimally invasive approach for valve surgery [12]. In our study, we compared staged PCI+conventional MVR (group I) to combined CABG+MVR (group II). We noticed no ECG changes in the form of arrhythmias in both groups. The AF patients preoperatively in both groups went through several changes in the rhythm and the rate intraoperatively before returning back to baseline AF again. This may be owing to the less morbid group of patients in our study, with good EF, low median

PAP, relatively good clinical status, and nearly no comorbidities.

The staged strategy ensures optimal myocardial protection during the mitral correction. It is our belief that myocardial protection is greatly enhanced with hybrid procedures. By achieving 100% completeness of revascularization before cross-clamping in all of our valve-PCI patients, cardioplegia administration to all regions of the heart was possible. In contrast, if surgeons are reluctant to attempt revascularization on high-risk or technically difficult to reach lesions, cardioprotection may be compromised, leading to low cardiac output postoperatively and worsened outcomes. The reduction in cross-clamp time for a hybrid procedure also provides significant myocardial protective benefit, as the heart is faced with a lower overall ischemic time and potentially less dysfunction upon reperfusion.

By performing PCI to treat the coronary artery disease, one obviates the necessity of performing concomitant CABG at the time of surgery, significantly reducing the complexity of the surgery and shortening the operative times, which was noted in our study when compared with conventional combined CABG and MVR. In our study, the median aortic cross-clamp and cardiopulmonary bypass times were 44 (IQR, 39–48) and 62 min (IQR, 59–68), respectively, for group I versus 60.5 (IQR, 55–65) and 82 min (IQR, 75–88), respectively, for group II (*P*=0.001); the difference between groups was statistically significant.

The less traumatic nature of isolated MVR and reduced operative times in group I likely conferred lower bleeding and transfusion requirements. The median bleeding loss (ml) postoperatively was 925 (IQR, 650–1200) in group I versus 1075 (IQR, 900–1400) in group II (*P*=0.021), which was statistically significant, with a median of 2 U of packed RBCs transfused (IQR, 1–2) in group I compared with a median of two packed RBC units transfused (IQR, 2–3) in group II (*P*=0.002), which was statistically significant also. However, the rate of re-exploration for bleeding did not differ significantly between both groups, with one (2.5%) case only in group I versus two (5%) cases in group II (*P*=0.556). All reoperations for bleeding cases were related to sternal wire placement, and no postoperative delayed cardiac tamponade was noted in any of the two groups.

Although our study was not powered to detect a statistically significant difference, shorter operative times and less blood product use during cardiac surgery are associated with fewer infections and a lower morbidity and mortality [13,14]. However, composite postoperative complications [prolonged mechanical ventilation (>24 h), respiratory complications, wound infection, cerebrovascular accidents, reoperation for bleeding, acute kidney injury, and 30-day mortality] occurred less frequently in group I than in group II.

With the goal being to optimize stent patency while minimizing the risks of bleeding, there is concern regarding the risk of bleeding if the surgery is performed after the PCI and the possibility of stent thrombosis with protamine reversal. Of particular concern is the risk of bleeding with dual antiplatelet therapy, largely based on known higher rates of bleeding after CABG in patients receiving clopidogrel [15]. In the current study, median time of PCI to MV surgery was 93 days. The patients had their antiplatelet agents stopped 5 days before surgery and resumed their antiplatelet regimen within 24–48 h after surgery.

In the previously mentioned study by Byrne *et al.* [16], because of the use of dual antiplatelet therapy, a high incidence of bleeding occurred, with 22 (85%) of the 26 patients requiring blood transfusions. In an attempt to reduce the incidence of bleeding, Brinster *et al.* [17] performed the PCI the day of, or evening before, the scheduled minimally invasive aortic valve replacement in 18 patients. There were no reoperations for bleeding, and only eight (44%) patients required blood transfusions.

Santana and colleagues compared the outcomes of patients taking clopidogrel with those who were not taking clopidogrel. In the intraoperative period, there were no differences in the requirement of blood products, whereas in the postoperative period, there was a significantly higher number of patients taking clopidogrel who required blood products compared with those not taking clopidogrel. Out of concern for the possible development of stent thrombosis, they prefer the continuation of antiplatelet therapy at the time of valve operation [18].

In the study of Mihos *et al.* [19], even though there was a higher use of preoperative clopidogrel in those undergoing PCI+MIMVS, there were fewer intraoperative transfusions required, when compared with CABG+MVS. The lower need for blood products in the PCI+MIVS group is most likely due to the fact that, by its less traumatic nature, minimally invasive valve surgery is associated with less blood loss. Moreover, by virtue of the fact that there was no need to place bypass grafts, the operative times were much shorter in this group, thereby having less bleeding [20]. Importantly, there were no cases of acute stent thrombosis perioperatively. In their previous work, they evaluated 222 patients who had PCI+MIMVS, 183 of which were on clopidogrel and were compared with 38 who were not [18]. In the intraoperative period, there were no differences in the requirement of blood products between the two groups. Postoperatively, there were a higher proportion of patients on clopidogrel requiring blood products compared with those who did not take it (50.5 vs. 26.3%, *P*=0.005); however, there was no significant difference in the need for reoperation for bleeding. Because clopidogrel use perioperatively appears to be safe [21], their clinical practice has been to continue antiplatelet therapy at the time of valve surgery to minimize the risk of acute stent thrombosis.

Ideally, these patients would be best managed by either a longer staging duration so that the clopidogrel can be stopped (3–6 months with DES) or by a very short staging duration (under 6 h), so that clopidogrel's actions are just beginning to take effect once the surgery has been completed. Our study differs from the previously mentioned studies in that we had a significant variation on the use of antiplatelet agents; our group I patients had their antiplatelet agents stopped 5 days before surgery. The median time of PCI to MV surgery in our study was 93 days, so we feel it is safe to withhold the antiplatelet therapy.

In these hybrid procedures, the optimal timing of the valve operation once PCI has been performed is not known. At our institution, the time delay between PCI and the valve operation is mainly driven by a desire to reduce the incidence of acute kidney injury counterbalanced with the urgency of the operation. It has been noted that the closer the two procedures are in time, the higher the incidence of acute kidney injury. Data from 4440 patients undergoing coronary angiography and cardiac operation on the same day demonstrated this approach to be an independent predictor for the development of acute kidney injury [22]. Another study evaluated the incidence of acute kidney injury in patients who had cardiac catheterization and cardiac operations during the same admission and compared it with a group of patients who had cardiac catheterization followed by operation at a later admission [23]. The incidence of acute kidney injury in the patients who had same-admission cardiac catheterization and operations was 50.2% compared with 33.7% in those who had operations at a later date (*P*=0.009). To reduce the incidence of acute kidney injury, several institutes prefer to wait at least 3 weeks after PCI to perform valve operations [22, 23].

We decided to wait 3 months after PCI to perform MVR, to avoid renal failure, and to be able to stop the antiplatelet therapy safely. We have got two (5%) patients in group I versus one (2.5%) in group II of acute kidney injury (*P*=0.556), in the form of elevated creatinine levels, which resolved medically, without the need for dialysis. This difference was not statistically significant. We attribute this to the period of 3 months between PCI and MVR, which provide us with the protection window against acute kidney injury.

Santana *et al.* [24] compared 65 patients who had a hybrid approach with 52 matched control patients who underwent conventional bypass grafting and valve operation. The results demonstrated a significant reduction in composite complications and hospital lengths of stay in the hybrid group when compared with conventional group. This is similar to the results per our study which showed less composite complications in group I, as well as statistically significant lower median ICU length of stay (hours) and hospital length of stay (days): 39 h (IQR, 32–45) and 5.5 days (IQR, 5–6), respectively, for group I versus 56.5 h (IQR, 49–69) and 8.5 days (IQR, 7–13), respectively, for group II (*P*=0.001).

The postoperative complications were comparable, with no statistically significant difference for groups I and II, with less prolonged mechanical ventilation (>24 h) [0 versus three (7.5%)] and less respiratory complications [0 versus one (2.5%)] for group I. This may be due to less aggressive and less time-consuming procedure in the isolated MVR than the combined CABG+MVR, which paves the way for faster extubation with less respiratory complications. The three patients of group II eventually got extubated, one of them got chest infection which was resolved using appropriate antibiotics. However, both approaches did include a sternotomy.

By virtue of avoiding a sternotomy, minimally invasive surgery results in less thoracic surgical trauma and alterations in pulmonary physiology and biomechanics, which contributes to an enhanced postoperative recovery and faster extubation, with a reported significantly lower incidence of prolonged mechanical ventilation occurring in 18.3% of the PCI+MIMVS cohort and 29% in CABG plus MV replacement, leading to shorter ICU length of stay with the PCI+MIMVS approach, when compared with sternotomy. We do not see this significant difference in our study, because both groups were approached through a median sternotomy, with low incidence of prolonged mechanical ventilation, most probably due to exclusion of any lung disease or other comorbidities from our study groups.

Our present study showed slightly less wound infection in group I [0 vs. two (5%)], most probably owing to less operative time, ICU and hospital stay, blood transfusion requirements, and other postoperative complications, which usually encourage infection. However, this difference is not significant, probably owing to the similar approach used in both groups, that is, sternotomy, and similar baseline characteristics between both groups.

The cerebrovascular accident encountered in our study was one stroke patient in group II without any residual deficit. No other cases were reported in both groups, probably owing to relatively good baseline characteristics of the patients included in our study, with good carotid duplex preoperatively, and exclusion of old patients above 60 years old with any central or peripheral vascular disease.

Several groups have investigated hybrid approaches of PCI combined with valve operations. In 2014, Santana *et al.* [24] published the results of more than 200 patients who underwent PCI for coronary revascularization followed by a minimally invasive valve procedure. They found a mortality rate of 3.6% and an all-cause mortality rate of 12% at 4.5 years. They also demonstrated a decreased complication rate and length of stay for the hybrid group compared with those undergoing conventional sternotomy.

George *et al.* [21] recently described a series of 26 patients who underwent a single-stage hybrid procedure involving PCI of a non-LAD vessel followed by a valve operation. Recalculating the STS risk after the PCI was performed. They found a 35% risk reduction in the re-operative group and a 17% risk reduction in the non-reoperative group. In addition, they had no in-hospital mortalities and very few complications. No coronary-stent thromboses were noted during a follow-up period of 2 years.

Specific to MV, Umakanthan *et al.* [25] described the Vanderbilt experience with 32 consecutive patients who underwent a hybrid procedure, including PCI and MV surgery. Of these procedures, 28 (89%) were performed as a single-stage procedure in a hybrid operating room. The observed in-hospital mortality rate was 3% (1/32) and survival at 1 and 2 years was 96 and 89%, respectively. The series was expanded to 39 patients and reported by Solenkova *et al.* [26], noting a predicted mortality for conventional CABG/ mitral of 14.1% versus an observed in-hospital mortality of only 2.6% (1/39).

This is different from our study which showed no operative/30-day mortality in both groups. This may be attributed to the baseline characteristics of our group of elective patients who are low risk patients with few or no comorbidities.

As demonstrated by 5-year outcomes from the Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery (SYNTAX) trial [27], a strong argument can now can be made for PCI in patients with left main or multivessel disease with low SYNTAX scores (<23). However, the SYNTAX trial also clearly demonstrates a survival benefit of CABG for patients with a higher burden of disease, as reflected by a high SYNTAX score (>33), and in specific patient subsets, such as patients with diabetes mellitus [28]. The benefit of CABG is primarily attributable to left IMA grafting to the LAD, and the patency of IMA grafting consistently exceeds 95% at 10 years, setting the gold standard with which other revascularization strategies should be compared. Yet, significant limitations of both PCI and CABG persist. However, PCI is burdened by the need for repeat target lesion interventions. SVG failure for non-LAD targets in CABG can reach 30% at 1 year, and at 10–15 years, only 50–60% of the SVGs have been reported to be patent [29]. Conversely, the early restenosis and thrombosis rate of the DES in non-LAD vessels is lower than that reported for SVG failure [30].

This is more or less in line with the results per our study. Postoperative routine TTE follow-ups upon discharge, after 3 months, 6 months, and 1 year were done for all patients in both groups. Follow-up was completed after 1 year. Regional wall motion abnormalities were noted in 15 (37.5%) patients of group I versus 17 (42.5%) patients of group II (P=0.648), who all underwent stress ECG, of whom nine (22.5%) patients in group I versus 11 (27.5%) patients in group II showed positive results (P=0.606) and were qualified for diagnostic coronary angiography, which confirmed the need for reoperation for myocardial ischemia/infarction within the first year of follow-up postoperatively in four (10%) patients of group I versus eight (20%) patients of group II (P=0.210). However, all these follow-up outcomes showed no significant difference between both groups within the first year of follow-up. None of the patients in both groups had major cardiac events or CCU admission. We attribute this to the nature of our patients in both groups, who have single non-LAD vessel disease supplying limited heart territories with good functional reserve. Long-term data are needed for more informative conclusion.

As more hybrid PCI/valve procedures are being performed, many questions remain unanswered, including the optimal order for the procedures, their timing, the management of dual antiplatelet therapy, and the optimal costs and logistics of the procedures [8].

Limitations

The primary limitation of the present study is the associated potential for treatment selection bias. The patients who underwent PCI were selected on the basis of favorable coronary anatomy for this procedure, which is an important selection bias. Moreover, all patients had single-vessel coronary artery disease with normal left ventricular EFs, and few or no comorbidities. High-risk patients were excluded from this study.

The follow-up of the patients was limited to 1 year, and thus no statement may be made regarding long-term differences in outcomes, as might be expected when comparing PCI and CABG.

Conclusion

A staged approach of PCI followed by MVR is an alternative to the conventional combined CABG and MVR, can be performed safely in some patients with single coronary artery and MV disease, and is associated with good short and follow-up outcomes. As per our study, it was associated with (a) significantly less operative time; (b) significantly faster post-operative recovery, as evidenced by a shorter ICU and hospital lengths of stay; (c) significantly less bleeding and blood transfusions, with no significant difference regarding re-exploration for bleeding; and (d) comparable morbidity, mortality, and early follow-up outcomes. Although our valve-PCI cohort primarily underwent surgery through conventional sternotomy, we expect to see even greater clinical benefits regarding lower transfusion, pain, and length of stay when undergoing minimally invasive, robotic, or small incision valvular surgery.

Nevertheless, important questions remain, including the optimal timing of the individual procedures, and the optimal antiplatelet therapy after PCI. With ongoing advances in stent technology, procedural techniques, and anticoagulation strategies, as well as the accumulation of long-term outcomes data, hybrid approaches to concomitant coronary artery and MV disease will likely become increasingly common. Tailoring the approach to individual patient pathology and comorbidities is feasible and offers potentially better treatment paradigms.

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Conflicts of interest

There are no conflicts of interest.

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