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# Comparison of Clinical Outcomes among Patients Undergoing Coronary Artery Bypass Grafting (CABG) with or without Prior Percutaneous Coronary Intervention (PCI)

**Mohamed A Alassal[1,2*], Hany Elrakhawy[1,2], Ahmed H Omar[2,5], Magdy Hassenien[3,4], Mohamed Aldahmashi[5], Bedir Ibrahim[6], Nabil Elsadeck[7] and Mohamed F Ibrahim[2]**

[1]*Cardiothoracic Surgery Department, Benha University, Egypt*

[2]*King Salman Heart Center, King Fahd Medical City, Riyadh, Saudi Arabia*

[3]*Department of Cardio-thoracic Surgery, National heart institute, Egypt*

[4]*Cardiothoracic Surgery Department, Ain shams University, Egypt*

[5]*Cardiothoracic Surgery Department, Thamar University, Yemen*

[6]*Cardiothoracic Surgery Department, Tanta University, Egypt*

[7]*Cardiothoracic Surgery Department, Zagazig University, Egypt*

[*]**Corresponding author:** Mohamed Abdulwahab Alassal, King Salman Heart Center, King Fahd Medical City, Riyadh, Saudi Arabia, Tel: +966112889999, +966543178563; Email: dmohamedabdelwahab@gmail.com

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## Abstract

**Background:** There are increasing number of patients who are referred for coronary artery bypass grafting (CABG) after prior percutaneous coronary intervention (PCI). The intent here is to characterize the risk, if any, that is associated with PCI experience prior to CABG.

**Methodology and patients:** 2358 consecutive patients underwent coronary artery bypass grafting between January 2008 to December 2013 at two tertiary cardiac centers in Middle East (one center in Egypt and one in Saudi Arabia) divided in 2 groups: 1st group-492 patients with Prior PCI to CABG (PPCABG), and the 2nd group-1866 patients underwent CABG without previous PCI (Native Vessel CABG-NVCABG). We chose the 2 groups with similar cardiac morbidities and extra cardiac co-morbidities.

**Results:** Except for emergency cases, clopidogrel, statin use and the distribution of NYHA classification, the two groups were similar in terms of baseline demographic and pre-operative characteristics. Summarized intra-operative and post-operative data showed that PPCABG group had significantly higher cross clamp time, total bypass time, higher incidence of post-operative complications such as bleeding, renal impairment than NVCABG and also significant higher in-hospital mortality rate in PPCABG group than NVCABG group.

**Conclusion:** Future re-interventions after PCI are common and both extent of disease and re-stenosis of stents are responsible for re-intervention. PCI prior to CABG increases morbidity post operatively and seem to have an independent factor in increasing mortality. So, in the best interest of the patient, proper consensus among cardiologists and cardiac surgeons must be reached before subjecting to PCI, especially in cases of multivessel coronary artery disease.

**Keywords:** PCI; CABG; In-stent restenosis; Coronary endarterectomy; CABG post PCI

## Abbreviations:

CABG: Coronary Artery Bypass Grafting; PCI: Percutaneous Coronary Intervention; PPCABG: Prior PCI to CABG; NVCABG: Native Vessel CABG; NYHA: New York Heart Association; LAD: Left Anterior Descending Artery; LIMA: Left Internal Mammary Artery; EF: Ejection Fraction; IAB: Intra-Aortic Balloon

## Introduction

Percutaneous coronary intervention (PCI) is emerging as the main treatment option for coronary artery disease and the number of PCI procedures are rapidly increasing worldwide [1].

Today, coronary artery bypass grafting is very commonly performed in patients who have recurrent symptoms after previously successful PCI either because of late failure of the deployed PCI or more commonly because of progression of the native disease. The widespread use of PCI has resulted in an increasing number of patients being referred for CABG surgery who have undergone prior PCI [2,3].

While the efficacy and outcomes for PCI and coronary artery bypass grafting as the primary treatment for coronary disease are well documented, there is little recent data available that specifically focuses

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on those patients who ultimately receive a surgical graft after a supposedly initially successful PCI [4-6].

| Variables | PPCABG (n=492) | NVCABG (n=1866) | p-values |
|---|---|---|---|
| **Male gender** | 366 (74.4%) | 1398 (74.9%) | ns |
| **Age (years)** | 58.6 (± 9.4) | 56.7 (± 10.7) | ns |
| **Height** | 163.6 (± 20) | 161.2 (± 15.7) | ns |
| **Weight** | 84 (± 21.3) | 76 (± 15.4) | ns |
| **Body surface area** | 1.83 (± 2.3) | 1.81 (± 2.0) | ns |
| **Urgent Presentation** | 156 (31.7%) | 126 (6.8%) | <0.05* |
| **Recent MI** | 270 (54.91%) | 1302 (69.8%) | ns |
| **Diabetes** | 402 (81.7%) | 1344 (72.0%) | ns |
| **Hypertension** | 408 (82.9%) | 1332 (71.4%) | ns |
| **Smoking** | 246 (50.0%) | 1044 (55.9%) | ns |
| **Positive family history** | 120 (24.4%) | 480 (25.7%) | ns |
| **Dyslipidemia** | 438 (89.0%) | 1350 (72.3%) | ns |
| **Clopidogril use** | 348 (70.7%) | 0 (0%) | <0.05* |
| **Statin use** | 460 (93.5%) | 618 (33.2%) | <0.05* |
| **NYHA class** | | | |
| **No SOB** | 78 (15.9%) | 12 (0.6%) | <0.05* |
| **I** | 120 (24.4%) | 834 (44.7%) | |
| **II** | 192 (39%) | 576 (30.9%) | |
| **III** | 84 (17%) | 354 (19%) | |
| **IV** | 18 (3.7%) | 90 (4.8%) | ns |
| **EF** | 45.2 (10.6 ±) | 47.1 (9.3±) | ns |
| **Diastolic dysfunction** | | | |
| **NO** | 108 (22%) | 546 (29.3%) | ns |
| **Mild** | 90 (18.3%) | 228 (12.2%) | |
| **Moderate** | 246 (50%) | 286 (46%) | |
| **Severe** | 68 (13.82%) | 234 (12.5%) | |
| **More than two vessels** | 460 (93.5%) | 1698 (91%) | ns |
| **LM Disease** | 108 (21.2%) | 300 (16.1%) | ns |

**Table 1:** Demographic and preoperative characteristics in the two groups.

There are a number of hypotheses as to why previous PCI may adversely affect outcomes with CABG. Patients may present with more advanced disease due to the effect of PCI in delaying surgery until later in life when the disease has progressed and even the patients may present in a more unstable clinical state. Another reason can be compromise of left ventricular function and loss of collateral circulation due to occlusion of side branches especially when many stents are deployed. Distal micro-embolization from stents is another possible cause of left ventricular dysfunction. Endothelial dysfunction induced by stenting is well known. Furthermore, the necessity to bypass the coronary artery more distally where it is smaller with more diffuse disease especially in patients with multiple stents can also be a cause of worse outcomes after CABG [7,8].

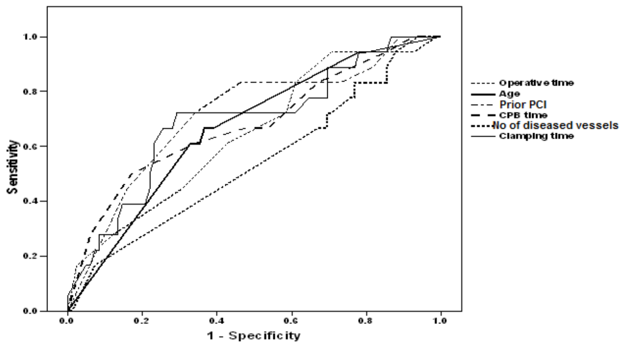


**Figure 1:** ROC curve analysis of evaluated parameters as predictors for development of additional morbidities of PO CABG patients with prior PCI showed that: the presence of prior PCI, aortic clamping time, CPB time and total operative time are the significant predictors.

In our study, we tried to analyse those patients who underwent initially successful PCI and developed recurrent symptoms, and then ultimately required a CABG procedure. Outcomes were studied for these patients and were compared to those patients that were treated by primary elective CABG over the same time period.

## Patients and Methodology

This is a retrospective randomized study that was done by analysing data from files of 2358 consecutive patients with ischemic heart disease who had symptoms not relieved by medical management and underwent CABG between January 2008 and December 2013 at two tertiary cardiac centers in Middle East (one center in Egypt and one in Saudi Arabia). We excluded all patients with organic valvular disease and/or underwent previous open heart surgery.

Patients were divided into two groups:

**First Group:** 492 patients who underwent initial successful PCI who developed recurrent symptoms, and then ultimately required CABG (Prior PCI CABG- PPCABG) and **Second Group:** 1866 patients treated by primary elective CABG (Native Vessel CABG- NVCABG).

On admission, the patients were subjected to the following: clinical evaluation, routine laboratory evaluation (including cardiac enzymes), plain chest x-ray, standard preoperative 12-leads ECG and echocardiography.

### Operative data

All procedures were performed using full median sternotomy; cardio-pulmonary bypass was of conventional standardized fashion, typically with high ascending aortic cannulation, and 2-stage single venous cannulation of the right atrium. Myocardial protection was afforded by antegrade intermittent cold blood cardioplegia and mild hypothermia (32°C). After arrest of the heart, all of our patients underwent conventional coronary artery bypass grafting procedure except for some cases who required certain procedures like sequential anastomoses, and/or creation of more than one bypass to the LAD territory, and/or open endarterectomy combined with different means of complex coronary reconstruction, and/or removal of stents in a 'full-metal jacket' LAD, followed by vein patch and anastomosis to the internal mammary graft or LIMA graft as an "onlay" patch to LAD.

| | | Parameter | β | t | Sig. |
|---|---|---|---|---|---|
| Morbidity | Model 1 | CPB time | 0.281 | 2.886 | 0.005 |
| | | Clamping time | 0.266 | 2.928 | 0.004 |
| | | Prior PCI | 0.256 | 3.169 | 0.002 |
| | Model 2 | Prior PCI | 0.286 | 3.041 | 0.003 |
| | | Clamping time | 0.264 | 2.809 | 0.006 |
| | Model 3 | Prior PCI | 0.273 | 2.808 | 0.006 |
| Mortality | Model 1 | Age | 0.231 | 2.513 | 0.014 |
| | | Clamping time | 0.239 | 2.593 | 0.011 |
| | | Prior PCI | 0.293 | 3.187 | 0.002 |
| | Model 2 | Clamping time | 0.256 | 2.716 | 0.008 |
| | | Prior PCI | 0.289 | 2.716 | 0.002 |
| | Model 3 | Prior PCI | 0.263 | 2.894 | 0.005 |

**Table 2:** Regression analysis for evaluated parameters as predictors for postoperative morbidities and mortality. β: Standardized coefficient; Sig.: significance; PO: postoperative; CPB: cardiopulmonary time.

The patient is then weaned from cardiopulmonary bypass and the sternum is closed after routine hemostasis was secured and insertion of chest tubes.

The data regarding post CABG hospital stay, post CABG intra-aortic balloon, need for inotropic support, re-exploration, blood or blood products transfusion, myocardial infarction, ventricular arrhythmias or repeat revascularization, and survival in both groups was recorded.

## Follow-up protocol

The studied patients were scheduled for follow-up in the outpatient clinic in two weeks, one month, three months, and six months-intervals after discharge from hospital. Each patient was subjected to clinical evaluation, routine laboratory evaluation, plain chest X-ray, 12-lead ECG and Doppler echocardiography.

## Statistical analysis

Obtained data was presented as mean SD, ranges, numbers and ratios. Results were analysed using Wilcoxon; ranked test for unrelated data (Z-test) and Chi-square test ($\chi^2$ test). Sensitivity and specificity of estimated parameters as predictors for postoperative mortality were evaluated using the receiver operating characteristic (ROC) curve analysis judged by the area under the curve (AUC) compared versus the null hypothesis that AUC=0.05. Regression analysis (Stepwise method) was used for stratification of studied parameters as predictors for postoperative mortality after CABG. Statistical analysis was conducted using the SPSS (Version 15, 2006) for Windows statistical package. P value<0.05 was considered statistically significant.

| Variables | PPCABG (n=492) | NVCABG (n=1866) | p-values |
|---|---|---|---|
| Use of left Internal Mammary artery | 474 (96.3%) | 1794 (96.1%) | ns |
| Use of both internal mammary arteries | 20 (4.06%) | 76 (4.1%) | ns |
| Cross clamp time | 126.9 (± 34.6) | 84.2 (± 31.1) | <0.05* |
| Bypass time | 146.3 (± 43.7) | 94.7 (± 39.0) | <0.05* |
| Coronary endarterectomy | 48 (9.8%) | 18 (0.96%) | <0.05* |
| Total Hospital Stay (days) | 15 (± 4.2) | 11(± 3.9) | <0.05* |
| Bleeding required blood +/- blood products transfusion transfusion | 48 (9.8%) | 36 (1.9%) | <0.05* |
| Reopening for bleeding | 30 (6.1%) | 76 (4.1%) | ns |
| Low cardiac output syndrome | 70 (14.2%) | 134 (7.2%) | <0.05* |
| IABP | 18 (3.7%) | 48 (2.9%) | ns |
| Prolonged-Ventilation | 102 (20.7%) | 234 (12.5%) | ns |
| Renal Impairment | 18 (3.7%) | 20 (1.1%) | <0.05* |
| Mortality | 18 (3.66%) | 18 (0.96%) | <0.05* |

**Table 3:** Operative and post-operative data in the two groups. Data are presented as mean ± SD and numbers; ranges and percentages are in parenthesis. *p significant<0.05, ns=No significance.

## Results

Except for the emergency cases, dyslipidemia, clopidogrel use and the distribution of NYHA classification, the two groups were similar in terms of baseline demographic and preoperative characteristics (Table 1).

ROC curve analysis for evaluated parameters as predictors for development of post-operative morbidities showed that: the presence of prior PCI, aortic clamping time, CPB time and total operative time are the significant predictors (Figure 1). While for prediction for post-operative mortality: prior PCI, aortic clamping time, CPB time and age are the significant predictors, (Table 2 and Figure 2). To verify these predictors, regression analysis defined prior PCI as significant predictor for both postoperative morbidity and mortality in three models, followed by duration of ischemia manifested as aortic artery clamping time in two models and both of CPB time and age in one model (Table 3).

Summarized intra-operative and post-operative data showed that PPCABG group had higher coronary endarterectomy and demanding complex coronary procedures, cross clamp time, total bypass time, post- operative bleeding, post-operative low cardiac output syndrome and use of inotropic support, total hospital stay and renal impairment than NVCABG (Table 4). Also, the mortality in NVCABG group was 18/1866 cases (0.96%) which were found to be less percentage than the other group which was 18/492 cases (3.66%) (p<0.05*) (Table 4).

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| | Parameter | AUC | Std. Error | Sig. | Confidence Interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| Morbidity | Age | 0.615 | 0.064 | >0.05 | 0.489 | 0.741 |
| | Clamping time | 0.648 | 0.058 | 0.018 | 0.534 | 0.763 |
| | CPB time | 0.648 | 0.058 | 0.018 | 0.534 | 0.763 |
| | Operative time | 0.632 | 0.064 | 0.036 | 0.506 | 0.757 |
| | No. of diseased vessels | 0.558 | 0.062 | >0.05 | 0.436 | 0.679 |
| | Prior PCI | 0.668 | 0.058 | 0.007 | 0.555 | 0.782 |
| Mortality | Age | 0.667 | 0.067 | 0.027 | 0.535 | 0.799 |
| | Clamping time | 0.692 | 0.071 | 0.011 | 0.552 | 0.832 |
| | CPB time | 0.68 | 0.075 | 0.017 | 0.533 | 0.826 |
| | Operative time | 0.644 | 0.071 | >0.05 | 0.506 | 0.783 |
| | No. of diseased vessels | 0.539 | 0.077 | >0.05 | 0.388 | 0.69 |
| | Prior PCI | 0.713 | 0.069 | 0.005 | 0.577 | 0.849 |

**Table 4:** ROC curve analysis for evaluated parameters as predictors for postoperative morbidities and mortality. AUC: Area under curve; Std error: Standard Error; Sig.: Significance; Preop: Preoperative; PO: Postoperative; CPB: Cardiopulmonary Time.

## Discussion

Since the introduction of PCI as an alternative myocardial revascularization procedure to CABG, several studies have been published comparing the outcomes of CABG and PCI as the primary treatment for coronary artery disease. On the other hand there are an increasing number of patients with a previous successful PCI undergoing CABG [9,10]. The differences between this patient-population and patients treated by primary CABG as the therapy for coronary artery disease have hardly ever been studied [11,12]. Here, we present our study on the preoperative, operative and postoperative differences between patients treated primarily by CABG and patients initially treated by PCI and later required CABG.

After analysis of our study results, we found that pre-operative urgent presentation and emergency CABG were significantly higher in PPCABG group (31.7%) than NVCABG group (6.8%) with p value<0.05. Moreover, pre-operative recent MI was insignificantly higher in NVCABG group (69.8%) than PPCABG group (52.4%), p value is non-significant. This does not coincide with the results in other series done by Bonaros et al. who reported that previous recent MI was 54% in group "without prior PCI" and 34% in group with "primary PCI preceding CABG", p<0.05. Also, he documented emergency cases were 3% in the 1st group with prior PCI and 0% in the 2nd group [12].

In contrast to our study, some authors demonstrated that patients with prior PCI had a significantly higher pre-operative ejection fraction, less extensive coronary disease, and fewer bypass grafts [13].

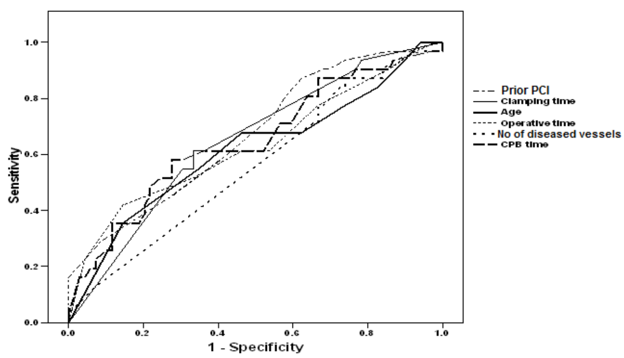


**Figure 2:** ROC curve analysis of evaluated parameters as predictors for mortality of PO CABG patients with prior PCI showing that prior PCI, aortic clamping time, CPB time and age are the significant predictors.

Analysing intra-operative data in our study showed insignificant difference as regard to the number of affected vessels and the percentage of use of internal mammary arteries in both groups, while in another study done by Thielmann et al., the mean number established by passes was significantly different among both groups (2.43 vs. 2.08, p=ns) and mean number of arterial bypass grafts used for revascularization showed significant results as well (1.26 vs. 1.7, p=ns), but they agreed with us that both cross clamp time and total bypass time were longer in post PCI group [14].

In our study, during post-operative course, the amount of post-operative bleeding was higher in PPCABG group than in NVCABG group. While others documented that, the amount of post-operative bleeding was higher in primary CABG group than in CABG post PCI group, and blood products utilization especially of platelets transfusion was higher in CABG post PCI group. This could possibly explain as one of the reasons for limited blood loss after surgery, and re-exploration rates were similar for the two groups [15].

Post-operatively, there were significant differences in in-hospital stay and in-hospital mortality in our two groups. This was similar to many other studies, but in these studies there was no significant difference in percentages of renal complications that was significantly higher in our PPCABG group [16].

Similar to other studies, it showed that the PCI group had a significantly higher risk of myocardial ischemia after CABG surgery (unstable angina requiring hospitalization) than the non-PCI group [17].

Some investigators have shown evidence that previous PCI has a negative influence on perioperative morbidity and mortality after elective CABG. They claimed that mortality was higher in short and mid-term after CABG with prior PCI due to coronary artery's pathology; and more urgent presentation requiring urgent surgery and more aggressive atherosclerotic changes with stent promoting a higher rate of restenosis and development of new lesions distal to PCI site and prevention of formation of protective collateral vessels, which result in more urgent presentation. Finally, prior PCI sometimes obligate surgeons to do their anastomosis more distal to the stent to avoid endarterectomy which leads to anastomosis in smaller calibre diameter and sub-optimal run-off, thus compromising the degree to which the patient was completely re-vascularized and negatively affect the durability of the used graft [7,8,17].

In meta-analysis done by Biancari et al., they concluded that prior PCI is associated with an increased risk of early in-hospital mortality after CABG but seems not to affect late mortality [18].

Also, in a study done by Mohr et al., 5 years follow-up to SYNTAX trial, which compared CABG with PCI for the treatment of patients with left main coronary disease or three-vessel disease, they concluded that CABG should remain the standard of care for patients with complex lesions (high or intermediate SYNTAX scores). For patients with less complex disease (low SYNTAX scores) or left main coronary disease (low or intermediate SYNTAX scores), PCI is an acceptable alternative. All patients with complex multivessel coronary artery disease should be reviewed and discussed by both a cardiac surgeon and interventional cardiologist to reach consensus on optimum treatment and this was similar to the results and interpretation of our study [19].

## Conclusion

From our study we can conclude that:

- Percutaneous interventions are successful method of revascularization and delays surgery, but future re-interventions are common and both extent of disease and re-stenosis of stents are responsible for re-intervention
- “PCI preceding CABG” increased morbidity post operatively and seems to have an independent risk factor in increasing post-operative mortality as well

So, we think that patients who present for “CABG after PCI” should at the very least be classified to be at a higher perioperative risk.

We can safely recommend here that, in the best interest of the patient, proper consensus among cardiologists and cardiac surgery team must be reached before subjecting to PCI, especially in cases of multivessel coronary artery disease.

## Study Limitations

We can put on-hand on several limitations for this study such as:

- The potential bias of any retrospective study
- We couldn't get full detailed information about types of previous stents in most of the patients, for example, drug eluting or bare-metal stents, that may affect the outcome
- We also don’t have information on the number of patients who may have not survived after primary PCI and therefore never received a CABG
- Our study was done in two tertiary centers only, and may require bigger patient volume for more precise evaluation and assessment

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