Korean J Thorac Cardiovasc Surg 2016;49:171-176 □ Clinical Research □
ISSN: 2233-601X (Print) ISSN: 2093-6516 (Online) http://dx.doi.org/10.5090/kjtcs.2016.49.3.171

Factors Associated with Early Adverse Events after Coronary Artery Bypass Grafting Subsequent to Percutaneous Coronary Intervention

Yasser Ali Kamal, M.Sc., Yasser Shaban Mubarak, M.D., Ashraf Ali Alshorbagy, M.D.

Background: A previous percutaneous coronary intervention (PCI) may affect the outcomes of patients who undergo coronary artery bypass grafting (CABG). The objective of this study was to compare the early in-hospital postoperative outcomes between patients who underwent CABG with or without previous PCI. ***Methods:*** The present study included 160 patients who underwent isolated elective on-pump CABG at the department of cardiothoracic surgery, Minia University Hospital from January 2010 to December 2014. Patients who previously underwent PCI (n=38) were compared to patients who did not (n=122). Preoperative, operative, and early in-hospital postoperative data were analyzed. The end points of the study were in-hospital mortality and postoperative major adverse events. ***Results:*** Non-significant differences were found between the study groups regarding preoperative demographic data, risk factors, left ventricular ejection fraction, New York Heart Association class, EuroSCORE, the presence of left main disease, reoperation for bleeding, postoperative acute myocardial infarction, a neurological deficit, need for renal dialysis, hospital stay, and in-hospital mortality. The average time from PCI to CABG was 13.9±5.4 years. The previous PCI group exhibited a significantly larger proportion of patients who experienced in-hospital major adverse events (15.8% vs. 2.5%, p=0.002). On multivariate analysis, only previous PCI was found to be a significant predictor of major adverse events (odds ratio, 0.16; 95% confidence interval, 0.03 to 0.71; p=0.01). ***Conclusion:*** Previous PCI was found to have a significant effect on the incidence of early major adverse events after CABG. Further large-scale and long-term studies are recommended.

Key words: 1. Coronary artery bypass
2. Percutaneous coronary intervention
3. Stents

INTRODUCTION

Percutaneous coronary intervention (PCI) has become a strategy for initial revascularization in the treatment of selected patients with coronary artery disease [1,2]. The primary goal of PCI is to provide a less invasive strategy for revascularization than coronary artery bypass grafting (CABG). The subsequent development of coronary stents has almost eliminated, or at least has dramatically reduced, the need for emergency CABG related to PCI [3].

Currently, the minimally invasive nature of stents in combination with advances in stent technology has led to the widespread use of PCI. However, a significant number of patients initially treated using PCI may require CABG [4,5]. Therefore, the aim of this study was to evaluate the effect of previous PCI on the early outcomes of CABG regarding the

Department of Cardiothoracic Surgery, Minia University Hospital
Received: November 26, 2015, Revised: February 3, 2016, Accepted: February 4, 2016, Published online: June 5, 2016
Corresponding author: Yasser Ali Kamal, Department of Cardiothoracic Surgery, Minia University Hospital, Minia 61519, Egypt
(Tel) 20-01123234736 (Fax) 20-86-2322505 (E-mail) yaser_ali_kamal@yahoo.com

postoperative occurrence of major events, based on a comparison with patients who underwent CABG on native coronary arteries.

METHODS

This retrospective study included 160 patients who underwent CABG with or without a history of previous PCI over a period of five years, extending from January 2010 to December 2014, at the department of cardiothoracic surgery, Minia University Hospital, Egypt, and fulfilled the inclusion criteria. Thirty-eight patients had a history of PCI and 122 underwent CABG for native vessels without prior interventions. Data were retrieved from patient files and discharge information. Patients were excluded if they had a myocardial infarction less than one week before CABG, a concomitant valve or other cardiac procedure, emergent surgery, redo CABG, or off-pump CABG.

Preoperative risk conditions were defined based on clinical, echocardiographic, laboratory, and radiological workups, and included: (1) obesity, as defined by a body mass index ≥30 kg/m^2; (2) chronic pulmonary disease, as reflected by the long-term use of bronchodilators or steroids for lung disease; (3) extracardiac arteriopathy, as defined by claudication, carotid occlusion, or >50% stenosis, and/or previous or planned interventions in the abdominal aorta, limb arteries, or carotids; (4) neurological dysfunction, with disease severely affecting ambulation or day-to-day functioning; (5) active endocarditis, with the patient still on antibiotic treatment for endocarditis at the time of surgery; (6) a critical preoperative state indicated by the presence of ventricular tachycardia, ventricular fibrillation, or aborted sudden death, preoperative cardiac massage, preoperative ventilation before standardly planned anesthesia, preoperative inotropes or an intra-aortic balloon pump, preoperative acute renal failure (anuria or oliguria of <10 mL/hr); (7) unstable angina as defined by resting angina requiring intravenous nitrates until arrival in the anesthetic room; (8) recent myocardial infarction (MI), as defined by a history of MI occurring within 90 days; (9) pulmonary hypertension as defined by a systolic pulmonary artery pressure >60 mmHg; (10) renal impairment based on creatinine clearance calculated using the Cockcroft–Gault formula, and defined as on dialysis (regardless of serum creatinine level), moderately impaired renal function (50–85 mL/min), or severely impaired renal function (<50 mL/min); (11) low left ventricular ejection fraction (LVEF) as defined by an ejection fraction of ≤50%; and (12) left main disease, defined as >50% narrowing of the left main coronary artery.

The patients were categorized into three groups according to the additive EuroSCORE: low risk (EuroSCORE of 1–2), medium risk (EuroSCORE of 3–5), and high risk (EuroSCORE ≥6) [6].

All patients underwent standard elective on-pump CABG. Cardiopulmonary bypass (CPB) was established via standard aortic and single venous cannulation using a roller pump. During CPB, oxygenation was achieved with an adult membrane oxygenator. Distal anastomoses were performed during aortic cross-clamping and proximal anastomoses were performed with partial clamping during rewarming. Revascularization was performed using only the left internal mammary artery and a saphenous vein graft in all patients.

The primary outcomes were operative (in-hospital) mortality and the occurrence of one or more major adverse events during the postoperative in-hospital stay (within 30 days), which included: re-operation for bleeding, acute postoperative MI within 24 hours, permanent stroke that did not resolve within 24 hours, prolonged ventilation (>24 hours), acute renal failure, and the need for new-onset renal dialysis. The data collected and analyzed included demographics, risk factors, echocardiographic findings, angiographic data, operative outcomes, postoperative major adverse events, and in-hospital death.

Statistical analysis was performed with IBM SPSS ver. 20.0 (IBM Co., Armonk, NY, USA). The quantitative data were expressed as mean±standard deviation, while qualitative data were expressed as number and percent. The Student t-test was used to compare the means between two independent groups. Proportions were compared using the chi-square test or Fisher's exact test. In order to estimate associations between postoperative major adverse events and different risk factors, odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. In order to determine the independent risk factors for major adverse events after surgery, variables with a p-value less than 0.20 on univariate analysis were in-

Table 1. Preoperative patient characteristics

Variable	Previous PCI (n=38)	No previous PCI (n=122)	p-value
Age (yr)	59.2±5.60	58.09±6.52	0.33
Gender (male/female)	27/11	97/25	0.27
Family history of coronary artery disease	6 (15.8)	12 (9.8)	0.31
Smoking	28 (73.7)	87 (71.3)	0.77
Diabetes mellitus	8 (21.1)	15 (12.3)	0.17
Obesity	8 (21.1)	22 (18.0)	0.67
Chronic pulmonary disease	6 (15.8)	12 (9.8)	0.31
Hypertension	5 (13.2)	22 (18.0)	0.48
Hyperlipidemia	5 (13.2)	15 (12.3)	0.88
Renal impairment	1 (2.6)	3 (2.5)	0.95
Cerebrovascular disease	1 (2.6)	1 (1.6)	0.69
Peripheral vascular disease	1 (2.6)	3 (2.5)	0.95
Left ventricular ejection fraction (%)	57.9±9.04	60.50±8.20	0.10
Unstable angina	3 (7.9)	14 (11.5)	0.53
New York Heart Association class III/IV	11 (28.9)	29 (23.8)	0.52
EuroSCORE	2.02±1.97	1.59±1.42	0.13
Left main disease	5 (13.2)	11 (9.0)	0.45
Multi-vessel disease	29 (76.3)	78 (63.9)	0.15

Values are presented as mean±standard deviation or number (%).
PCI, percutaneous coronary intervention.

Table 2. Detailed angiographic information for 38 patients with a history of previous PCI

Variable	Previous PCI patients (n=38)
Average time to restenosis (yr)	14±5.4
Type of PCI	
Stenting	22 (58.0)
Percutaneous transluminal coronary angioplasty alone	16 (42.0)
Targets of previous PCI	
Three vessels	3 (8.0)
Two vessels	15 (38.4)
One vessel	20 (52.6)
Targets for subsequent coronary artery bypass grafting	
Three-vessel disease	29 (76.3)
Two-vessel disease	7 (18.4)
One-vessel disease	2 (5.2)
Left main disease (>50% stenosis)	5 (13.2)

Values are presented as mean±standard deviation or number (%).
PCI, percutaneous coronary intervention.

cluded in the full model of multivariate binary logistic regression [7]. Differences were considered significant at $p<0.05$.

RESULTS

No significant differences were found between the study groups in terms of preoperative characteristics, including demographic data, risk factors, LVEF, New York Heart Association (NYHA) class, EuroSCORE, and the extent of coronary artery disease (Table 1). In the group with a history of previous PCI, the average time from PCI to CABG was 13.9±5.4 years, and one patient had a history of multiple PCI (2.6%).

In patients with previous PCI, the average time to restenosis was 14.0±5.4 years (Table 2). The previous PCI involved stenting in 22 patients (58%) and percutaneous transluminal coronary angioplasty alone in 16 patients (42%). The previous PCI targeted one vessel in 20 patients (52.6%), two vessels in 15 patients (38.4%), and three vessels in three patients (8%). The targets for subsequent CABG were three-vessel disease in 29 patients (76.3%), two-vessel disease in seven patients (18.4%), and one-vessel disease in two patients (5.2%). Left main disease (>50% stenosis) was reported in five patients (13.2%).

Regarding operative and postoperative outcomes, no significant differences were found between the groups in terms

Table 3. Operative and postoperative outcomes

Variable	Previous PCI (n=38)	No previous PCI (n=122)	p-value
Bypass time	87.7±16.09	86.48±18.33	0.70
Cross-clamping time	66.78±15.25	64.87±14.77	0.49
No. of grafts	2.73±0.86	2.50±1.00	0.19
Reoperation for bleeding	2 (5.3)	3 (2.5)	0.38
Acute myocardial infarction	1 (2.6)	1 (0.8)	0.38
Neurological deficit	2 (5.3)	1 (0.8)	0.07
Prolonged ventilation	2 (5.3)	2 (1.6)	0.21
Need for renal dialysis	1 (2.6)	0	0.07
Any major adverse event[a)]	6 (15.8)	3 (2.5)	0.002[b)]
In-hospital mortality	2 (5.3)	2 (1.6)	0.21
Hospital stay (day)	17.1±6.7	16.3±6.1	0.47

Values are presented as mean±standard deviation or number (%).
PCI, percutaneous coronary intervention.
[a)]Some patients had more than one major adverse event. [b)]Significant difference.

Table 4. Associations of preoperative risk factors with the incidence of an in-hospital adverse event after coronary artery bypass grafting

Risk factors	Any major adverse event		Univariate analysis		Multivariate analysis	
	Yes (n=9)	No (n=151)	OR (95% CI)	p-value	OR (95% CI)	p-value
Age ≥60 yr	4 (44.4)	67 (44.4)	1 (0.25–3.8)	0.99	-	-
Gender (female)	1 (11.1)	35 (23.2)	0.41 (0.05–3.4)	0.40	-	-
Family history of coronary artery disease	2 (22.2)	16 (10.6)	2.4 (0.46–12.6)	0.28	-	-
Smoking (current or past)	5 (55.6)	110 (72.8)	0.46 (0.11–1.8)	0.26	-	-
Diabetes mellitus	3 (33.3)	20 (13.62)	3.2 (0.75–14.1)	0.09	0.39 (0.08–1.9)	0.24
Obesity (body mass index ≥30 kg/m^2)	1 (11.1)	29 (19.2)	0.52 (0.06–4.3)	0.54	-	-
Chronic pulmonary disease	2 (22.2)	16 (10.6)	2.41 (0.46–12.6)	0.28	-	-
Left ventricular ejection fraction ≤50%	1 (11.1)	19 (12.9)	0.86 (0.11–7.3)	0.89	-	-
New York Heart Association class III/IV	5 (55.6)	35 (23.2)	4.1 (1–16.2)	0.02[a)]	0.44 (0.10–1.89)	0.27
Left main disease	2 (22.2)	14 (9.3)	2.7 (0.52–14.7)	0.20	0.40 (0.06–2.3)	0.31
Multi-vessel disease	7 (77.8)	100 (66.2)	1.78 (0.35–8.9)	0.47	-	-
Previous percutaneous coronary intervention	6 (66.7)	33 (21.9)	4.47 (1.13–17.5)	0.002[a)]	0.16 (0.03–0.71)	0.01[a)]

Values are presented as number (%).
OR, odds ratio; CI, confidence interval.
[a)]Significant difference.

of bypass time, cross-clamping time, the number of grafts, the incidence of postoperative acute MI, postoperative neurological deficits, and the postoperative need for renal dialysis (Table 3). The rate of reoperation for bleeding in the previous PCI group was higher than in the group with no history of PCI (5.3% vs. 2.5%), but it was not statistically significant (p=0.38). The incidence of operative (in-hospital) mortality was 5.3% in patients with previous PCI and 1.6% in patients with no previous PCI, which was not found to be a significant difference (p=0.21). Patients with previous PCI exhibited a larger proportion of patients experiencing in-hospital major adverse events (15.8% vs. 2.5%, p=0.002).

Univariate analysis found that a history of diabetes mellitus, NYHA class III or IV function, the presence of left main disease, and previous PCI exhibited significant associations with the incidence of major adverse events after CABG. On logistic multivariate analysis, only previous PCI was found to be a significant predictor for major adverse events (OR, 0.16;

95% CI, 0.03 to 0.71; p=0.01) (Table 4).

DISCUSSION

The need for subsequent re-vascularization has been reported in 20%–40% of coronary artery disease patients who are initially treated with PCI [8]. These patients have been found to have worse outcomes after repeated PCI [9] and when undergoing non-cardiac surgery [10], and it is therefore suspected that they will have also worse outcomes after CABG [11,12].

In the literature, multiple comparative studies have evaluated the effects of previous PCI on clinical outcomes after CABG, with controversial results. In the study of Hassan et al. [13], the rate of in-hospital mortality after CABG was higher in patients with prior PCI (3.6% vs. 2.3%, p=0.02). Prior PCI emerged as an independent predictor of postoperative in-hospital mortality (OR, 1.93; p=0.003). The study by Lisboa et al. [14] reported previous PCI to be an independent predictor of postoperative in-hospital mortality (OR, 1.94; 95% CI, 1.02 to 3.68; p=0.044) that was as strong as diabetes (OR, 1.86; 95% CI, 1.07 to 3.24; p=0.028).

In a large study performed by Mehta et al. [15], operative mortality was similar in both groups (2.3% vs. 1.9%, p=0.13). Previous PCI patients had more major complications (15.0% vs. 12.0%, $p<0.001$), in addition to longer hospitalization (p=0.01), and higher readmission rates (p=0.01). Additionally, multivariate analysis found that previous PCI was an independent predictor of major complications after CABG (OR, 1.15; p=0.01).

In contrast, the large registry study of Yap et al. [12] showed no associations between prior PCI and increased short-term or medium-term mortality after CABG. Prior PCI was not a predictor of in-hospital mortality (OR, 1.22; 95% CI, 0.76 to 2.0; p=0.41) or mid-term mortality over six years of follow-up (hazard ratio, 0.94; 95% CI, 0.75 to 1.18; p=0.62).

The primary outcome in the present study confirmed that CABG subsequent to PCI was associated with more major complications than CABG on native vessels (OR, 0.16; 95% CI, 0.03 to 0.71; p=0.01). Several mechanisms have been demonstrated through which previous initial PCI may affect the outcomes of CABG, including: (1) limitations in distal anastomosis if the stent was positioned distally; (2) reduction of the graft patency due to compromised collateral blood flow caused by multiple overlapping stents; (3) the effect of stents on coronary artery endothelial function; (4) the possibility that previous PCI may result in poor targets or debility disproportionate to age; and (5) the possibility that patients with PCI requiring subsequent CABG may have more aggressive atherosclerosis [12,16,17].

Despite the influence of previous PCI on morbidity after CABG in this study, the rate of operative (in-hospital) mortality exhibited no significant difference between the two groups. This may be attributed to the non-significant differences in preoperative comorbidities between the groups and the small number of patients with a history of multiple PCI (only one patient). This explanation is supported by the findings of a recent meta-analysis of comparative studies [18], which showed that the adverse effect of previous PCI on in-hospital mortality was statistically significant in cohorts with a high proportion of patients who had previous multiple PCIs, but it was not significant in cohorts with a low proportion of patients with a history of multiple PCIs.

In conclusion, we found a significant association between previous PCI and the incidence of major adverse events after CABG. The limitations of our study are its retrospective nature, small number of patients, and the fact that it reflects experiences within a single center, urging us to recommend further multi-center, large-scale, and long-term studies.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Holmes DR Jr, Williams DO. *Catheter-based treatment of coronary artery disease: past, present, and future*. Circ Cardiovasc Interv 2008;1:60-73.
2. Nabel EG, Braunwald E. *A tale of coronary artery disease and myocardial infarction*. N Engl J Med 2012;366:54-63.
3. Singh M, Rihal CS, Gersh BJ, et al. *Twenty-five-year trends in in-hospital and long-term outcome after percutaneous coronary intervention: a single-institution experience*. Circulation

2007;115:2835-41.

4. Mohr FW, Morice MC, Kappetein AP, et al. *Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial*. Lancet 2013;381:629-38.
5. Biancari F, Mariscalco G, Rubino AS, et al. *The effect of prior percutaneous coronary intervention on the immediate and late outcome after coronary artery bypass grafting: systematic review and meta-analysis*. Heart Lung Vessel 2014; 6:244-52.
6. Shanmugam G, West M, Berg G. *Additive and logistic EuroSCORE performance in high risk patients*. Interact Cardiovasc Thorac Surg 2005;4:299-303.
7. Vittinghoff E, Glidden DV, Shiboski SC, McCulloch CE. *Regression methods in biostatistics: linear, logistic, survival, and repeated measures models*. New York (NY): Springer; 2005.
8. Taggart DP. Thomas B. *Ferguson lecture: coronary artery bypass grafting is still the best treatment for multivessel and left main disease, but patients need to know*. Ann Thorac Surg 2006;82:1966-75.
9. Arjomand H, Willerson JT, Holmes DR Jr, et al. *Outcome of patients with prior percutaneous revascularization undergoing repeat coronary intervention (from the PRESTO Trial)*. Am J Cardiol 2005;96:741-6.
10. Vicenzi MN, Meislitzer T, Heitzinger B, Halaj M, Fleisher LA, Metzler H. *Coronary artery stenting and non-cardiac surgery: a prospective outcome study*. Br J Anaesth 2006;96: 686-93.
11. Johnson RG, Sirois C, Watkins JF, et al. *CABG after successful PTCA: a case-control study*. Ann Thorac Surg 1995; 59:1391-6.
12. Yap CH, Yan BP, Akowuah E, et al. *Does prior percutaneous coronary intervention adversely affect early and mid-term survival after coronary artery surgery?* JACC Cardiovasc Interv 2009;2:758-64.
13. Hassan A, Buth KJ, Baskett RJ, et al. *The association between prior percutaneous coronary intervention and short-term outcomes after coronary artery bypass grafting*. Am Heart J 2005;150:1026-31.
14. Lisboa LA, Mejia OA, Dallan LA, et al. *Previous percutaneous coronary intervention as risk factor for coronary artery bypass grafting*. Arq Bras Cardiol 2012;99:586-95.
15. Mehta GS, LaPar DJ, Bhamidipati CM, et al. *Previous percutaneous coronary intervention increases morbidity after coronary artery bypass grafting*. Surgery 2012;152:5-11.
16. Stone PH, Coskun AU, Yeghiazarians Y, et al. *Prediction of sites of coronary atherosclerosis progression: in vivo profiling of endothelial shear stress, lumen, and outer vessel wall characteristics to predict vascular behavior*. Curr Opin Cardiol 2003;18:458-70.
17. Muhlestein JB. *Endothelial dysfunction associated with drug-eluting stents what, where, when, and how?* J Am Coll Cardiol 2008;51:2139-40.
18. Ueki C, Sakaguchi G, Akimoto T, Shintani T, Ohashi Y, Sato H. *Influence of previous percutaneous coronary intervention on clinical outcome of coronary artery bypass grafting: a meta-analysis of comparative studies*. Interact Cardiovasc Thorac Surg 2015;20:531-7.