

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 Aldahmashi⁵, Bedir Ibrahim⁶, Nabil Elsadeck⁷ and Mohamed F Ibrahim²

¹Cardiothoracic Surgery Department, Benha University, Egypt

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

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

⁴Cardiothoracic Surgery Department, Ain shams University, Egypt

⁵Cardiothoracic Surgery Department, Tamar University, Yemen

⁶Cardiothoracic Surgery Department, Tanta University, Egypt

⁷Cardiothoracic 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

Received date: Aug 27, 2015; Accepted date: Oct 19, 2015; Published date: Oct 25, 2015

Copyright: ©2015 Alassal MA, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

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

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].

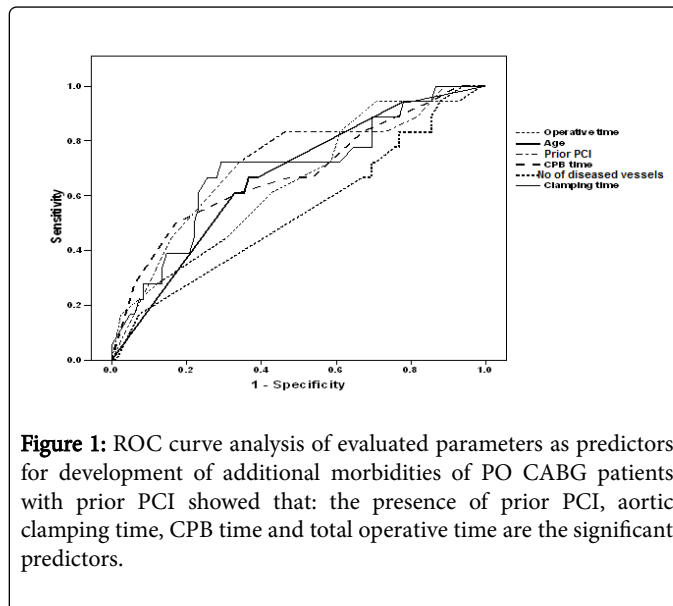


Figure 1: ROC curve analysis of evaluated parameters as predictors for development of additional morbidities of PO CABG patients with prior PCI showed that: the presence of prior PCI, aortic clamping time, CPB time and total operative time are the significant predictors.

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 (χ^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	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).

	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].

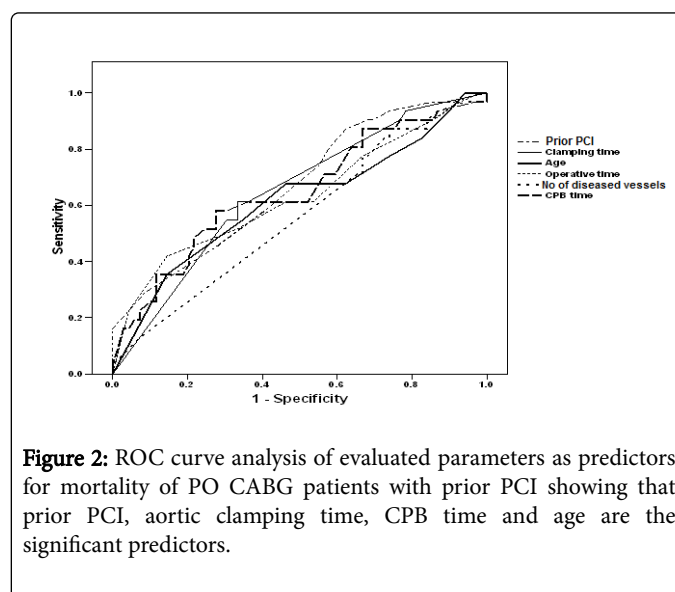


Figure 2: ROC curve analysis of evaluated parameters as predictors for mortality of PO CABG patients with prior PCI showing that prior PCI, aortic clamping time, CPB time and age are the significant predictors.

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

Acknowledgement

The authors thank statistician consultants M Mubasher, N Baker and Sumanth N Raghunayakula, for their contribution to this research and for their assistance in conception, design and processing of our project.

References

1. Cook S, Walker A, Hügli O, Togni M, Meier B (2007) Percutaneous coronary interventions in Europe: prevalence, numerical estimates, and projections based on data up to 2004. *Clin Res Cardiol* 96: 375-382.
2. Shahabuddin S, Sami S, Ansari J, Perveen S, Furnaz S, et al. (2012) Coronary artery bypass grafting after percutaneous coronary intervention. *J Coll Physicians Surg Pak* 22: 340-341.
3. Gilbert CS, James T, Peter DS, Andrew N, Cheng-Hon Y, et al. (2009) Does Prior Percutaneous Coronary Intervention Adversely Affect Early and Mid-Term Survival After Coronary Artery Surgery? *J Am Coll Cardiol Intv* 2: 758-764.
4. Tran HA, Barnett SD, Hunt SL, Chon A, Ad N (2009) The effect of previous coronary artery stenting on short- and intermediate-term outcome after surgical revascularization in patients with diabetes mellitus. *J Thorac Cardiovasc Surg* 138: 316-323.
5. Taggart DP (2008) Does prior PCI increase the risk of subsequent CABG? *Eur Heart J* 29: 573-575.
6. Davis PK, Parascandola SA, Miller CA, Campbell DB, Myers JL, et al. (1989) Mortality of coronary artery bypass grafting before and after the advent of angioplasty. *Ann Thorac Surg* 47: 493-497.
7. Judith MD, van den B, Luc Noyez, Freek WAV (2005) Risk of coronary surgery for hospital and early morbidity and mortality after initially successful percutaneous intervention. *Interact CardioVasc Thorac Surg* 4: 96-100.
8. Johnson RG, Sirois C, Thurer RL, Sellke FW, Cohn WE, et al. (1997) Predictors of CABG within one year of successful PTCA: a retrospective, case-control study. *Ann Thorac Surg* 64: 3-7.
9. Kamiya H, Ushhijima T, Mukai K, Ikeda C, Ueyama K, et al. (2004) Late patency of the internal thoracic artery graft in patients with and without previous successful percutaneous transluminal coronary angioplasty. *Interactive CardioVasc Thorac Surg* 3: 110-113.
10. Kalaycioglu S, Sinci V, Oktar L (1998) Coronary artery bypasses grafting (CABG) after successful percutaneous transluminal coronary angioplasty (PTCA): Is PTCA a risk for CABG? *Int Surg* 83: 190-193.
11. Hassan A, Buth KJ, Baskett RJE, Ali IS, Maitland A, et al. (2005) The association between prior percutaneous coronary intervention and short-

- term outcomes after coronary artery bypass grafting. *Am Heart J* 150: 1026-1031.
12. Bonaros N, Vill D, Wiedemann D, Fischler K, Friedrich G, et al. Major risk stratification models do not predict perioperative outcome after coronary artery bypass grafting in patients with previous percutaneous intervention. *Eur J Cardiothorac Surg* 39: e164-e169.
 13. Eifert S, Mair H, Boulesteix AL, Kilian E, Adamczak M, et al. (2010) Mid-term outcomes of patients with PCI prior to CABG in comparison to patients with primary CABG. *Vasc Health Risk Manag* 6: 495-501.
 14. Thielmann M, Leyh R, Massoudy P, Neuha M, Aleksic I, et al. (2006) Prognostic significance of multiple previous percutaneous coronary interventions in patients undergoing elective coronary artery bypass surgery. *Circulation* 114: I441-I447.
 15. Yap CH, Yan BP, Akowuah E, Dinh DT, Smith JA, et al. (2009) Does prior percutaneous coronary intervention adversely affect early and mid-term survival after coronary artery surgery? *J Am Coll Cardiovasc Interv* 2: 758-764.
 16. Massoudy P, Thielmann M, Lehmann N, Marr A, Kleikamp G, et al. (2009) Impact of prior percutaneous coronary intervention on the outcome of coronary artery bypass surgery: a multicenter analysis. *J Thorac Cardiovasc Surg* 137: 840-845.
 17. Chocron S, Baillot R, Rouleau JL, Warnica WJ, Block P, et al. (2008) Impact of previous percutaneous transluminal coronary angioplasty and/or stenting revascularization on outcomes after surgical revascularization: insights from the IMAGINE study. *Eur Heart J* 29: 673-679.
 18. Biancari F, Mariscalco G, Rubino AS, Vinco G, Onorati F, et al. (2014) 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* 6: 244-252.
 19. Mohr FW, Morice MC, Kappetein AP, Feldman TE, Stahle E, et al. (2013) 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* 381: 629-638.