

Previous Percutaneous Coronary Intervention as Risk Factor for Coronary Artery Bypass Grafting

Luiz Augusto Ferreira Lisboa, Omar Asdrúbal Vilca Mejía, Luís Alberto Oliveira Dallan, Luiz Felipe Pinho Moreira, Luiz Boro Puig, Fabio Biscegli Jatene, Noedir Antonio Groppo Stolf

Instituto do Coração do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo - SP, Brazil

Abstract

Background: Percutaneous coronary intervention (PCI) has increased as the initial revascularization strategy in chronic coronary artery disease. Consequently, more patients undergoing coronary artery bypass grafting (CABG) have history of coronary stent.

Objective: Evaluate the impact of previous PCI on in-hospital mortality after CABG in patients with multivessel coronary artery disease.

Methods: Between May/2007 and June/2009, 1099 consecutive patients underwent CABG on cardiopulmonary bypass. Patients with no PCI (n=938, 85.3%) were compared with patients with previous PCI (n=161, 14.6%). Logistic regression models and propensity score matching analysis were used to assess the risk-adjusted impact of previous PCI on in-hospital mortality.

Results: Both groups were similar, except for the fact that patients with previous PCI were more likely to have unstable angina (16.1% x 9.9%, p=0.019). In-hospital mortality after CABG was higher in patients with previous PCI (9.3% x 5.1%, p=0.034) and it was comparable with EuroSCORE and 2000 Bernstein-Parsonnet risk score. Using multivariate logistic regression analysis, previous PCI emerged as an independent predictor of postoperative in-hospital mortality (odds ratio 1.94, 95% CI 1.02-3.68, p=0.044) as strong as diabetes (odds ratio 1.86, 95% CI 1.07-3.24, p=0.028). After computed propensity score matching based on preoperative risk factors, in-hospital mortality remained higher among patients with previous PCI (odds ratio 3.46, 95% CI 1.10-10.93, p=0.034).

Conclusions: Previous PCI in patients with multivessel coronary artery disease is an independent risk factor for in-hospital mortality after CABG. This fact must be considered when PCI is indicated as initial alternative in patients with more severe coronary artery disease. (Arq Bras Cardiol 2012;99(1):586-595)

Keywords: Myocardial revascularization; angioplasty, balloon, coronary; risk factors; mortality.

Introduction

Despite all scientific evidences and the guidelines for the treatment of chronic coronary artery disease demonstrating the benefits of coronary artery bypass grafting (CABG), especially in patients with multivessel disease, there has been an exponential growth in percutaneous coronary intervention (PCI) with stents^{1,2}. With technological advances and the experience accumulated over the years, the indication for PCI has expanded and procedures in multivessel coronary disease have become more common^{3,4}.

In this so-called "stent era", patients with coronary artery disease and class I indication for CABG are frequently submitted to PCI as initial alternative, before

being convinced to surgical treatment⁵. Some studies have shown restenosis rates after PCI with stent, with need of reintervention due to symptom recurrence, ranging from 20% to 40%^{6,7}. More recently, it has been discussed whether previous PCI is a risk factor with negative impact on the outcomes of CABG⁸⁻¹⁰. A significant inflammatory process and endothelial function abnormalities in the coronary arteries have been related to the treatment with stent, especially when drug-eluting stents were used¹¹⁻¹³. However, the actual clinical impact of the presence of stents in the coronary artery in the prognosis of CABG has not been clearly established and it is controversy^{14,15}. The increase in mortality is the main event that can influence changes in the guidelines.

The objective of this study is to assess the impact of previous PCI with stent as risk factor for in-hospital mortality in patients with multivessel chronic coronary artery disease who requiring later surgical treatment for myocardial revascularization.

Mailing Address: Luiz Augusto Ferreira Lisboa •

Instituto do Coração - Av. Dr. Enéas de Carvalho Aguiar, 44, 2º andar sala 11.

Postal Code 05403-000, São Paulo, SP - Brazil

E-mail: lisboa@cardiol.br, luiz.lisboa@incor.usp.br

Manuscript received February 09, 2012; manuscript revised February 14, 2012; manuscript accepted February 27, 2012.

Patients and methods

A prospective observational design was used. All patients who underwent first-time isolated CABG surgery on cardiopulmonary bypass between May 2007 and July 2009 were included in this study. The study group consisted of 1,099 consecutive patients of mean age 63.6 ± 12.6 years who underwent elective, urgent or emergency CABG surgery. All patients had multivessel atherosclerotic coronary disease. Patients with combined cardiac surgery were excluded. CABG without cardiopulmonary bypass and reoperations were excluded to minimize surgical technique interferences. Patients underwent previous PCI in the same hospitalization as the surgery, were also excluded. All patients were operated at Heart Institute University of Sao Paulo Medical School, a tertiary referral national center and data were prospectively collected, creating a database.

Patient characteristics and preoperative risk factors were analyzed, following the additive European System for Cardiac Operative Risk Evaluation (EuroSCORE) and 2000 Bernstein-Parsonnet logistic risk model^{16,17}. The correlation of predicted and observed mortality was compared with these two models, for better evaluation. The outcome was in-hospital surgical mortality, defined as death occurring in the time interval between surgery and hospital discharge.

This study was approved by the Scientific and Ethics Committee of Heart Institute, University of São Paulo Medical School.

Surgical procedure

CABG was performed with cardiopulmonary bypass, using the classic technique by median sternotomy in all patients. Five hundred UI/Kg of heparin was used to obtain an activated coagulation time greater than 400 seconds. Myocardial protection was achieved with intermittent hyperkalemic antegrade warm blood cardioplegia or with intermittent aortic clamping. Protamine was used for heparin reversal at a ratio of 1:1. At the end of surgery, patients were transferred to the intensive care unit and managed according to the unit protocol.

Patients receiving dual anti-platelet therapy with acetylsalicylic acid and clopidogrel prior surgery were treated as follows: acetylsalicylic acid was discontinued on surgery day and was reintroduced the day following surgery, clopidogrel was discontinued at least 2 to 5 days prior surgery and, if required, it was reintroduced within at least 2 days after surgery.

Statistical analysis

Variables are shown in contingency tables with absolute (n) and relative (%) frequencies. Association among them, taking into consideration the groups with and without prior PCI, was evaluated by the chi-squared test, the likelihood ratio test or Fisher's exact test.

Quantitative variables were shown in tables including the median, and 1st and 3rd quartile values. The distribution of variables was evaluated by Mann-Whitney's test.

The Hosmer–Lemeshow goodness-of-fit statistic test was used to compare the observed and predicted mortality with 95% confidence intervals. A well-calibrated model gives corresponding $p > 0.05$.

Univariate and multivariate logistic regression models were used to identify associated factors and independent preoperative predictors for in-hospital mortality. The variables identified by the univariate analysis with a p value ≤ 0.10 were used to the adjustment of the multivariate logistic regression model (forward procedure).

In an additional effort to minimize the influence from a non-randomized study, a second analysis was performed using the propensity score matching. Patients with prior PCI (study group) were matched with patients without prior PCI (control group), at a 1:1 ratio. After matching, in-hospital mortality was compared between the two groups. Paired samples were also reevaluated using the univariate and multivariate logistic regression tests, in order to control eventual risk factor selection bias.

The analysis was done using two-tailed tests and $p < 0.05$ was considered statistically significant. The SPSS software version 18.0 was used for statistical analysis (SPSS Inc, Chicago, Illinois).

Results

Patients characteristics

From May 2007 to July 2009, 1551 patients were submitted to first time isolated CABG at the Heart Institute University of Sao Paulo Medical School. Four hundred and twenty-nine patients were excluded because they were operated without cardiopulmonary bypass or because they were submitted to PCI during the same hospitalization as the surgical treatment, 15 patients were excluded because they were submitted to vascular procedures associated to CABG and 8 patients were excluded due to incomplete information regarding prior angioplasty. The other 1099 patients were the final study population.

Of the 1099 patients included in the study, 938 (85.3%) patients underwent CABG without previous PCI and 161 (14.6%) patients had previous PCI. Of these, 147 (91.3%) had been submitted to PCI using bare metal stents and 14 (8.7%) using drug-eluting stents. The comparison of patients with and without prior PCI taking into consideration clinical manifestation and preoperative risk factors showed that patients with prior PCI had a more frequent unstable angina (16.1% vs. 9.9%, $p=0.019$) at the time of hospitalization. There were no others statistical differences between the two groups as to the remaining clinical manifestations and preoperative cardiovascular risk factors (Table 1).

Surgical treatment

In the intraoperative, patients with prior PCI had lower mean number of revascularized coronary arteries (3.0 vs 3.2 – $p=0.446$), longer aortic clamping time (76.1 vs. 74.8 minutes, $p=0.673$) and longer cardiopulmonary bypass time (90.7 vs 85.3 minutes, $p=0.584$), however, there was no statistical significance. There were also no differences between the two groups regarding the use of left internal thoracic artery (95.2% vs 97.3%, $p=0.386$).

In-Hospital mortality

The overall mortality according to the additive EuroSCORE and 2000 Bernstein-Parsonnet risk model are showing, respectively, in Table 2 and Table 3. Patients with prior PCI had a significantly higher in-hospital mortality than those who did not have a prior intervention (9.3% vs. 5.1%, $p=0.034$). After adjustment with univariate analysis and later on with multivariate logistic regression for differences in clinical manifestations and preoperative risk factors, prior PCI emerged as an independent risk factor for in-hospital mortality after CABG with odds ratio of 1.94 (95% confidence interval 1.02 - 3.68; $p=0.044$). Other factors such as age, pulmonary hypertension, diabetes, congestive heart failure and preoperative intra-aortic balloon pump were also classified (Table 4).

Patient matching

Propensity score matching was performed taking into consideration preoperative factors with a greater impact on surgery to match study group (patients with previous PCI) and control group (patients without previous PCI). The following parameters were selected: gender, age, diabetes, systemic hypertension, congestive heart failure, unstable angina, recent myocardial infarction. For this analysis, 161 study group patients were successfully paired with 161 corresponding controls at a ratio of 1;1 (Table 5). When in-hospital mortality was compared between the two groups, patients with prior PCI had significantly higher in-hospital mortality after CABG (9.3% vs. 3.1%, $p=0.021$). After univariate and multivariate analysis with the paired groups, to control eventual variables not selected for the matching, PCI emerged once again as an independent predictor for in-hospital mortality after CABG with odds ratio of 3.46 (95% confidence interval 1.10- 10.93; $p=0.034$) (Table 6).

Discussion

Impact of prior PCI on in-hospital mortality after CABG

Cardiovascular surgeons have more and more often been faced with patients referred for CABG after a successful previous PCI. This study clearly showed, based on a database created for a prospective analysis with adjustment of risk factors, that previous PCI is an independent risk factor for in-hospital mortality after CABG.

Mortality risk factors after cardiac surgery have been studied since the late 80s. Initially only using associations and later with risk stratification models^{18,19}. Many variables, including PCI at the same hospitalization, have been studied and known for a long time as in-hospital mortality predictors after CABG^{16,17,20}. The influence of previous PCI on CABG has been observed for cardiac surgeons in daily practice. However, it has not been extensively studied and only recently, it has been taken into account more seriously.

In 1995, Johnson et al²¹ observed negative impact of a previous PCI on CABG. Comparing 234 patients successfully submitted to angioplasty who later required CABG, they observed that surgical risk at the time of surgery was 4.0%, significantly higher than the 2.8% prior angioplasty ($p=0.04$). In 1996, Jones et al²² in extensive review of seven large

databases with 172,184 patients underwent CABG were the first to identify previous PCI as a risk factor. At the time, it was classified as level 2, i.e., not clearly related to mortality after surgery. In 1998, Kalaycioglu et al²³ in a propensity score matching with 80 patients underwent CABG observed worse outcomes in the group of patients with previous coronary angioplasty. More recently, Hassan et al⁸ in a large study with 6504 patients underwent CABG (919 patients with a previous PCI), clearly demonstrated that previous PCI is an independent predictor for in-hospital mortality after CABG, odds ratio of 1.93 ($p=0.003$). However, nowadays still have doubt if previous PCI is a risk factor for patients who undergoing CABG.

In the last years, there is an increasing number of interventional procedures using stents in intermediate risk patients as well as in patients with more severe multivessel coronary disease, which used to be considered inadequate for PCI^{3,4,24}. As consequence, there are an increasing number of patients who have been submitted to PCI with stents before being finally referred for CABG. In the literature, this incidence ranges from 10% to 20%⁸⁻¹⁰. From our study group, 161 patients (14.6%) had previous PCI. In this context, it is important to reassess the clinical relevance of previous PCI and the prognostic value of risks in patients who may require later CABG.

Recent report, with post hoc analysis, patients with history of PCI had worse prognosis after CABG and an increase in cardiovascular events during clinical follow-up²⁵. Bonaros et al²⁶ confirmed these data in study with 306 patients with previous PCI who were matched with similar group without PCI prior to CABG. Patients with previous PCI had higher in-hospital mortality (4.4% vs. 2.4%, $p<0.001$).

In the present study, the analysis of 1099 consecutive patients underwent CABG on cardiopulmonary bypass the overall hospital mortality was 5.7%. This observed mortality reflect the high complexity presented in tertiary service of national reference and it was comparable with predicted mortality based on the additive EuroSCORE and 2000 Bernstein-Parsonnet logistic risk model^{27,28}. The mortality was greater in patients with a history of previous PCI (9.3% vs 5.1%, $p<0.034$). Logistic regression models indicated that previous PCI with stent was an independent predictor for in-hospital mortality after CABG with an odds ratio of 1.94 ($p=0.044$). Propensity score matching confirmed previous PCI as a risk factor for in-hospital mortality after CABG (odds ratio of 3.46, $p=0.034$).

Even though several studies have shown that the previous PCI using stents is risk factor for in-hospital mortality after CABG, this correlation is still controversial. Some groups believe there is no correlation between previous PCI and subsequent CABG¹⁴. Others have found this correlation only in patients receiving multiple coronary interventions or in diabetic patients^{9,29-31}. Yap et al¹⁴ analyzed 13,184 patients (1,457 with history of PCI) underwent CABG and did not find an association between previous PCI and early or mid term mortality (odds ratio of 1.11, $p=0.41$). Thielmann et al²⁹ analyzed 2626 patients undergoing CABG and found an association between previous PCI and hospital mortality, however, it was only significant in the presence of multiple previous PCIs (odds ratio of 2.24; $p<0.001$). Massoud et al⁹

Table 1 - Comparison of clinical manifestations and preoperative cardiovascular risk factors between patients submitted to isolated CABG with previous PCI and those without PCI

Variables	Without previous PCI (n=938)		With previous PCI (n=161)		p	
Age (years)	62 (56 - 70)		63 (56 - 69)		0.863	c
Female sex	254	27.1%	36	22.4%	0.209	a
Ejection fraction (%)	60 (45 - 65)		56 (45 - 62)		0.135	c
Left main disease > 50%	188	20.0%	24	14.9%	0.127	a
Clinical manifestation						
Congestive heart failure	419	44.7%	79	49.1%	0.300	a
Unstable angina	93	9.9%	26	16.1%	0.019	a
Recent AMI	247	26.3%	53	32.9%	0.083	a
AMI with < 48hs	35	3.7%	10	6.2%	0.142	a
Cardiogenic shock	5	0.5%	1	0.6%	1.000	b
Preoperative IABP	32	3.4%	9	5.6%	0.178	a
CV risk factors						
Diabetes	449	47.9%	71	44.1%	0.376	a
Systemic hypertension	819	87.3%	147	91.3%	0.151	a
Morbid obesity	109	11.6%	19	11.8%	0.947	a
Renal insufficiency	48	5.1%	8	5.0%	0.937	a
Dialysis	12	1.3%	1	0.6%	0.705	b
COPD	20	2.1%	3	1.9%	1.000	a
Pulmonary hypertension	65	6.9%	10	6.2%	0.738	a
Emergency surgery	26	2.8%	6	3.7%	0.506	a

a-chi-squared test; b-Fisher's exact test; c-Mann-Whitney's test. Variables are shown in contingency table with absolute (n) and relative (%) frequencies. Quantitative variables were shown in table including the median, and 1st and 3rd quartile values. CABG - Coronary artery bypass grafting; PCI - Percutaneous coronary intervention; AMI - Acute myocardial infarction; IABP - Intra-aortic balloon pump; CV - Cardiovascular; COPD - Chronic obstructive pulmonary disease.

Table 2 – Predicted and observed mortality by additive EuroSCORE risk model for whole study group

EuroSCORE group	Patients	Mortality *	
		% observed (95% CI)	% predicted (95% CI)
≤ 2	459	1,53	1,74
		(0,40; 2,65)	(0,55; 2,94)
3 – 5	397	4,28	4,03
		(2,29; 6,27)	(2,10; 5,96)
≥ 6	243	16,05	16,05
		(11,43; 20,66)	(11,43; 20,66)

* Hosmer–Lemeshow goodness-of-fit test (p=0,412)

Table 3 – Predicted and observed mortality by 2000 Bernstein-Parsonnet risk model for whole study group

2000 Bernstein Parsonnet Risk group	Patients	Mortality *	
		% observed (IC a 95%)	% predicted (IC a 95%)
≤ 6	218	1,38 (0,17; 2,92)	1,38 (0,17; 2,92)
6,1 – 11,0	237	0,84 (0,32; 2,01)	1,69 (0,05; 3,33)
11,1 – 15,0	216	3,70 (1,19; 6,22)	3,24 (0,88; 5,60)
15,1 – 20,9	226	4,42 (1,74; 7,11)	5,75 (2,72; 8,79)
≥ 21	202	19,80 (14,31; 25,30)	17,82 (12,54; 23,10)

* Hosmer–Lemeshow goodness-of-fit test (p=0,890)

Table 4 - Univariate and multivariate logistic regression analysis of variables associated with in-hospital mortality after CABG

Variables	Univariate analysis		Multivariate analysis	
	odds ratio (95% CI)	p	odds ratio (95% CI)	p
Age (years)	1.07 (1.04 – 1.10)	<0.001	1.06 (1.03 – 1.09)	<0.001
Female sex	1.66 (0.97 – 2.82)	0.063		
Ejection fraction (%)	0.97 (0.96 – 0.99)	0.003		
Left main disease > 50%	1.74 (0.98-3.07)	0.037		
Clinical manifestation				
Congestive heart failure	2.97 (1.71 – 5.16)	<0.001	2.15 (1.2 – 3.85)	0.010
Unstable angina	4.06 (1.94 – 8.49)	<0.001		
Recent AMI	2.10 (1.25 – 3.52)	0.005		
AMI with < 48hs	3.93 (1.75 – 8.84)	0.001		
Cardiogenic shock	8.46 (1.52 – 47.09)	0.015		
Preoperative IABP	9.36 (4.57 – 19.16)	<0.001	6.6 (3.09 – 14.08)	<0.001
CV risk factors				
Diabetes	1.63 (0.97 – 2.73)	0.064	1.86 (1.07 – 3.25)	0.028
Systemic hypertension	1.33 (0.56 – 3.14)	0.519		
Morbid obesity	1.47 (0.73 – 2.96)	0.284		
Renal insufficiency	4.06 (1.94 – 8.49)	<0.001		
Dialysis	1.38 (0.18 – 10.76)	0.761		
COPD	2.54 (0.73 - 8,79)	0.141		
Pulmonary hypertension	3.63 (1.84 – 7.16)	<0.001	1.02 (1.01 – 1.04)	0.006
Emergency surgery	6.13 (2.64 – 14.28)	<0.001		
Previous PCI	1.90 (1.04 – 3.491)	0.037	1.94 (1.02 – 3.68)	0.044

CABG - Coronary artery bypass grafting; CI - Confidence interval; AMI - Acute myocardial infarction; IABP - Intra-aortic balloon pump; CV - Cardiovascular; COPD, -Chronic obstructive pulmonary disease; PCI - Percutaneous coronary intervention.

Table 5 - Preoperative characteristics in patients matched on propensity score with previous PCI (study group) and those without previous PCI (control group)

Variable	Without previous PCI (n=161)		With previous PCI (n=161)		p	
Age (years)	63 (56 - 69)		70 (61 - 76)		0.800	c
Female sex	38	23.6%	23	36.5%	0.791	a
Ejection fraction (%)	57 (42 - 62)		56 (45 - 62)		0.809	c
Left main disease > 50%	33	20.5%	24	14.9%	0.189	a
Clinical manifestation						
Congestive heart failure	83	51.5%	79	49.1%	0.656	a
Unstable angina	20	12.4%	26	16.1%	0.339	a
Recent AMI	53	32.9%	53	32.9%	1.000	a
AMI with < 48hs	5	3.1%	10	6.2%	0.186	b
Cardiogenic shock	1	0.6%	1	0.6%	1.000	b
Preoperative IABP	7	4.3%	9	5.6%	0.608	b
CV risk factors						
Diabetes	71	44.1%	71	44.1%	1.000	a
Systemic hypertension	140	87.0%	147	91.3%	0.210	a
Morbid obesity	15	9.3%	19	11.8%	0.468	a
Renal insufficiency	11	6.8%	8	5.0%	0.478	a
Dialysis	1	0.6%	1	0.6%	1.000	b
COPD	2	1.2%	3	1.9%	0.686	b
Pulmonary hypertension	12	7.4%	10	6.2%	0.659	a
Emergency surgery	6	3.7%	6	3.7%	1.000	b

a-chi-squared test; b-Fisher's exact test; c-Mann-Whitney's test. Variables are shown in contingency table with absolute (n) and relative (%) frequencies. Quantitative variables were shown in table including the median, and 1st and 3rd quartile values. PCI - Percutaneous coronary intervention; AMI - Acute myocardial infarction; IABP - Intra-aortic balloon pump; CV - Cardiovascular; COPD - Chronic obstructive pulmonary disease.

in multicenter study with almost 30,000 patients confirmed the history of multiple previous PCIs as risk factor for hospital mortality after CABG (odds ratio of 2.02; p=0.0005). In a sub-analysis with 749 diabetic patients, Thielmann et al³¹, observed the association of hospital mortality after CABG with odds ratio of 2.87 (p=0.03) for diabetic patients with a history of previous PCI. In our study group (with previous PCI), 90 patients (56.0%) did not have diabetes and 136 patients (84.5%) had only one previous PCI, even so previous PCI was an independent risk factor. This risk had similar impact as diabetes (odds ratio of 1.86, p=0.028) and chronic renal failure (odds ratio of 4.80, p=0.029), risk factors which have long been known and accepted by the medical community.

Negative influence mechanism

There are several possible causes that may explain the negative impact of previous PCI using stents on CABG:

1- One of them might be stent thrombosis, which takes place more frequently in the first six months after the procedure, and mainly when antiplatelet drugs are discontinued early on to carry out surgery. This thrombotic risk is greater when more than one stent is used, with long stents, stents placed in bifurcations,

drug-eluting stents, diabetic patients and in renal failure³². In our casuistic, this could explain the cause of approximately 1/3 of the patients operated on within less than 12 months of the PCI.

2 - Another cause might be the number of coronary anastomoses or incomplete revascularization in this group of patients. The most common reasons are occluded coronary arteries or those with multiple stents. Incomplete revascularization may lead to postoperative events such as myocardial infarct and death³³. In our casuistic, patients with previous PCI had a lower number of coronary anastomosis per patient (3.0 vs. 3.2 in the group without a previous intervention), however there was no statistical difference.

3 - The need to perform coronary anastomosis more distally than usual (as a result of the presence of stents in the mid third of the arteries) may also affect surgery. In this region, arteries have a smaller diameter, greater flow resistance and it is more difficult to perform coronary anastomosis. This is a mechanic cause, related to the surgical technique, which is difficult to quantify and assess, but definitely plays a major role in the early outcomes of the surgical treatment.

4 - A fourth cause may be the presence of multiple coronary interventions, impairing native blood flow by collaterals

Table 6 - Univariate and multivariate logistic regression analysis of variables associated with in-hospital mortality after CABG in patients matched on propensity score

Variable	Univariate analysis		Multivariate analysis	
	odds ratio (95% CI)	P	odds ratio (95% CI)	P
Age (years)	2.41 (0.31 – 18.58)	0.398	1.11 (1.04 – 1.18)	0.001
Female sex	1.13 (0.4 – 3.21)	0.825		
Ejection fraction (%)	0.99 (0.96 – 1.02)	0.501		
Left main disease > 50%	1.60 (0.56 – 4.6)	0.381		
Clinical manifestation				
Congestive heart failure	2.43 (0.91 – 6.49)	0.077		
Unstable angina	4.63 (1.78 – 12.06)	0.002		
Recent AMI	4.17 (1.61 – 10.8)	0.003		
AMI with < 48hs	13.95 (4.36 – 44.68)	<0.001	16.43 (4.17 – 64.65)	<0.001
Cardiogenic shock	-	-		
Preoperative IABP	17.53 (5.64 – 54.44)	<0.001		
CV risk factors				
Diabetes	1.29 (0.52 – 3.19)	0.584		
Systemic hypertension	2.41 (0.31 – 18.58)	0.398		
Morbid obesity	3.14 (1.06 – 9.26)	0.038	4.15 (1.21 – 14.19)	0.023
Renal insufficiency	4.78 (1.42 – 16.08)	0.011	4.80 (1.17 – 19.74)	0.029
Dialysis	-	-		
COPD	-	-		
Pulmonary hypertension	2.63 (0.71 – 9.76)	0.149		
Emergency surgery	3.24 (0.66 – 15.93)	0.147		
Previous PCI	3.21 (1.14 – 9.04)	0.028	3.46 (1.1 – 10.93)	0.034

CABG - Coronary artery bypass grafting; CI - Confidence interval; AMI - Acute myocardial infarction; IABP - Intra-aortic balloon pump; CV - Cardiovascular; COPD - Chronic obstructive pulmonary disease; PCI - Percutaneous coronary intervention.

causing micro myocardial infarctions. As a consequence, there is more flow resistance of the grafts and lower myocardial irrigation^{9,34}. In our experience, most of the patients (84.5%) had only one previous PCI and this fact could be the cause of only 15% of the patients.

5 – The severity of the progression of coronary atherosclerotic disease may justify the greater mortality. Currently, patients undergoing PCI with a stent have more severe atherosclerotic disease, but not as severe as those undergoing surgical treatment. When treatment fails, these patients are referred for surgical revascularization, however the atherosclerotic disease is then more severe and diffuse³⁵. In our casuistic, preoperative clinical factors and the presence of left main lesion were similar between the two groups, which leads to the conclusion that the presence of the stent may have worsened the progression of atherosclerotic disease and delayed the optimal time for surgical treatment.

6 – More recently, endothelial abnormalities caused by the presence of stents have been studied. There is evidence indicating the coronary stents cause lesions in the arterial wall, leading to endothelial dysfunction with a chronic inflammatory response and platelet and neutrophil activation. The

inflammatory and proliferative abnormalities are not limited to the treated coronary. It affects other coronary arteries, surrounding tissues, including the myocardium, causing adverse cardiovascular effects. Endothelial abnormalities may also render coronary anastomosis more difficult, affecting the perviousness of the grafts¹¹⁻¹³. This is common in bare metal stents and is even more intense in drug-eluting stents¹³. In our casuistic, only 8% of the patients had a previous intervention with drug-eluting stents. If on one hand, there are evidences that drug-eluting stents cause greater inflammatory and chronic response and therefore may further increase surgical risk, on the other hand they may reduce the need of reinterventions and decrease the number of patients requiring CABG after PCI. This association should be further studied.

The mechanism associated with worse prognostic after CABG in patients with previous PCI is multifactorial and probably is caused by a chronic inflammatory reaction, endothelial dysfunction, myocardial ischemic events and changes or difficulty of the surgical technique^{15,36}. Critical analysis and larger and more comprehensive studies should be carried out to establish this association and its respective mechanisms.

Study limitations

This type of study cannot be randomized and the comparison between groups with and without previous PCI has clear limitations, especially regarding the different sample sizes. Even if the propensity score matching is used, the analysis is not ideal, since it depends on selected variables for matching. The type of previous PCI was also not detailed. It was not known whether there was any other procedure in addition to stent implantation or whether there was any other complication. Different causes for surgical treatment indication were also not separated among patients with a previous PCI, such as restenosis, occlusion, thrombosis or disease progression.

Conclusion

Previous PCI is an independent risk factor for in-hospital mortality in patients with multivessel coronary artery disease

who requiring later CABG for coronary artery disease. The cardiac surgeons have to be mindful of this, just as they are already had with other factors, such as renal failure and diabetes.

Potential Conflict of Interest

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

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is part of the thesis of full professor the submitted by Luiz Augusto Ferreira Lisboa, from Faculdade de Medicina - Universidade de São Paulo.

References

1. Kolh P, Wijns W, Danchin N, Di Mario C, Falk V, Folliguet T, et al; Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC), the European Association for Cardio-Thoracic Surgery (EACTS), European Association for Percutaneous Cardiovascular Interventions (EAPCI). Guidelines on myocardial revascularization. *Eur J Cardiothorac Surg.* 2010;38 Suppl:S1-S52.
2. Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, et al. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons. *J Am Coll Cardiol.* 2011;58(24):e123-210.
3. Kappetein AP, Dawkins KD, Mohr FW, Morice MC, Mack MJ, Russell ME, et al. Current percutaneous coronary intervention and coronary artery bypass grafting practices for three-vessel and left main coronary artery disease. Insights from the SYNTAX run-in phase. *Eur J Cardiothorac Surg.* 2006;29(4):486-91.
4. Epstein AJ, Polsky D, Yang F, Yang L, Groeneveld PW. Coronary revascularization trends in the United States, 2001-2008. *JAMA.* 2011;305(17):1769-76.
5. Hannan EL, Racz MJ, Gold J, Cozzens K, Stamato NJ, Powell T, et al. Adherence of catheterization laboratory cardiologists to American College of Cardiology/American Heart Association guidelines for percutaneous coronary interventions and coronary artery bypass graft surgery: what happens in actual practice? *Circulation.* 2010;121(2):267-75.
6. Hlatky MA, Boothroyd DB, Bravata DM, Boersma E, Booth J, Brooks MM, et al. Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials. *Lancet.* 2009;373(9670):1190-7.
7. Daemen J, Boersma E, Flather M, Booth J, Stables R, Rodriguez A, et al. Long-term safety and efficacy of percutaneous coronary intervention with stenting and coronary artery bypass surgery for multivessel coronary artery disease: a meta-analysis with 5-year patient-level data from the ARTS, ERACI-II, MASS-II, and SoS trials. *Circulation.* 2008;118(11):1146-54.
8. Hassan A, Buth KJ, Baskett RJ, Ali IS, Maitland A, Sullivan JA, et al. The association between prior percutaneous coronary intervention and short-term outcomes after coronary artery bypass grafting. *Am Heart J.* 2005;150(5):1026-31.
9. Massoudy P, Thielmann M, Lehmann N, Marr A, Kleikamp G, Maleszka A, et al. Impact of prior percutaneous coronary intervention on the outcome of coronary artery bypass surgery: a multicenter analysis. *J Thorac Cardiovasc Surg.* 2009;137(4):840-5.
10. Bonaros N, Vill D, Wiedemann D, Fischler K, Friedrich G, Pachinger O, 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.* 2011;39(6):e164-9.
11. Gomes WJ, Giannotti-Filho O, Paez RP, Hossne NA Jr, Catani R, Buffolo E. Coronary artery and myocardial inflammatory reaction induced by intracoronary stent. *Ann Thorac Surg.* 2003;76(5):1528-32.
12. Gomes WJ, Buffolo E. Coronary stenting and inflammation: implications for further surgical and medical treatment. *Ann Thorac Surg.* 2006;81(5):1918-25.
13. Lüscher TF, Steffel J, Eberli FR, Joner M, Nakazawa G, Tanner FC, et al. Drug-eluting stent and coronary thrombosis: biological mechanisms and clinical implications. *Circulation.* 2007;115(8):1051-8.
14. Yap CH, Yan BP, Akowuah E, Dinh DT, Smith JA, Shardey GC, et al. Does prior percutaneous coronary intervention adversely affect early and mid-term survival after coronary artery surgery? *JACC Cardiovasc Interv.* 2009;2(8):758-64.
15. Mack M. Does percutaneous coronary intervention compromise the outcome of subsequent coronary artery bypass grafting? *JACC Cardiovasc Interv.* 2009;2(8):765-6.
16. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). *Eur J Cardiothorac Surg.* 1999;16(1):9-13.
17. Bernstein AD, Parsonnet V. Bedside estimation of risk as an aid for decision-making in cardiac surgery. *Ann Thorac Surg.* 2000;69(3):823-8.
18. Hannan EL, Kilburn H Jr, O'Donnell JF, Lukacik C, Shields EP. Adult open heart surgery in New York State: an analysis of risk factors and hospital mortality rates. *JAMA.* 1990;264(21):2768-74.
19. O'Connor GT, Plume SK, Olmstead EM, Coffin LH, Morton JR, Maloney CT, et al. A regional prospective study of in-hospital mortality associated with coronary artery bypass grafting. The Northern New England Cardiovascular Disease Study Group. *JAMA.* 1991;266(6):803-9.
20. Edwards FH, Grover FL, Shroyer AL, Schwartz M, Bero J. The Society of Thoracic Surgeons National Cardiac Surgery Database: current risk assessment. *Ann Thorac Surg.* 1997;63(3):903-8.

21. Johnson RG, Sirois C, Watkins JF, Thurer RL, Sellke FW, Cohn WE, et al. CABG after successful PTCA: a case-control study. *Ann Thorac Surg.* 1995;59(6):1391-6.
22. Jones RH, Hannan EL, Hammermeister KE, Delong ER, O'Connor CT, Luepker RV, et al. Identification of preoperative variables needed for risk adjustment of short-term mortality after coronary artery bypass graft surgery. The Working Group Panel on the Cooperative CABG Database Project. *J Am Coll Cardiol.* 1996;28(6):1478-87.
23. Kalaycioglu S, Sinci V, Oktar L. Coronary artery bypass grafting (CABG) after successful percutaneous transluminal coronary angioplasty (PTCA): is PTCA a risk for CABG? *Int Surg.* 1998;83(3):190-3.
24. Cook S, Walker A, Hugli O, Togni M, Meier B. Percutaneous coronary interventions in Europe: prevalence, numerical estimates, and projections based on data up to 2004. *Clin Res Cardiol.* 2007;96(6):375-82.
25. Chocron S, Baillot R, Rouleau JL, Warnica WJ, Block P, Johnstone D, et al. Impact of previous percutaneous transluminal coronary angioplasty and/or stenting revascularization on outcomes after surgical revascularization: insights from the imagine study. *Eur Heart J.* 2008;29(5):673-9.
26. Bonaros N, Hennerbichler D, Friedrich G, Kocher A, Pachinger O, Laufer G, et al. Increased mortality and perioperative complications in patients with previous elective percutaneous coronary interventions undergoing coronary artery bypass surgery. *J Thorac Cardiovasc Surg.* 2009;137(4):846-52.
27. Lisboa LA, Moreira LF, Mejia OV, Dallan LA, Pomerantzeff PM, Costa R, et al. [Evolution of cardiovascular surgery at the Instituto do Coração: analysis of 71,305 surgeries]. *Arq Bras Cardiol.* 2010;94(2):162-8.
28. Mejía OA, Lisboa LA, Puig LB, Dias RR, Dallan LA, Pomerantzeff PM, et al. The 2000 Bernstein-Parsonnet score and EuroSCORE are similar in predicting mortality at the Heart Institute, USP. *Rev Bras Cir Cardiovasc.* 2011;26(1):1-6.
29. Thielmann M, Leyh R, Massoudy P, Neuhäuser M, Aleksic I, Kamler M, et al. Prognostic significance of multiple previous percutaneous coronary interventions in patients undergoing elective coronary artery bypass surgery. *Circulation.* 2006;114(1 Suppl):I441-7.
30. Tran HA, Barnett SD, Hunt SL, Chon A, Ad N. 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.* 2009;138(2):316-23.
31. Thielmann M, Neuhäuser M, Knipp S, Kottenberg-Assenmacher E, Marr A, Pizanis N, et al. Prognostic impact of previous percutaneous coronary intervention in patients with diabetes mellitus and triple-vessel disease undergoing coronary artery bypass surgery. *J Thorac Cardiovasc Surg.* 2007;134(2):470-6.
32. Cutlip DE, Baim DS, Ho KK, Popma JJ, Lansky AJ, Cohen DJ, et al. Stent thrombosis in the modern era: a pooled analysis of multicenter coronary stent clinical trials. *Circulation.* 2001;103(15):1967-71.
33. Hannan EL, Wu C, Walford G, Holmes DR, Jones RH, Sharma S, et al. Incomplete revascularization in the era of drug-eluting stents: impact on adverse outcomes. *JACC Cardiovasc Interv.* 2009;2(1):17-25.
34. Alfonso F, Hernandez C, Pérez-Viscayno MJ, Hernández R, Fernández-Ortiz A, Escaned J, et al. Fate of stent-related side branches after coronary intervention in patients with in-stent restenosis. *J Am Coll Cardiol.* 2000;36(5):1549-56.
35. Borges JC, Lopes N, Soares PR, Góis AF, Stolf NA, Oliveira SA, et al. Five-year follow-up of angiographic disease progression after medicine, angioplasty, or surgery. *J Cardiothorac Surg.* 2010;5:91.
36. Taggart DP. Does prior PCI increase the risk of subsequent CABG? *Eur Heart J.* 2008;29(5):573-5.

