ORIGINAL ARTICLE

Previous Percutaneous Coronary Intervention Does Not Increase In-Hospital Mortality After Surgical Revascularization: Analysis of 63420 Cases

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ABSTRACT

Background
Recent publications indicate higher in-hospital mortality following myocardial revascularization in patients with previous history of successful percutaneous coronary intervention. Yet, no risk models of surgical mortality have included percutaneous intervention as a risk factor.

Objectives
The purpose of this study was to analyze whether previous percutaneous coronary intervention is a risk factor of in-hospital mortality in coronary artery bypass grafting.

Methods
The study included 78794 patients retrieved from the Spanish Ministry of Health database, who underwent coronary artery bypass graft surgery between January 1997 and December 2007. After applying exclusion criteria, 63420 patients were included in the study, 2942 (4.6%) of whom had previously undergone percutaneous coronary intervention. Continuous variables were compared using the Mann-Whitney U test or Student's t test, and categorical variables using the chi-square test. Univariate and multivariate logistic regression analyses and a multivariate analysis including a propensity score were performed.

Results
Previous percutaneous coronary intervention was not an independent risk factor of in-hospital mortality in the multivariate logistic regression analysis (odds ratio 0.88; 95% confidence interval, 0.72-1.07; p=0.20) or after adjusting for propensity score (odds ratio 0.9; 95% confidence interval, 0.75-1.08; p=0.27).

Conclusion
Previous percutaneous coronary intervention is not an independent risk factor of in-hospital mortality in patients undergoing coronary artery bypass grafting.

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Key words > Thoracic Surgery - Myocardial Revascularization - Angioplasty - Stents

Abbreviations >

PCABG	Coronary artery bypass graft surgery	**PCI**	Percutaneous coronary intervention

INTRODUCTION
Coronary artery disease is currently the leading cause of death worldwide (1). Both percutaneous coronary intervention (PCI) and cardiovascular surgery represent the revascularization modalities of coronary artery disease. Despite PCI has been established as first-line therapy of coronary artery disease, the current guidelines still recommend coronary artery bypass graft surgery (CABG) as the treatment of choice in patients with severe stenosis of the left main coronary artery, three-vessel disease and two-vessel disease with proximal left anterior descending coronary artery stenosis, with the greatest benefit achieved in patients with left ventricular dysfunction or diabetes (2).

According to different publications, the incidence of CABG after PCI varies from 3% to 13%, depending on the year of publication, use of drug eluting stents,

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preference of repeating a PCI procedure, severity of the patients included and length of follow-up. (3-10)

Up to the present time, risk stratification models for cardiac surgery have not included previous PCI as a risk factor (11) and the Society of Thoracic Surgeons Score has only considered previous PCI interval < 6 hours as a risk factor (12). In 1996, Jones et al. published a study identifying variables associated with short-term mortality after CABG. The level 2 group, which considered variables not clearly shown to relate directly to short-term CABG but with potential research or administrative interest, included PCI previous to CABG (13). During the last years, several articles have been published reporting greater in-hospital mortality in patients undergoing CABG with a history of previous successful PCI. The number of publications has been limited, with small samples and contradictory information. (14-25)

The goal of the present study is to analyze the difference of in-hospital mortality of patients undergoing CABG with or without previous history of successful PCI.

METHODS

Study design

We conducted a retrospective, multicenter study of 78794 patients undergoing CABG from January 1997 to December 2007, whose data were retrieved from the database of the Health Information System of the Spanish Ministry of Health, Social Services and Equality. This clinical and administrative database has information regarding demographic variables and the codes of diagnoses and procedures according to the international classification (ICD-9-CM) of all the patients hospitalized in the Spanish Healthcare System.

Patients with and without previous PCI were compared. The following exclusion criteria were considered: absence of type of discharge code, reoperations, combined procedures (revascularization with valve surgery or revascularization with ascending aorta surgery) and PCI and CABG during the same hospitalization.

The variables were selected based on the relevance reported by previous studies and the capacity of discriminating risk factors using the codes retrieved from the database (8, 26, 27). The following variables were included in the analysis: age, gender, year of surgery, hospital stay (preoperative, operative and total stay), previous PCI, type of hospitalization (emergency or scheduled), emergency CABG, diabetes, dyslipidemia, hypertension, smoking habits, previous myocardial infarction, atrial fibrillation, chronic obstructive pulmonary disease, renal failure, congestive heart failure, peripheral vascular disease, cerebrovascular disease, myocardial infarction and CABG within the same hospital admission, cardiogenic shock at admission, cardiopulmonary bypass, perioperative intraaortic balloon pump, number of coronary artery grafts, use of internal mammary artery graft and in-hospital mortality.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation. Normality of distribution was assessed using the Kolmogorov Smirnov test and the Mann-Whitney U test or Student's t test was used for comparisons. Categorical variables were expressed as percentages and were compared using the chi square test. Univariate and multivariate logistic regression analyses were performed to identify independent preoperative predictors of in-hospital mortality. Preoperative variables identified at univariate analysis with a p value ≤ 0.1 for at least one study objective were included in the multivariate logistic regression model. Emergency CABG was not included in the multivariate analysis as values from 6016 cases were lost. Type of hospitalization (354 cases lost) and gender (10 cases lost) were included in the model.

A multivariate logistic regression model which included a propensity score was used to correct for selection bias introduced by non-random allocation. The following variables were matched with the outcome variable (previous PCI) in a multivariate logistic regression model to estimate the propensity scores: age (< 50 years, 50 to 59 years, 60 to 69 years, 70 to 79 years, ≥ 80 years), gender, year of surgery (1997 to 2002 or 2003 to 2007), type of hospitalization, emergency surgery, diabetes, dyslipidemia, hypertension, smoking habits, previous myocardial infarction, atrial fibrillation, chronic obstructive pulmonary disease, chronic renal failure, congestive heart failure, peripheral vascular disease, cerebrovascular disease, myocardial infarction at admission and cardiogenic shock at admission. The propensity score and previous PCI were introduced in a logistic regression model with in-hospital mortality as outcome variable, and the odds ratio adjusted for previous PCI was obtained.

A two-tailed p value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 17.0 statistical package for Windows (SPSS Inc., Chicago, Illinois).

RESULTS

The Health Information Institute database of the Ministry of Health, Social Services and Equality identified 78794 patients undergoing CABG between January 1997 and December 2007. The following subgroups of patients were excluded according to the exclusion criteria of the study: absence of type of discharge code (n = 405), reoperation (n=1125), combined revascularization with valve surgery (n=13670), and combined revascularization with ascending aorta surgery (n= 174). A total of 63420 patients were included, 2942 (4.6%) of whom had previous history of PCI in a different hospital admission. Patient preoperative characteristics are shown in Table 1. The group with previous PCI was significantly younger and had a significantly greater number of patients undergoing CABG between 2003 and 2007, with diabetes, dyslipidemia, hypertension, smoking habits, previous myocardial infarction and peripheral vascular disease. The group without previous PCI was significantly older, had longer postoperative hospital stay and a significantly greater number of patients with emergency surgery, atrial fibrillation, renal failure, congestive heart failure and myocardial infarction and CABG within the same hospital admission.

Patient operative characteristics are shown in Table 2. The mean number of grafts implanted was lower in patients with previous PCI. The use of internal mammary artery grafts, CABG without cardiopulmonary bypass and the need of intraaortic balloon pump was significantly greater in the group with previous PCI.

Table 1. Preoperative characteristics

	Previous PCI (n=2942)	No previous PCI (n=60 478)	p
Age (years)	63.0±9.9	64.8±9,8	<0.001
<50	304 (10.3)	4688 (7.8)	<0.001
50-59	729 (24.8)	11941 (19.7)	<0.001
60-69	903 (30.7)	18878 (31.2)	0.55
70-79	924 (31.4)	22469 (37.2)	<0.001
≥80	65 (2.2)	1642 (2.7)	0.09
Gender (women)	550 (18.7)	11866 (19.6)	0.21
Year of surgery			
1997-2002	1297 (44.1)	33897 (56)	<0.001
2003-2007	1645 (55.9)	26581 (44)	<0.001
Preoperative hospital stay (days)	8.5±8.8	8.7±10.0	0.33
Postoperative hospital stay (days)	11.9±12.7	12.8±14.2	<0.001
Total stay (days)	20.1±15.6	20.8±17	0.43
Emergency admission	1150 (39.5)	23959 (39.8)	0.75
Emergency CABG	29 (1.1)	949 (1.7)	0.008
Diabetes mellitus	947 (32.2)	18356 (30.4)	0.034
Dyslipidemia	1395 (47.4)	23028 (38.1)	<0.001
Hypertension	1500 (51)	28890 (47.8)	0.001
Current smoking	1111 (37.8)	19532 (32.3)	<0.001
Previous AMI	1008 (34.3)	11417 (18.9)	<0.001
Atrial fibrillation	335 (11.4)	8751 (14.5)	<0.001
COPD	41 (1.4)	892 (1.5)	0.72
Renal failure	54 (1.8)	1515 (2.5)	0.022
Heart failure	119 (4)	3683 (6.1)	<0.001
Peripheral vascular disease	247 (8.4)	4232 (7)	0.004
Cerebrovascular disease	88 (3)	2182 (3.6)	0.079
AMI at admission	402 (13.7)	12012 (19.9)	<0.001
Cardiogenic shock at admission	53 (1.8)	1400 (2.3)	0.069

Data are shown as mean ± standard deviation or as numbers (percentages). CABG: Coronary artery bypass graft surgery. COPD: Chronic obstructive pulmonary disease. AMI: Acute myocardial infarction. PCI: Percutaneous coronary intervention.

Table 2. Intraoperative characteristics

	Previous PCI	No previous PCI	p
Cardiopulmonary bypass.	1848 (62.8)	41124 (68)	<0.001
IABP	184 (6.3)	3106 (5.1)	0.008
Number of grafts			
One	884 (30)	14289 (23.6)	<0.001
Two	999 (34)	18138 (30)	<0.001
Three	844 (28.7)	22516 (37.2)	<0.001
≥ Four	215 (7.3)	5535 (9.2)	0.001
Use of IMA	2316 (78.7)	42596 (70.4)	<0.001
Use of 2 IMA	297 (10.1)	5852 (9.7)	0.45
In-hospital mortality	136 (4.6)	4003 (6.6)	<0.001

Data are shown as numbers (percentages).). IMA: Internal mammary artery. IABP: Intraaortic balloon pump. PCI: Percutaneous coronary intervention

At univariate analysis, in-hospital mortality was significantly greater in the group without previous PCI. After including the preoperative variables in a multivariate logistic regression model, previous PCI was not an independent predictor of in-hospital mortality (Table 3). The multivariate analysis that included a propensity score showed similar results (odds ratio, 0.9; 95% confidence interval, 0.75-1.08, p=0.27).

DISCUSSION

The present study, performed in 63420 CABG patients is the largest study ever published analyzing PCI as a risk factor for in-hospital mortality in CABG. Several publications have reported that patients undergoing CABG with previous PCI have greater in-hospital mortality. These results, however, have not been confirmed by our study as previous PCI has not been identified as an independent predictor of in-hospital mortality in patients undergoing CABG in the global series and in the subgroups analyzed.

Most of the possible mechanisms associated with greater in-hospital mortality after CABG in patients with previous PCI are speculative. Prior PCI may limit the number of distal anastomoses, which are performed during subsequent CABG; it may be technically difficult to graft the coronary artery distal to a stent if the stent has been positioned in the distal portion of the vessel (17). Leaving vessels with patent stent ungrafted may lead to postoperative myocardial infarction given the prothrombotic state of patients after CABG and the cessation of antiplatelet agents (17). Prior PCI may reduce the patency of coronary artery bypass grafts as distal run-off from the graft may be decreased by multiple overlapping stents compromising collateral blood flow or because the surgeon is forced to graft more distal parts of the coronary artery due to a proximally placed stent (17-19, 21, 23). Stents in general and drug-eluting stents in particular may affect coronary artery endothelial function, producing local and systemic inflammatory response (28,

Table 3. Univariate and multivariate logistic regression analysis of the variables associated with in-hospital mortality

	Univariate analysis		Multivariate analysis	
Variable	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
<50 years	0.41 (0.35-0.48)	<0.001	0.21 (0.15-0.28)	<0.001
50-59 years	0.41 (0.36-0.45)	<0.001	0.24 (0.19-0.31)	<0.001
60-69 years	0.84 (0.78-0.90)	<0.001	0.41 (0.33-0.52)	<0.001
70-79 years	1.81 (1.70-1.93)	<0.001	0.63 (0.51-0.79)	<0.001
≥80 years	2.26 (1.96-2.61)	<0.001	1.04 (0.80-1.35)	0.75
Gender (women)	1.37 (1.27-1.47)	<0.001	1.10 (1.01-1.20)	0.026
CABG 1997-2002	1.35 (1.27-1.44)	<0.001	1.48 (1.37-1.60)	<0.001
CABG 2003-2007	0.73 (0.69-0.78)	<0.001	-	-
Previous PCI	0.68 (0.57-0.81)	<0.001	0.88 (0.72-1.07)	0.20
Emergency admission	1.84 (1.73-1.96)	<0.001	1.33 (1.23-1.42)	<0.001
Emergency CABG	3.44 (2.92-4.07)	<0.001	-	-
Diabetes mellitus	0.88 (0.82-0.95)	0.001	0.94 (0.86-1.01)	0.13
Dyslipidemia	0.43 (0.40-0.47)	<0.001	0.59 (0.54-0.64)	<0.001
Hypertension	0.64 (0.60-0.68)	<0.001	0.73 (0.68-0.79)	<0.001
Current smoking	0.46 (0.42-0.50)	<0.001	0.64 (0.59-0.70)	<0.001
Previous AMI	0.79 (0.73-0.86)	<0.001	1.01 (0.92-1.11)	0.76
Atrial fibrillation	1.21 (1.11-1.32)	<0.001	0.91 (0.83-1.01)	0.085
COPD	1.03 (0.80-1.34)	0.77	-	-
Renal failure	2.61 (2.26-3.01)	<0.001	2.26 (1.92-2.65)	<0.001
Heart failure	3.98 (3.65-4.35)	<0.001	2.20 (1.98-2.44)	<0.001
Peripheral vascular disease	1.39 (1.24-1.55)	<0.001	1.39 (1.23-1.58)	<0.001
Cerebrovascular disease	2.06 (1.81-2.34)	<0.001	2.01 (1.74-2.32)	<0.001
AMI at admission	3.19 (2.99-3.41)	<0.001	2.05 (1.90-2.22)	<0.001
Cardiogenic shock at admission	39.38 (35.07-44.21)	<0.001	27.54 (24.30-31.22)	<0.001

CABG: Coronary artery bypass graft surgery. COPD: Chronic obstructive pulmonary disease. AMI: Acute myocardial infarction. PCI: Percutaneous coronary intervention.

29). Patients undergoing initial PCI may represent a cohort of patients who may have been assessed as likely to have suboptimal outcomes from CABG, due to cobormidity or unsuitable coronary vessels presenting more advanced atherosclerosis (17). Patients who have PCI and are subsequently submitted to CABG may represent a cohort of patients with more aggressive atherosclerosis (21).

Table 4 shows the publications analyzing in-hospital mortality in patients undergoing CABG with or without prior PCI. The studies by Kalacyoglu et al. (14), Barakate et al.(15) and Bonaros et al. (24) did not use multivariate analysis, while Yap et al. (17), Hassan et al. (18), Thielmann et al. (19) and Massoudy et al. (23) included a propensity score in the statistical analysis. The National Adult Cardiac Surgical Database Report of the Society for Cardiothoracic Surgery in Great Britain and Ireland (30) published in 2008, included the greatest number of patients. In this registry, in-hospital mortality was similar in both groups: 1.8% in the group with previous PCI and 1.7% without previous PCI. However, this publication is a registry without statistical analysis. Thielmann et al. (19) and Massoudy et al. (23) reported that only two or more previous PCI procedures were independent risk factors for in-hospital mortality. In the present study, we did not know the number of PCI procedures before CABG because this information was not available in

Table 4. Characteristics of the studies comparing in-hospital mortality after CABG with or without previous PCI

	Previous PCI (n)	No previous PCI (n)	Results (in-hospital mortality/multivariate analysis)
Kalaycioglu et al. (14)	40	40	Not significant differences
Barakate et al. (15)	361	11909	Not significant differences
Van den Brule et al. (16)	113	1141	Not significant differences / PCI is not a risk factor
Database Great Britain (30)	7815	90112	No statistical analysis
Yap et al. (17)	1457	11727	Not significant differences / PCI is not a risk factor
Boening et al. (25)	185	907	Significantly greater mortality in the group with previous PCI / PCI is not a risk factor
Hassan et al. (18)	919	5113	Significantly greater mortality in the group with previous PCI / PCI is an independent risk factor of in-hospital mortality
Thielmann et al. (19)	649	2626	Two or more PCI are independent risk factors of mortality
Gurbuz et al. (31)	192	399	PCI is an independent risk factor of in-hospital mortality
Thielmann et al. (20)	128	621	Significantly greater mortality in the group with previous PCI / PCI is an independent risk factor of in-hospital mortality
Chocron et al. (32)	430	2059	Significantly greater mortality in the group with previous PCI
Tran et al. (21)	221	1537	Significantly greater mortality in the group with previous PCI / PCI is an independent risk factor of in-hospital mortality
Carnero et al. (22)	116	680	Significantly greater mortality in the group with previous PCI / PCI is an independent risk factor of in-hospital mortality
Massoudy et al. (23)	4176	25752	Two or more PCI are independent risk factors of mortality
Bonaros et al. (24)	306	452	Significantly greater mortality in the group with previous PCI

CABG: Coronary artery bypass graft surgery. PCI: Percutaneous coronary intervention.

the database used. The study by Carnero et al. (22) only included patients undergoing CABG without cardiopulmonary bypass. In the present study, surgery was performed with cardiopulmonary bypass in 62.8% of patients with previous PCI and in 68% of patients without previous PCI. The publications by Thielmann et al. (20), Tran et al. (21) and Boening et al. (25) were conducted on diabetic patients with dissimilar results. Atherosclerosis is more aggressive in these patients and the outcomes of PCI are worse than those of non-diabetics. The present study included 19303 diabetic patients, and 4.90% had a history of prior PCI.

The group with previous PCI was younger, had more cardiovascular coronary risk factors, history of myocardial infarction, peripheral vascular disease and the number of grafts implanted was lower. Patients without previous PCI were older, had higher prevalence of myocardial infarction at admission, emergency surgery and comorbidities. These differences in the distribution of preoperative variables are similar to those reported in other studies (14-25, 31-32).

At univariate analysis, in-hospital mortality was significantly greater in the group without previous PCI. Yap et al. found that the group without previous PCI was associated with lower survival rates at one, three and five years (17) and Boening et al. reported greater 30-day mortality in the group without previous PCI (25). In our series, this might be due to the fact that this group was older and had more comorbidities as atrial fibrillation, chronic renal failure and congestive heart failure. In addition, myocardial infarction and CABG within the same hospital admission was more frequent in these patients. In the study by Yap et al., the group without previous PCI also had more comorbidities (17).

In the multivariate analysis and the model including a propensity score, previous PCI was not associated with greater in-hospital mortality. Female gender, surgery between 1997 and 2002, emergency hospitalization, chronic renal failure, congestive heart failure, peripheral vascular disease, cerebrovascular disease, myocardial infarction at admission and cardiogenic shock at admission were identified as independent predictors of in-hospital mortality in the multivariate analysis. These risk factors have also been identified in different publications and risk scores (11, 12).

Study limitations

The present study is observational and retrospective. Statistical analysis was performed using multivariate logistic regression analysis and a model including a propensity score to avoid selection bias. This multicenter study included all the public health care centers of the Spanish National Health System during a long period of time. There is no information about the results of coronary angiographies performed before the initial PCI (balloon angioplasty, atherectomy, or stents), the time interval between PCI and CABG and the number of PCI procedures performed. Also, there is lack of information about mortality and morbidity between PCI and CABG. Several registries have shown that patients with multi-vessel coronary artery disease managed initially with PCI have elevated mortality, ranging between 6% and 9.5% at 12 months (7, 8, 33). Therefore, in these patients it is not safe to perform firstly a PCI followed by CABG in case of restenosis or progression of coronary artery disease.

CONCLUSIONS

The analysis of this registry demonstrated that previous PCI is not an independent risk factor for in-hospital mortality in patients undergoing CABG for the first time and as a single procedure.

RESUMEN

El intervencionismo coronario percutáneo previo no aumenta la mortalidad hospitalaria en cirugía coronaria: análisis de una serie de 63.420 casos

Introducción
En diversas publicaciones de los últimos años se señala una mortalidad hospitalaria mayor de la cirugía de revascularización miocárdica en pacientes con antecedente de intervencionismo coronario percutáneo previo exitoso; por su parte, los modelos de riesgo de mortalidad en cirugía cardíaca publicados hasta la actualidad no han incluido este antecedente como factor de riesgo.

Objetivo
Analizar si el intervencionismo coronario percutáneo previo es un factor de riesgo de mortalidad hospitalaria en la cirugía de revascularización coronaria.

Material y métodos
Entre enero de 1997 y diciembre de 2007 se analizaron un total de 78.794 pacientes sometidos a cirugía coronaria, recogidos en la base de datos del Ministerio de Sanidad de España. Tras aplicar los criterios de exclusión, el estudio se realizó sobre un total de 63.420 pacientes, de los que 2.942 (4,6%) tenían intervencionismo coronario percutáneo previo. Las variables continuas se compararon con las pruebas de U de Mann-Whitney o de la t de Student y las variables categóricas, mediante chi cuadrado. Se realizó un análisis de regresión logística univariado y multivariado y un análisis multivariado que incluía un índice de propensión.

Resultados
El intervencionismo coronario percutáneo previo no fue un predictor independiente de mortalidad hospitalaria en el análisis multivariado (odds ratio 0,88; intervalo de confianza del 95% 0,72-1,07; p = 0,20) ni en el modelo que incluía un índice de propensión (odds ratio 0,9; intervalo de confianza 95% 0,75-1,08; p = 0,27).

Conclusión
El intervencionismo coronario percutáneo previo no es un factor de riesgo independiente de mortalidad hospitalaria en pacientes con intervención quirúrgica coronaria.

Palabras clave > Cirugía cardíaca - Revascularización miocárdica - Angioplastia - Stents

Conflicts of interest
None declared.

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