ORIGINAL ARTICLE

Impact of previous percutaneous coronary interventions on the course and clinical outcomes of coronary artery bypass grafting

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Abstract

Background: Despite the increasing number of patients after percutaneous coronary intervention (PCI) requiring coronary artery bypass grafting (CABG), studies on the impact of these procedures on surgical revascularisation outcomes are sparse. Furthermore, advances in cardiology require reassessment of their potential prognostic significance.

Aim: We sought to assess the influence of previous PCI on CABG outcomes.

Methods: A total of 211 consecutive patients scheduled for CABG were enrolled into this prospective study. Patients after PCI (group 1, n = 99) were compared with subjects with no history of PCI (group 2, n = 112) in terms of preoperative, operative, and postoperative data. All the patients were followed-up for the incidence of in-hospital (cardiogenic shock, myocardial infarction, stroke, acute renal failure, reoperation, death) and long-term (overall mortality, occlusion of at least one graft in 64-row computed tomography) clinical endpoints.

Results: Group 1 had more advanced heart failure and coronary artery disease as reflected by New York Heart Association (2.43 ± 0.57 vs. 2.17 ± 0.68; p < 0.001) and Canadian Cardiovascular Society (2.44 ± 0.59 vs. 2.03 ± 0.65; p < 0.001) scales, respectively. Compared with group 2, longer aortic cross-clamp (33.5 ± 9.9 vs. 29.5 ± 8.4; p < 0.05) and cardiopulmonary bypass (67.5 ± 28.2 vs. 56.5 ± 17.9; p < 0.001) times were observed as well as a higher number of implanted grafts (3.0 ± 0.7 vs. 2.8 ± 0.70; p < 0.05). No significant differences were observed in terms of in-hospital clinical endpoints. During 12 ± 3.41 months of follow-up group 1 had higher mortality (5.05% vs. 0%; p < 0.05) but similar graft patency.

Conclusions: "Stent-loaded" patients undergo more time-consuming CABG with a higher number of grafts. Furthermore, they have higher long-term mortality but similar graft patency and in-hospital mortality/morbidity.

Key words: myocardial revascularisation, graft patency, percutaneous coronary intervention, coronary artery bypass grafting

Kardiol Pol 2018; 76, 6: 953–959

INTRODUCTION

In recent years, indications for percutaneous coronary intervention (PCI) have extended to patients with more advanced and complex coronary artery disease (CAD) [1]. At the same time, despite progress in stent design and procedural techniques as well as more aggressive pharmacological treatment, in-stent restenosis and progression of coronary atherosclerosis in untreated native coronary segments still remain a significant problem. Therefore, there is an increasing number of patients with a history of PCI who require coronary artery bypass graft

(CABG) surgery. Available data suggest that 10% to 20% of patients with prior PCI are referred for CABG three to five years after PCI [2].

Increased incidence of adverse cardiac events in patients with prior PCI undergoing non-cardiac surgical procedures as well as repeated PCI has attracted interest in the effect of prior PCI on patients undergoing CABG [3, 4]. Studies on the impact of these procedures on patients undergoing surgical revascularisation give conflicting results. Although there is a large body of evidence indicating that previous PCI

adversely affects clinical outcomes of CABG, this is not supported by other published data [5–10]. Some studies reported that patients after multiple PCI procedures have significantly increased risk of in-hospital mortality and major adverse cardiac events (MACEs) compared with patients with a history of no or a single PCI [11, 12].

Dynamic progress in stent technology and more effective pharmacotherapy, as well as progress in cardiac surgery techniques, require reassessment of the potential prognostic significance of prior PCI in patients undergoing CABG. We therefore sought to reassess the influence of previous PCI on the course and clinical outcomes of CABG surgery by comparing the two subsets of patients referred for surgical revascularisation. This should allow cardiac surgery teams preparing for CABG procedures to recognise possible risks related to previous interventions.

METHODS
Study population
A total of 211 consecutive patients with stable CAD scheduled for elective on-pump CABG were enrolled in a prospective single-centre study. To minimise bias, the study population was restricted to patients with isolated CAD without indications for concomitant valve surgery or any previous cardiac surgical procedure. Furthermore, patients who underwent PCI during the same admission as well as subjects with PCI-related complications necessitating urgent cardiac surgery were excluded from the present study.

Preoperative, operative, and postoperative data were collected from consecutive patients undergoing CABG, including 99 patients with previous PCI (group 1) and 112 patients without previous PCI (group 2). All of the PCI patients underwent left coronary artery stenting, whereas 79.8% of them underwent right coronary artery stenting. The mean number of implanted stents per patient was 2.6 ± 1.5 (range 1–6 stents). The mean period between PCI and CABG procedures was 13.1 ± 23.1 months (range 4–120 months).

All patients were prospectively followed-up for the incidence of in-hospital (cardiogenic shock, myocardial infarction, stroke, acute renal failure, reoperation, cardiovascular death) and long-term (overall mortality, occlusion of at least one graft in 64-row computed tomography) clinical endpoints. Mean follow-up was 12 ± 3.41 months. Both groups of patients were compared in terms of preoperative, operative, and postoperative data.

Assessment of bypass graft patency
After a mean follow-up of 12 ± 3.41 months, bypass graft patency was assessed using 64-row multidetector computed tomography (Siemens Somatom Sensation 64, Erlangen, Germany). During the diagnostic procedure a nonionic monomeric iodinated contrast agent was used (Iomeron 400, Bracco, UK). Heart rate < 70 bpm was maintained with the use of β-blocker, if necessary. The β-blocker metoprolol (Betaloc,

AstraZeneca, UK) was administered prior to the examination if patient's heart rate was above the aforementioned threshold.

Ethics
Informed consent was obtained from all individual participants included in the study. The present study was conducted in accordance with the Declaration of Helsinki and approved by the Local Ethics Committee.

Statistical analysis
Statistical analysis was performed with Statistica v. 9.0 (Statsoft Inc., Tulsa, OK, USA) and StatXact 8 (Cytel Software Corp, Cambridge, MA, USA) software. Quantitative variables are expressed as the mean and standard deviation (mean ± SD). The Shapiro-Wilk test was performed to determine whether a sample of values followed normal distribution. If normal distribution was confirmed, intergroup comparisons were made by the Student t test (when the assumption of homogeneity of variances was confirmed) or Welch's test (when the assumption of homogeneity of variances was violated). The assumption of homogeneity of variances was tested using Levene's test. The nonparametric Mann-Whitney U test was used if the analysed variables were not normally distributed.

The abovementioned nonparametric test was used to make comparisons between groups. Categorical variables are expressed as absolute numbers and their frequencies in percentages. A p-value < 0.05 was considered significant.

RESULTS
Preoperative characteristics
A higher percentage of men was observed in group 1. Furthermore, patients in this group had higher incidence of left main disease (LMD) (Fig. 1) and more severe CAD and heart failure, as reflected by the Canadian Cardiovascular Society (CCS) and New York Heart Association (NYHA) scales, respectively. A comparison of preoperative characteristics of patients with vs. without prior PCI scheduled for isolated elective CABG is presented in Table 1. The two groups of patients did not differ in terms of the of biochemical test results, including markers of glycaemic control. A comparison of the results of preoperative biochemical tests in patients scheduled for elective CABG with vs. without previous PCI showed no significant differences in plasma levels of haemoglobin, electrolytes, fasting glucose, creatinine, transaminases, high-sensitivity C-reactive protein, and N-terminal pro-B-type natriuretic peptide.

Intraoperative characteristics
In group 1 a higher number of grafts were implanted (3.0 ± 0.7 vs. 2.8 ± 0.7; p < 0.05). Furthermore, longer cardiopulmonary bypass (CPB) time as well as cross-clamp time (CCT) were observed in this group (Figs. 2, 3). The abovementioned intraoperative variables were also adjusted for the number of implanted grafts. Compared to group 2, patients from group 1 had longer CPB time (22.6 ± 8.1 min
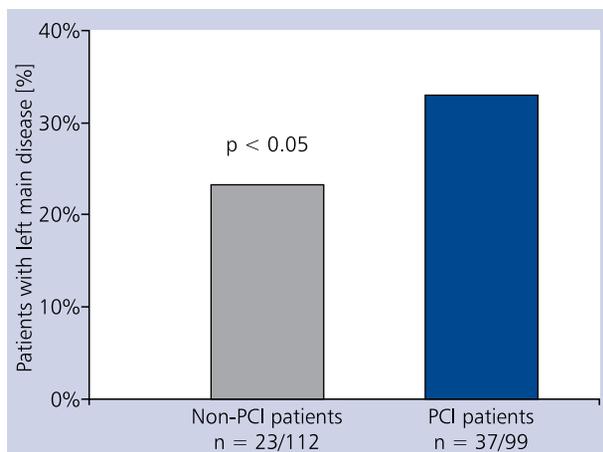
Figure 1. Comparison of the incidence of left main disease in patients undergoing coronary artery bypass grafting with percutaneous coronary intervention (PCI patients) vs. without previous PCI (non-PCI patients)

vs. 20.4 ± 5.2 min; $p < 0.001$) as well as CCT per graft (11.2 ± 2.2 min vs. 10.7 ± 2.4 min; $p < 0.05$). A comparison of all intraoperative variables in patients undergoing CABG with vs. without previous PCI is presented in Table 2.

Postoperative characteristics and long-term follow-up

Patients were followed-up for 12 ± 3.41 months. During that time higher long-term mortality in group 1 was observed. However, despite that fact, no significant differences in graft patency between the analysed groups were observed (Table 3). Similarly, no significant differences were observed in other postoperative variables (Table 4).

DISCUSSION

In recent years, along with progress in interventional cardiology, indications for PCI have extended to patients with more advanced and complex CAD, who had been considered unsuitable for that treatment in the past [1]. On the other hand, despite advances in stent design and procedural techniques as well as more aggressive lipid-lowering therapy, in-stent restenosis and progression of coronary atherosclerosis in untreated segments still remain a significant problem. Consequently, there is an increasing number of patients with a history of PCI

Table 1. Comparison of preoperative characteristics of patients scheduled for elective coronary artery bypass grafting after previous percutaneous coronary intervention (PCI; group 1) versus without previous PCI (group 2)

	Group 1 (n = 99)	Group 2 (n = 112)	p
Women	22 (22.22%)	32 (28.57%)	0.040
Age [years]	60.6 ± 8.5	61.6 ± 9.7	0.428
Body mass index [kg/m²]	28.7 ± 4.1	28.2 ± 3.8	0.896
EuroSCORE II [%]	2.63 ± 1.74	2.88 ± 1.96	0.420
Logistic EuroSCORE II [%]	2.09 ± 3.08	2.35 ± 4.30	0.697
CCS	2.44 ± 0.59	2.03 ± 0.65	0.00001
NYHA	2.43 ± 0.57	2.17 ± 0.68	0.005
Heart rate [bpm]	72.18 ± 9.06	73.38 ± 9.79	0.349
Systolic BP [mmHg]	126.7 ± 14.21	129.5 ± 16.73	0.426
Diastolic BP [mmHg]	77.68 ± 8.87	78.16 ± 10.55	0.915
CAD [years since diagnosis]	4.4 ± 5.2	4.0 ± 4.9	0.567
History of MI	66.0 ± 58.93	61 (54.46%)	0.754
Diabetes mellitus	28 (28.28%)	25 (22.32%)	0.343
Hypercholesterolaemia	77 (77.78%)	76 (67.86%)	0.218
Chronic kidney disease	10 (10.1%)	4 (3.57%)	0.177
COPD	21 (21.21%)	14 (12.5%)	0.459
Hypertension	89 (89.9%)	73 (65.18%)	0.333
History of stroke	9 (9.09%)	6 (5.36%)	0.389
Cigarette smoking	12 (12.12%)	8 (7.14%)	0.599
Left main disease	37 (33.04%)	23 (23.23%)	0.009
Ejection fraction [%]	45.97 ± 6.1	44.9 ± 5.9	0.235

Data are shown as mean ± standard deviation or number (percentage). BP — blood pressure; CAD — coronary artery disease; CCS — Canadian Cardiovascular Society angina scale; COPD — chronic obstructive pulmonary disease; MI — myocardial infarction; NYHA — New York Heart Association heart failure scale
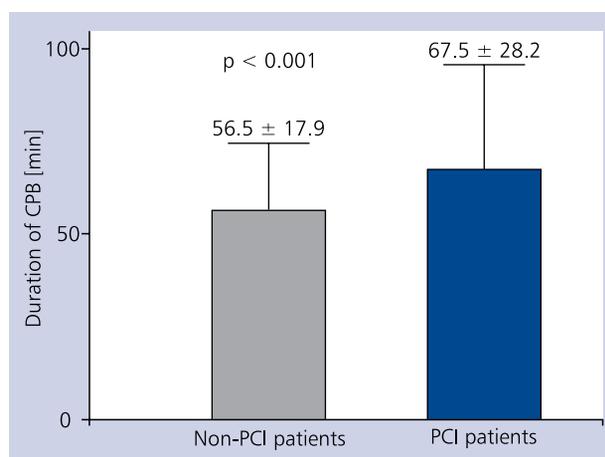
Figure 2. Comparison of the duration of cardiopulmonary bypass (CPB) in patients undergoing coronary artery bypass grafting with percutaneous coronary intervention (PCI patients) vs. without previous PCI (non-PCI patients) (p < 0.001)
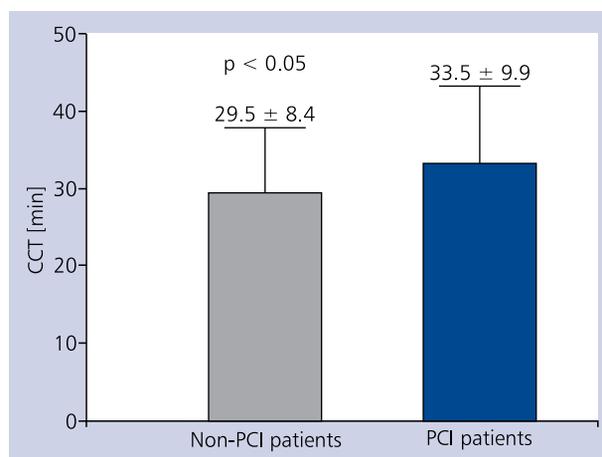
Figure 3. Comparison of cross-clamp time (CCT) in patients undergoing coronary artery bypass grafting with percutaneous coronary intervention (PCI patients) vs. without previous PCI (non-PCI patients) (p < 0.05)

Table 2. Comparison of intraoperative variables in patients undergoing elective coronary artery bypass grafting after previous percutaneous coronary intervention (PCI; group 1) versus without previous PCI (group 2)

	Group 1 (n = 99)	Group 2 (n = 112)	p
Duration of CPB [min]	67.5 ± 28.2	56.5 ± 17.9	0.001
Cross-clamp time [min]	33.5 ± 9.9	29.5 ± 8.4	0.0036
Total arterial revascularisation	18 (18.18%)	18 (16.07%)	0.247
Number of arterial grafts	1.44 ± 0.71	1.4 ± 0.68	0.765
Number of venous grafts	1.56 ± 0.94	1.38 ± 0.95	0.190
Total number of grafts	3.0 ± 0.7	2.8 ± 0.70	0.049

Data are shown as mean ± standard deviation or number (percentage). CBP — cardiopulmonary bypass

Table 3. Comparison of bypass graft patency as assessed by computed tomography scans, and overall mortality in elective coronary artery bypass grafting patients after previous percutaneous coronary intervention (PCI; group 1) versus without previous PCI (group 2) in 12-month follow-up

	Group 1 (n = 99)	Group 2 (n = 112)	p
Occlusion of a venous graft	0.21 ± 0.53	0.2 ± 0.4	0.612
Occlusion of an arterial graft	0.13 ± 0.34	0.09 ± 0.29	0.376
Overall mortality	5 (5.05%)	0 (0%)	0.021

Data are shown as mean ± standard deviation or number (percentage).

who require CABG. Many studies revealed that PCI adversely affects clinical outcomes of non-cardiac surgical procedures as well as repeated PCIs [3,4]. In this context, it is not surprising that the potential influence of previous PCI on clinical outcomes of CABG has become the focus of attention. The main finding of the present study, which was intended to be a part of this heated debate, is that "stent-loaded" patients undergo more difficult CABG procedures with a higher num-

ber of grafts. Furthermore, compared with subjects without previous PCI, they have higher long-term mortality but similar graft patency and in-hospital morbidity/mortality. The two groups of patients did not differ in terms of most of baseline demographics, except for a significantly higher proportion of women in the group 2, more advanced CAD and heart failure (as reflected by CCS and NYHA scales, respectively), as well as higher incidence of LMD in group 1. One of the reasons for

Table 4. Comparison of postoperative variables in patients undergoing elective coronary artery bypass grafting after previous percutaneous coronary intervention (PCI; group 1) versus without previous PCI (group 2)

	Group 1 (n = 99)	Group 2 (n = 112)	p
Intensive coronary unit stay [days]	2.26 ± 0.92	2.22 ± 0.89	0.854
Ventilation time [h]	11.17 ± 14.74	11.49 ± 15.65	0.847
Perioperative myocardial infarction	7 (7.07%)	5 (4.46%)	0.737
Cardiogenic shock	5 (5.05%)	4 (3.57%)	0.554
Intra-aortal balloon pump support	9 (9.09%)	12 (10.71%)	0.819
Saphenous vein harvest wound complications	16 (16.16%)	17 (15.18%)	0.852
Sternal wound complications	6 (6.06%)	13 (11.61%)	0.228
Reoperation	9 (9.09%)	13 (11.61%)	0.654
Acute renal failure	7 (7.07%)	8 (7.14%)	1.0
Stroke	4 (4.04%)	4 (3.57%)	1.0
In-hospital mortality	2 (2.02%)	2 (1.79%)	1.0

Data are shown as mean ± standard deviation or number (percentage).

a higher proportion of women in group 2 could be attributed to atypical manifestation of CAD observed in this sex, which hampers early recognition of the disease [13]. This highlights the need for a more female-tailored strategy that will lead to earlier recognition and more effective treatment of CAD, especially taking into account that mortality after CABG is higher in women compared with men [14].

As mentioned earlier, higher incidence of LMD in group 1 was observed. This may be associated with the fact that, in accordance with European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) guidelines on myocardial revascularisation, LMD is much more suitable for PCI treatment compared with multivessel disease (MVD) [1], of course after careful assessment by the Heart Team. Available data suggest that neither PCI nor CABG alone can provide a solution for the entire spectrum of CAD patients [1]. Recent advances in interventional cardiology have led to PCI becoming a rival to CABG in patients with LMD/MVD who had previously been referred for cardiac surgery. Thus, it cannot be ruled out that LMD patients had previously been treated by PCI and later referred for CABG in the case of percutaneous treatment failure or restenosis. Another possible explanation is stenosis of the left main coronary artery, resulting from endothelial injury caused by the guiding catheter and other equipment used in PCI [15, 16]. However, this mechanism should not be overestimated. Nowadays, thanks to less traumatic low-profile soft-tip catheters and more advanced interventional cardiology equipment, the risk of injury of the left main coronary artery is incomparably low. Nevertheless, this rare iatrogenic complication cannot be completely ruled out.

Another finding of the present study is that no differences in EuroSCORE II and logistic EuroSCORE II were observed between the study groups. Taking into account the fact that both groups were comparable in terms of perioperative outcomes, this seems to be logical and confirms the accuracy of the scoring system. In the study by Lisboa et al. [7] patients with previous PCI had higher in-hospital mortality after CABG, and it was also comparable with EuroSCORE and 2000 Bernstein-Parsonnet risk scores. However, these findings are not consistent with the results of Bonaros et al. [6], who did not confirm the accuracy of EuroSCORE in patients after PCI. Despite EuroSCORE-matched study groups, patients with previous PCI had worse perioperative outcomes in terms of mortality, higher incidence of MACE, bleeding complications, acute renal failure, and the need for renal replacement therapy. The authors suggested that the lack of predictive value of preoperative EuroSCORE is attributed to the fact that the scoring system does not take into consideration previous PCI in calculating risk of cardiac surgery. These results were also confirmed in another study conducted by the same scientific group, in which EuroSCORE as well as the STS risk model were inaccurate in predicting perioperative mortality after CABG in patients with a history of elective PCI [17]. Given the above-mentioned conflicting results and due to the fact that there are a growing number of patients with a history of PCI who require CABG, there is a necessity to develop a more reliable scoring system that takes into account patients' previous coronary interventions.

The results of the present study also indicate that patients with previous PCI undergo more time-consuming CABG procedures as compared with stent-naïve subjects. This was reflected by differences in absolute values of CCT and duration of CPB as well as their relative values adjusted for the number of bypass grafts. These results come as no surprise, given the fact that distal anastomoses of bypass grafts have to be placed more distally than usual. Smaller diameter of distal parts of target vessels is associated with prolonged and technically more difficult procedure. Thus, the presence of implanted stent (or

multiple stents) often makes the procedure suboptimal or, in cases of a so-called "full metal jacket," even impossible to perform. Our findings agree with common sense, but surprisingly they have not been confirmed in available studies. Many studies revealed no significant differences in CCT and duration of CPB between patients with and without prior PCI [6, 7, 18]. Analogical findings were reported by Thielmann et al. [5], who analysed a high-risk subset of patients with diabetes mellitus and triple-vessel disease. Yap et al. [10] noticed even shorter CCT and reduced duration of CPB in patients with prior PCI. Undoubtedly, the influence of previous PCI on these intraoperative variables requires further studies, especially taking into account that they may contribute to several adverse postoperative complications [19].

In the present study, compared to stent-naïve subjects, higher long-term mortality in PCI patients was observed. It is noteworthy that these patients had more advanced CAD and heart failure as reflected by CCS and NYHA scales, respectively. Previous PCI could have been a surrogate marker of more aggressive disease, in turn translating into worse prognosis. Furthermore, in logistic regression analysis, higher risk of long-term mortality and graft occlusion was observed in patients with diabetes, who had previously undergone PCI. This is consistent with the study of Nauffal et al. [20] reporting poorer long-term outcomes after CABG in diabetic patients with a history of PCI. At the same time, no significant differences between studied groups were observed in terms of in-hospital morbidity and mortality. These results are not consistent with the vast majority of available data. Thielmann et al. [5] reported that CABG performed in patients with previous PCI is associated with higher in-hospital mortality and MACE, compared with stent-naïve subjects. Importantly, in the study by Lisboa et al. [7] previous PCI emerged as an independent predictor of in-hospital mortality as strong as diabetes. Some of the studies also indicate that multiple PCIs are stronger predictors of the above-mentioned clinical endpoints compared to single previous PCI or no prior PCI [11, 12]. Along with the impact of prior PCI on perioperative mortality, Bonaros et al. [6] also reported higher perioperative morbidity (MACE, bleeding complications, acute renal failure, renal replacement therapy and the use of blood products). On the other hand, in the study by Mehta et al. [18] previous PCI was an independent predictor of perioperative complications, longer hospitalisation, and higher readmission rates, but the impact on mortality was not confirmed. In contrast to previously cited papers, Fukui et al. [21] did not confirm the prognostic impact of previous PCI on early and late outcomes of CABG. However, it should be noted that only patients undergoing off-pump CABG were enrolled. Thus, it is probable that worse clinical outcomes of CABG in previously cited papers could be partially attributed to the use of CPB that intensifies inflammatory reactions. In the study by Zhang et al. [9] there was also no association between prior PCI and

CABG outcomes including in-hospital mortality and MACE. However, the vast majority of patients had a single PCI procedure before referral for CABG. Analogically, Yap et al. [10] observed no differences between PCI and non-PCI patients in terms of short-term and mid-term mortality after CABG. In that paper, non-PCI patients were older, had higher EuroSCORE, and more frequently a history of myocardial infarction.

Despite important findings, several limitations of the present study need to be acknowledged. First, this is a single-centre study with a relatively small sample size and only a one-year follow-up period. Therefore, the results cannot be easily extrapolated to other cardiac centres performing CABG across the world. It cannot be ruled out that centres with higher volume of cardiac procedures would provide different results depending on their expertise and surgeon volume. Second, the findings of the present study can be undermined by its intrinsic limitation. It is well recognised that randomised trials are less likely to be affected by selection bias. Unfortunately, a study such as ours ("ex post facto research design"), despite its prospective nature, cannot be randomised, which may lead to problems with drawing unambiguous conclusions from comparisons. Third, there are no detailed data regarding pharmacotherapy, target vessels for prior PCI, quality of target vessels, as well as the types and locations of bypass grafts implanted during subsequent CABG. It should be pointed out that the results of our study should not be interpreted as evidence for worse prognosis of CABG patients as a result of PCI but as evidence of different clinical characteristics of subjects with a history of PCI prior to CABG, because we compared two groups of patients scheduled for surgery. Undoubtedly, confronting that information could lead to a better understanding of the link between previous PCI and CABG outcomes.

Our study suggests different characteristics of both subgroups of CABG patients. To assess a possible "purely mechanical" effect of implanted stents, a large-scale analysis of clinically comparable groups is warranted.

In conclusion, our results suggest that patients with prior PCI need more bypass grafts and undergo more time-consuming CABG procedures, as reflected by CCT and duration of CPB. There are no differences in terms of in-hospital mortality and morbidity between patients with previous PCI and subjects undergoing CABG as a primary revascularisation strategy. In addition, "stent-loaded" patients have similar graft patency but higher long-term mortality. The current study compares the two subpopulations of patients referred to surgical revascularisation: those with previous PCI and those having CABG as the first choice; therefore, the differences observed are mostly related to different clinical characteristics. However, to evaluate the pure effect of PCI on CABG outcome an analysis of matching subsets of patients should be performed. Thus, further investigations with higher sample sizes and longer follow-up period are warranted to assess the predictive value of previous PCI and to elucidate the impact of

PCI-related factors (number of PCIs, extent of stenting, types of implanted stents, etc.) on the course and clinical outcomes of CABG. Irrespective of future results from clinical studies, our findings reemphasise the importance of the Heart Team's approach to patients requiring myocardial revascularisation.

Conflict of interest: *none declared*

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