# Comparison of One-Year Outcomes of Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting in Patients With Unprotected Left Main Coronary Artery Disease and Acute Coronary Syndromes (from the CUSTOMIZE Registry)

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**Uncertainty surrounds the optimal revascularization strategy for patients with left main coronary artery disease presenting with acute coronary syndromes (ACSs), and adequately sized specific comparisons of percutaneous and surgical revascularization in this scenario are lacking. The aim of this study was to evaluate the incidence of 1-year major adverse cardiac events (MACEs) in patients with left main coronary artery disease and ACS treated with percutaneous coronary intervention (PCI) and drug-eluting stent implantation or coronary artery bypass grafting (CABG). A total of 583 patients were included. At 1 year, MACEs were significantly higher in patients treated with PCI (n = 222) compared to those treated with CABG (n = 361, 14.4% vs 5.3%, p <0.001), driven by a higher rate of target lesion revascularization (8.1% vs 1.7%, p = 0.001). This finding was consistent after statistical adjustment for MACEs (adjusted hazard ratio [HR] 2.7, 95% confidence interval [CI] 1.2 to 5.9, p = 0.01) and target lesion revascularization (adjusted HR 8.0, 95% CI 2.2 to 28.7, p = 0.001). No statistically significant differences between PCI and CABG were noted for death (adjusted HR 1.1, 95% CI 0.4 to 3.0, p = 0.81) and myocardial infarction (adjusted HR 4.8, 95% CI 0.3 to 68.6, p = 0.25). No interaction between clinical presentation (ST-segment elevation myocardial infarction or unstable angina/non–ST-segment elevation myocardial infarction) and treatment (PCI or CABG) was observed (p for interaction = 0.68). In conclusion, in patients with left main coronary artery disease and ACS, PCI is associated with similar safety compared to CABG but higher risk of MACEs driven by increased risk of repeat revascularization.**  **(Am J Cardiol 2011;108: 355–359)**

Coronary artery bypass grafting (CABG) is the gold standard of revascularization offered to patients with significant unprotected left main coronary artery disease.[1,2] However, current American College of Cardiology/American Heart Association guidelines allow percutaneous coronary intervention (PCI) of the left main coronary artery as a reasonable alternative to CABG in patients with anatomic conditions that are associated with a low risk of procedural complications and clinical co-morbidities that predict an increased risk of adverse surgical outcomes.[1] Although these guidelines apply to patients with stable angina, some uncertainty surrounds the optimal revascularization strategy for the large and heterogeneous group of patients with left main coronary artery disease presenting with acute coronary syndromes (ACSs). In particular, there is a lack of adequately sized specific comparisons of PCI to CABG in patients with left main coronary artery disease and ACS. To fill this gap we report on the 1-year clinical outcomes of patients with left main coronary artery disease and ACS undergoing revascularization by PCI or CABG in the contemporary era.

## Methods

The Appraise a Customized Strategy for Left Main Revascularization (CUSTOMIZE) Registry is an ongoing registry maintaining data from 2 participating centers that have performed PCIs with drug-eluting stents or CABGs in consecutive patients with unprotected left main coronary artery disease since 2002.[3] This prespecified analysis focuses on clinical outcomes of patients presenting with ACS (unstable angina/non–ST-segment elevation myocardial infarction or ST-segment elevation myocardial infarction). The local ethics committee at each center approved the use of clinical data for this study and all patients provided written informed consent.

Details on procedural and postprocedural practices of patients enrolled in the CUSTOMIZE Registry were reported elsewhere.[3] Briefly, patients underwent PCI instead of CABG because of a subject's or physician's preference or high risk associated with CABG. All PCIs were per-

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0002-9149/11/$ – see front matter 
doi:10.1016/j.amjcard.2011.03.050

Table 1
Baseline characteristics in patients with left main coronary artery disease who underwent percutaneous coronary intervention or coronary artery bypass grafting

| Variable | PCI (n = 222) | CABG (n = 361) | p Value |
|---|---|---|---|
| Age (years), mean ± SD | 67.2 ± 10 | 65.8 ± 10 | 0.11 |
| Men | 76.1% | 78.7% | 0.47 |
| Systemic hypertension | 71.6% | 73.7% | 0.59 |
| Hypercholesterolemia* | 55.4% | 52.9% | 0.56 |
| Smoking habitus | 43.7% | 44.9% | 0.78 |
| Diabetes mellitus | 35.6% | 40.4% | 0.24 |
| Creatinine >2 mg/dl | 4.5% | 1.4% | 0.02 |
| Previous myocardial infarction | 35.6% | 37.4% | 0.66 |
| Peripheral artery disease | 16.2% | 14.4% | 0.55 |
| Chronic obstructive pulmonary disease | 11.7% | 6.4% | 0.02 |
| Previous percutaneous coronary intervention | 26.6% | 14.4% | <0.001 |
| Clinical presentation | | | |
| Unstable angina/non–ST-segment elevation myocardial infarction | 91.4% | 99.2% | <0.001 |
| ST-segment elevation myocardial infarction | 8.6% | 0.8% | <0.001 |
| Left ventricular ejection fraction (%) | 47.4 ± 11 | 50.4 ± 9 | <0.001 |
| Left ventricular ejection fraction <30% | 14% | 4.2% | <0.001 |
| EuroSCORE | 6.3 ± 3 | 5.6 ± 2.5 | 0.002 |
| Coronary artery lesion location | | | |
| Ostium | 32.9% | 17.3% | <0.001 |
| Shaft | 15.3% | 6.1% | <0.001 |
| Distal | 51.8% | 76.6% | <0.001 |
| Coronary artery vessel | | | |
| Isolated left main | 7.7% | 6.6% | 0.67 |
| Left main + 1 other | 32.2% | 15.4% | <0.001 |
| Left main + 2 others | 35.5% | 27.5% | 0.06 |
| Left main + 3 others | 24.6% | 50.5% | <0.001 |
| Right | 45.9% | 69.4% | <0.001 |
| SYNTAX score | 26 ± 10.8 | 33.6 ± 13 | <0.001 |
| Complete revascularization† | 42.6% | 74.7% | <0.001 |

EuroSCORE = European System for Cardiac Operative Risk Evaluation score.
* Defined as serum cholesterol >200 mg/dl.
† Defined as successful treatment of all vessels ≥1.5 mm in diameter with stenosis ≥50% as identified by the interventional cardiologist and cardiac surgeon after coronary angiography and estimated after the procedure by the investigators.

formed according to current practice guidelines. Use of dilatation before the procedure, intra-aortic balloon pump, or intravascular ultrasound and choice of drug-eluting stent was at the operator's discretion. Lesions at the ostium or shaft without involvement of bifurcation were usually treated with single stents. Bifurcation lesions were treated using different stenting strategies at the operator's discretion including provisional stenting or crush technique in the vast majority of cases. Final kissing balloon dilatation was performed in most patients and was mandatory in cases with suboptimal results at the branch ostium. Antiplatelet therapy and periprocedural anticoagulation followed standard regimens.[1,2] After the procedure, patients treated with drug-eluting stents were prescribed clopidogrel for ≥6 months. Aspirin was prescribed for the life span.

Surgical revascularization was performed using standard bypass techniques. Whenever possible, the internal thoracic artery was used preferentially for revascularization of the left anterior descending coronary artery. Patients could be operated with or without extracorporeal circulation; in on-pump surgeries, type of cardioplegia was left to surgical judgment. The postprocedure medication regimen was chosen according to local clinical practice. For all patients, aspirin was continued indefinitely.

The primary objective was the incidence of major adverse cardiac events (MACEs) at 1-year follow-up. MACEs were defined as the composite of death, myocardial infarction, or target lesion revascularization (TLR). Secondary objectives were the subcomponent end points of the primary objective (death, myocardial infarction, TLR). Death was defined as postprocedure death from any cause. Myocardial infarction was defined as any typical increase and decrease of biochemical markers of myocardial necrosis with ≥1 of the following: cardiac symptoms, development of Q waves on electrocardiogram, or electrocardiographic changes indicative of ischemia. TLR was defined as any repeat revascularization in the target segment. All outcomes of interest were confirmed by source documentation collected at each center and were centrally adjudicated by an independent blinded endpoints committee.

Clinical follow-up data on medical therapy and clinical status were prospectively collected through scheduled outpatient clinic evaluations. Referring cardiologists, general practitioners, and patients were contacted if necessary for

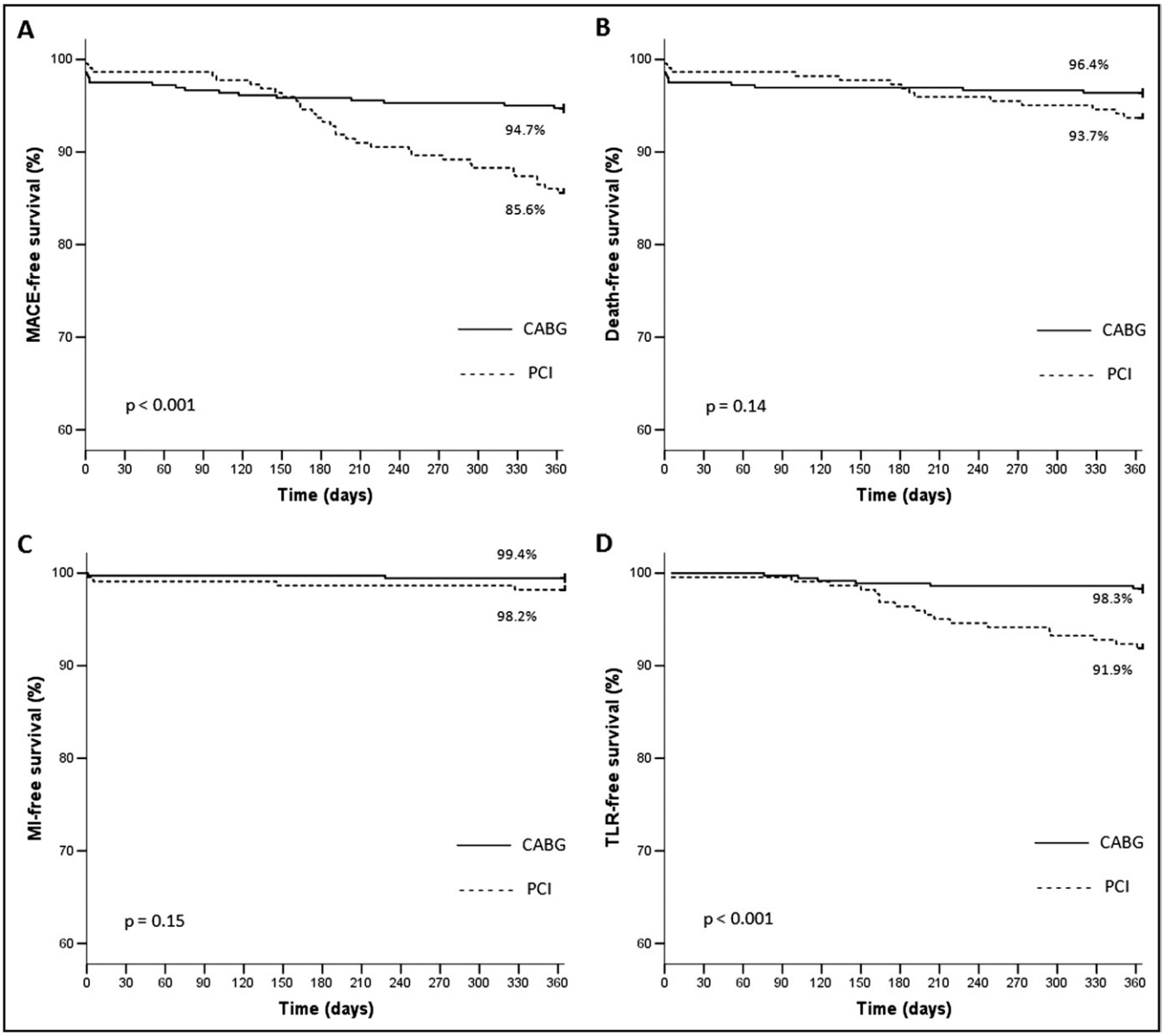


Figure 1. One-year Kaplan–Meier survival free from major adverse cardiac events *(A)*, death *(B)*, myocardial infarction (MI) *(C)*, and target lesion revascularization *(D)*.

Table 2
Unadjusted and adjusted risks of one-year adverse outcomes

| | | | Unadjusted | | Adjusted | |
|---|---|---|---|---|---|---|
| | PCI | CABG | HR (95% CI) | p Value | HR (95% CI) | p Value |
| Major adverse cardiac events | 14.4% | 5.3% | 2.8 (1.6–4.9) | <0.001 | 2.7 (1.2–5.9) | 0.01 |
| Death | 6.3% | 3.6% | 1.7 (0.8–3.7) | 0.15 | 1.1 (0.4–3.0) | 0.81 |
| Cardiac death | 3.6% | 3.0% | 1.2 (0.5–2.9) | 0.72 | 0.4 (0.2–2.0) | 0.38 |
| Myocardial infarction | 1.8% | 0.6% | 3.3 (0.6–17.8) | 0.17 | 4.8 (0.3–68.6) | 0.25 |
| Target lesion revascularization | 8.1% | 1.7% | 5.0 (2.0–12.6) | 0.001 | 8.0 (2.2–28.7) | 0.001 |

Crude event rates are presented as Kaplan–Meier estimates.

additional information. All revascularization (surgical or percutaneous) and rehospitalization data were prospectively gathered during follow-up through the centralized system of the participating institutions or direct contact with hospitals where patients were admitted or referred. Angiographic follow-up was recommended at 6 and 9 months after the index procedure in all patients who consented and had undergone PCI. Angiography was carried out beforehand if clinically indicated. Nevertheless, patients with high angiographic procedural risk and patients without signs or symptoms of ischemia or those who

declined the recommendation did not undergo routine follow-up angiography. For patients who underwent CABG, angiographic follow-up was suggested only for ischemic symptoms or signs during follow-up.

Continuous variables are presented as mean ± SD or median and interquartile range and were compared using Student's unpaired *t* test or Mann–Whitney rank-sum test based on tests for normal distribution. Categorical variables are presented as counts and percentages and were compared using the chi-square test when appropriate (expected frequency >5). Otherwise, the Fisher's exact test was used. Kaplan–Meier estimates were used to plot rates of clinical objectives in patients who underwent PCI and CABG and differences between groups were analyzed with the log-rank test.

To decrease the effect of selection bias and potential confounding in this observational study, outcome parameters were adjusted with a Cox multivariable proportional hazard regression model for observed differences for variables with a p value <0.20 in the univariate analysis, which were chronic renal failure, previous PCI, chronic obstructive pulmonary disease, left ventricular ejection fraction, European System for Cardiac Operative Risk Evaluation score (EuroSCORE), ST-segment elevation myocardial infarction, Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) score, distal left main coronary artery disease, left main coronary artery stenosis plus 1-vessel disease, left main coronary artery stenosis plus 3-vessel disease, right coronary artery disease, and complete revascularization. Assumption of proportional hazard was verified by a visual examination of the log-minus-log curves and linearity assumption was assessed by plotting Martingale residuals against continuous covariates.

Results are presented as hazard ratios (HRs) and associated exact 95% confidence intervals (CIs). First-order interaction between clinical presentation (unstable angina/non–ST-segment elevation myocardial infarction vs ST-segment elevation myocardial infarction) and treatment (PCI or CABG) were formally tested using Cox proportional hazard models, entering interaction terms and adjusting for potential confounders. Statistical analyses were performed using SPSS 17.0 (SPSS, Inc., Chicago, Illinois).

## Results

A total of 583 patients fulfilled the entry criteria and entered the present analysis. Of them, PCI with drug-eluting stents was performed in 222 patients (38.1%) and CABG in 361 patients (61.9%). Diagnosis of ST-segment elevation myocardial infarction was more frequent in patients treated with PCI compared to those treated with CABG (8.6% vs 0.8%, p <0.001).

In the unadjusted analysis, differences were noted for worse clinical risk profile in patients treated with PCI including more cases of chronic renal failure, chronic obstructive pulmonary disease and previous PCI, lower left ventricular ejection fraction, and higher EuroSCORE (Table 1). In contrast, patients who underwent CABG had a higher angiographic risk profile, being more likely to present with multivessel and left main bifurcation coronary artery disease, resulting in a higher SYNTAX score (Table 1). A larger proportion of patients in the CABG group achieved the goal of complete revascularization (74.7% vs 42.6%, p <0.001). Follow-up angiography was performed in 64.4% of patients who underwent PCI and 8.6% of patients who underwent CABG (p <0.001).

At 30 days, there were no significant differences in MACEs between PCI and CABG (1.4% vs 2.5%). Conversely, at 1-year follow up, the incidence of MACEs was significantly higher in patients treated with PCI (14.4% vs 5.3%). This difference was mainly driven by a higher rate of TLR (8.1% vs 1.7%), whereas rates of death and myocardial infarction were comparable (Figure 1, Table 2). Follow-up angiography was significantly associated with higher likelihoods of MACEs (p <0.001) and TLR (p <0.001) at 1-year follow-up.

After statistical adjustment for potential baseline and procedural confounders, PCI remained associated with a higher risk of MACEs (adjusted HR 2.7, 95% CI 1.2 to 5.9, p = 0.01) and TLR (adjusted HR 8.0, 95% CI 2.2 to 28.7, p = 0.001), whereas no statistically significant differences were noted for death and myocardial infarction (Table 2). No meaningful interaction between clinical presentation (unstable angina/non–ST-segment elevation myocardial infarction or ST-segment elevation myocardial infarction) and type of treatment (CABG or PCI) was observed in MACEs (p for interaction = 0.68).

## Discussion

We reported on midterm outcomes of PCI versus CABG in patients with left main coronary artery disease who underwent myocardial revascularization in the setting of ACS. At 1-year follow-up, PCI with drug-eluting stents was found to be similar to CABG in death and myocardial infarction but was associated with more frequent repeat revascularizations, leading to a significantly higher rate of MACEs. In addition, this analysis does not support the concept of a significant association between clinical presentation and treatment strategies in patients with left main coronary artery disease and ACS.

Left main coronary artery disease in the setting of ACS has been described in about 4% of patients, but this figure could be underestimated considering the large number of patients with ACS who died early or not undergone cardiac catheterization.[4] ACS has been shown to be independently associated with a ~2.4 increased risk of 2-year mortality and myocardial infarction in patients treated with drug-eluting stents.[5] It is well known that clinical outcomes are improved by any revascularization compared to medical treatment alone, and among revascularization strategies PCI is performed more liberally than CABG in higher-risk settings such as acute myocardial infarction, thus biasing any attempt to fairly compare surgical to percutaneous therapies.[4] However, observational data have a role when randomized data are lacking. During the previous 10 years PCI has become the most common revascularization treatment in patients with left main coronary artery disease and ACS, offering prompt reperfusion and lower risk of stroke and promising clinical outcomes improved by drug-eluting stents and dual antiplatelet therapy use.[6]

Montalescot et al[4] reported outcomes of 1,799 patients with significant left main coronary artery disease enrolled in the Global Registry of Acute Coronary Events (GRACE) who underwent PCI or CABG or no initial revascularization. From discharge to 6 months, PCI (HR 0.45, 95% CI 0.23 to 0.85) and CABG (HR 0.11, 95% CI 0.04 to 0.28) were significantly associated with improved survival compared to no initial revascularization strategy.[4] However, no adjusted data were reported on the comparative effectiveness of PCI versus CABG. Additional limitations included the small prevalence of drug-eluting stent use (30%), which limited the generalizability of the study findings in the contemporary era, and availability of only 6-month follow-up.[4]

Our analysis, focusing on a longer follow-up period, showed that the separation of survival curves for MACEs starts at about 6 months, most likely because of a higher rate of follow-up angiography and TLR in the PCI group. A longer follow-up period was reported by Buszman et al[7] in a small study involving 138 patients with severe left main coronary artery disease and ACS, but patients with ST-segment elevation myocardial infarction were excluded. The need for re-evaluating the difference between PCI and CABG after including patients with ST-segment elevation myocardial infarction is emphasized by the notion that ST-segment elevation myocardial infarction per se carries a significantly higher risk of patient- and device-oriented adverse cardiac outcomes compared to other clinical presentations including non–ST-segment elevation myocardial infarction, unstable angina, and stable angina.[8] Importantly, in the present study, we did not find any meaningful interaction between clinical presentation (unstable/non–ST-segment elevation myocardial infarction) and revascularization approach.

Our findings highlight that even in a complex and peculiar setting as left main coronary artery revascularization in ACS PCI is characterized by a higher rate of MACEs, mainly driven by an increased risk of TLR. These data are consistent with 2 small randomized trials, a post hoc analysis from the SYNTAX trial and a recent meta-analysis.[9–12]

The most important limitation of the present study is the lack of random assignment to treatment groups. Evaluating the impact of a specific treatment using a registry can lead to incorrect conclusions because of the influence of unassessed confounding variables. In this study, each treatment was not assigned randomly but by specific criteria in each case, generating an unavoidable risk of bias regarding treatment selection and possible prognosis. To partly compensate for the baseline and angiographic imbalance between groups, we performed adjustments with multivariate analysis. However, it is impossible to know if these adjustments were appropriate or if the relevant characteristics were correctly identified because only randomization can provide an unbiased estimation of effects of a treatment. In addition, the presumptive benefit of CABG is likely to increase over time. Therefore, longer follow-up would add meaningfully to the present report.


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