European Heart Journal (2005) **26**, 128–136
doi:10.1093/eurheartj/ehi061

Clinical research

Outcomes of patients with acute coronary syndromes and prior percutaneous coronary intervention: a pooled analysis of three randomized clinical trials

Marino Labinaz[1]*, Jasmine Mathias[2], Karen Pieper[2], Christopher B. Granger[2], A. Michael Lincoff[3], David J. Moliterno[3], Frans Van de Werf[4], John Simes[5], Harvey D. White[6], Maarten L. Simoons[7], Robert M. Califf[2], Eric J. Topol[3], Paul W. Armstrong[8], and Robert A. Harrington[2]

[1] *University of Ottawa Heart Institute, Division of Cardiology, 40 Ruskin Ave, Rm H-150 Ottawa, Ontario, K1Y 4W7 Canada*
[2] *Duke Clinical Research Institute, Duke University Medical Center, Durham, NC, USA*
[3] *Cleveland Clinic, Cleveland, OH, USA*
[4] *University of Leuven, Leuven, Belgium*
[5] *University of Sydney, New South Wales, Australia*
[6] *Green Lane Hospital, Auckland, New Zealand*
[7] *University Hospital, Rotterdam, The Netherlands*
[8] *University of Alberta, Edmonton, Alberta, Canada*

Received 20 October 2004; revised 8 October 2004; accepted 28 October 2004; online publish-ahead-of-print 9 December 2004

KEYWORDS
Percutaneous coronary intervention;
Acute coronary syndrome;
Myocardial infarction

Aims We sought to characterize the outcomes of patients with a prior percutaneous coronary intervention (PCI) who presented with a non-ST-segment elevation acute coronary syndrome (ACS).

Methods and results We analysed the 30 and 180 day outcomes of 3012 patients with prior PCI and 21 154 patients without prior PCI enrolled in three randomized ACS trials (GUSTO IIb, PURSUIT, and PARAGON-B). The median (25th, 75th percentile) interval between the prior PCI and randomization was 647 (123, 1585) days. Patients with prior PCI had significantly more adverse baseline clinical characteristics, left ventricular dysfunction, and multi-vessel coronary artery disease. After adjusting for baseline characteristics and treatment, we found that patients with prior PCI had a significantly lower mortality rate at 30 days [hazard ratio (HR), 0.60; 95% confidence interval (CI), 0.45–0.80; $P = 0.0006$] and 180 days (HR, 0.81; 95% CI, 0.66–0.98; $P = 0.029$). However, no difference was observed in the composite of death or myocardial infarction (MI) at 30 days (HR, 0.95; 95% CI, 0.83–1.08; $P = 0.42$) or 180 days (HR, 1.01; 95% CI, 0.90–1.13; $P = 0.90$). Patients with prior PCI had a higher rate of MI at 180 days (13.3 vs. 12.0%; $P = 0.045$). Prior-PCI patients had lower incidences of in-hospital cardiogenic shock, congestive heart failure (CHF), and atrial fibrillation.

Conclusion Patients with prior PCI who present with non-ST-segment elevation ACS have a lower mortality rate than those without prior PCI.

* Corresponding author. Tel: +1 613 761 5427; fax: +1 613 761 4690.
E-mail address: mlabinaz@ottawaheart.ca

Introduction

Since its inception in 1977, percutaneous coronary intervention (PCI) has become the most common method of coronary revascularization. Randomized trials have demonstrated that patients presenting with an acute coronary syndrome (ACS) and who subsequently undergo routine angiography and revascularization, predominantly by PCI, have improved outcomes compared with patients not treated with a routine invasive strategy.[1–3] Several studies have also examined the impact of a prior revascularization procedure on the outcome of patients with a subsequent ACS. Numerous studies have shown that patients with a history of a prior coronary artery bypass grafting (CABG) who present with either an ST-segment elevation or non-ST-segment elevation ACS have significantly worse outcomes compared with patients without this history.[4–7] However, other studies have suggested that patients with a prior PCI who subsequently have an acute ST-segment elevation myocardial infarction (MI) have improved outcomes.[8] Despite the increasing number of patients with a previous PCI, their outcomes after presenting with a new non-ST-segment elevation myocardial ACS have not been described in detail. To assess the effect of a prior PCI on the outcome of patients presenting with ACS, we performed a pooled analysis of three randomized non-ST-segment elevation ACS trials and compared the outcome of prior-PCI patients with patients without prior PCI.

Methods

Patient population

Individual data were collected from patients with non-ST-segment elevation enrolled in three ACS trials: Global Use of Strategies to Open occluded arteries in acute coronary syndromes (GUSTO IIb), Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin Therapy (PURSUIT), and Platelet IIb/IIIa Antagonist for the Reduction of Acute coronary events in a Global Organization Network (PARAGON)-B.[9–11] Data were pooled, and outcomes at 30 and 180 days were assessed. The details of each study's protocol have been previously published. In brief, in GUSTO IIb, 8011 patients with non-ST-segment elevation were randomly assigned to treatment with either hirudin or heparin. The primary endpoint was the composite of death or MI during the first 30 days following randomization. The endpoints of death and MI were also recorded at 180 days. MI was considered to have occurred at the time of enrolment if the creatinine kinase (CK)-MB concentration was elevated to above normal at baseline or 8 h after enrolment. If the CK-MB concentration was elevated at the 16 h sample, and no symptoms occurred between enrolment and the 16 h sample, this was considered an MI at enrolment. If the CK-MB concentration was elevated only at the 16 h sample, and symptoms of MI occurred after enrolment, the events committee coded the event according to information collected on the electrocardiogram (ECG), symptoms, and enzyme elevation. If the CK-MB concentration was not available, CK had to be >2 times above the upper limit of normal (ULN). An MI was also to be classified in the event of new significant Q-waves in at least two contiguous leads. For patients who had an MI before enrolment, a new MI was defined as a rise in the CK-MB concentration to above normal limits or at least two times above a prior value if above the ULN, with appropriate signs, symptoms, and ECG changes.[9]

The double-blind, placebo-controlled PURSUIT trial enrolled 10 948 patients with non-ST-segment elevation ACS. Patients were randomly assigned to receive placebo or a bolus and infusion of eptifibatide. The primary endpoint of the trial was the composite of death or MI in the first 30 days of follow-up. Data on death and MI were also collected at 180 days. A masked clinical events committee evaluated suspected infarcts. MI within 18 h after enrolment was diagnosed on the basis of ischaemic chest pain and new ST-segment elevation in at least two contiguous leads and lasting for 30 min. After 18 h, MI was considered to have occurred if there was a new or repeated elevation of the CK-MB concentration above the ULN or if there were new Q-waves in two ECG leads.[10]

In PARAGON-B, 5225 patients with non-ST-segment elevation ACS were randomly assigned to placebo or lamifiban adjusted for renal function. The primary endpoint was the composite of death, MI, or severe, recurrent ischaemia at 30 days. Follow-up data for death and MI were collected at 180 days. MI was considered to have occurred when the CK-MB concentration was elevated to ≥ 2 times the ULN or there were new significant Q waves in two contiguous ECG leads in patients without an MI at baseline. In patients with MI at baseline, a post-enrolment MI was defined by a re-elevation of the CK-MB concentration to ≥ 2 times the ULN if the prior CK-MB concentration was in the normal range and $>50\%$ above the prior level if the prior CK-MB concentration was above normal or if new significant Q-waves were present in two contiguous leads, discrete from an enrolment MI.[11] In all three trials, the clinical events committee independently and blindly adjudicated all suspected MIs.

Our analysis included all patients who had a previous PCI, as determined from the information that site investigators collected at the time of admission. Coronary angiography, PCI, and CABG were performed at the discretion of the treating physician and not subjected to randomization. The treating physician also performed the angiographic assessment at the site with visual analysis; coronary lesions $>50\%$ stenosis were considered significant. Data specifying which vessel was treated with the prior PCI were not collected. The time interval between prior PCI and randomization was not collected in the PARAGON-B trial.

Statistical analysis

Continuous baseline characteristics were reported as medians with 25th and 75th percentiles. Categorical variables were reported as frequencies and percentages. Differences in categorical baseline characteristics, including medication use, angiographic results, and complications and procedures in patients with and without a prior PCI, were compared using Pearson's χ^2 test. Differences for continuous variables were compared using the Wilcoxon rank-sum test.

Baseline characteristics were compared across the three trials and were found to be similar, as were the patient entry criteria. The Breslow–Day statistic was used to test differences across the three studies in associations between previous PCI and the outcomes of 30 day death and the composite of death or MI. Because the associations were homogeneous across the trials ($P = 0.85$ and 0.49, respectively), the trials were combined and all analyses were performed across the entire database.

To characterize the time course of events, the cumulative event rate was estimated using the Kaplan–Meier method, with the time to death and the time to the first event of death or MI used as the outcome variables. Previously published Cox

proportional hazards models were used to adjust for imbalances in baseline characteristics for 30 day death, 30 day death or MI, 180 day death, and 180 day death or MI.[12] The following variables were entered in the model of death: sex; age; weight; height; region of enrolment; history of hypertension; diabetes mellitus; smoking status; hypercholesterolaemia; prior MI; recent chest pain; congestive heart failure (CHF); prior CABG; enrolling trial; prior medications including aspirin, beta-blockers, calcium antagonists, nitrates, and angiotensin-converting enzyme (ACE) inhibitors; presenting characteristics including enzymatic MI at enrolment; systolic blood pressure; heart rate; Killip class; symptom onset to treatment; presence of ST-segment depression, and the interactions of age and pulse with enzymatic MI. The following variables were entered in the model of death or MI: sex; age; weight; height; region of enrolment; history of hypertension; diabetes mellitus; smoking status; prior MI; recent chest pain; CHF; prior stroke; peripheral vascular disease; prior CABG; enrolling trial; prior medications including aspirin, beta-blockers, calcium antagonists, nitrates, and ACE inhibitors; presenting characteristics including enzymatic MI at enrolment; systolic blood pressure; diastolic blood pressure; heart rate; Killip class; symptom onset to treatment; ST-segment depression, and the interactions of age, Killip class, and pulse with enzymatic MI. Only patients with complete data were included in the multivariable models. A test of proportional hazards was used on each covariate in the model. This test was generated by running a model which contained the factor of interest (X1) plus a time-dependent covariate factor which was programmed to be the log of time to the event *X1. In addition, Kaplan–Meier curves were generated for each to visualize this same issue. For continuous measurements, the factor was divided into quartiles or tertiles for plotting purposes. Had a factor deviated significantly from this assumption, it would have been included in the model as a stratum. For all analyses, a two-tailed P value of <0.05 was considered statistically significant. However, no adjustments have been made for the multiple comparisons, so the results should be interpreted as hypothesis generating. All analyses were performed using SAS statistical software (SAS Institute, Cary, NC, USA).

Results

Baseline characteristics

The study population consisted of 24 166 patients with non-ST-segment elevation ACS, of which 3012 (12.5%) had prior PCI and 21 154 (87.5%) had no prior PCI. Information on 30 day death was available in 99.9% of patients, and for death or MI in 99.7%. Information on 180 day death was available in 98.6% of patients, and for death or MI in 98.1%. The median (25th, 75th percentile) interval between the prior PCI and randomization was 647 (123, 1585) days. Although younger, patients with prior PCI had more adverse baseline clinical characteristics including diabetes mellitus, prior MI, prior stroke, hypercholesterolaemia, peripheral vascular disease, prior CABG, and CHF, and they were heavier (*Table 1*). There were fewer current smokers in the prior PCI group. Despite having lower blood pressure at the time of enrolment, patients with prior PCI more often had a history of hypertension. A higher proportion of patients with prior PCI were receiving aspirin, beta-blockers, calcium-channel blockers, ACE-inhibitors, and lipid-lowering agents compared with patients without a prior PCI (*Table 2*).

Patients with prior PCI underwent more coronary angiography during the index hospitalization (75 vs. 57%; $P < 0.001$). A higher percentage of this patient group had multi-vessel coronary disease and impaired left ventricular function (*Table 3*). There were no differences with respect to the maximum stenosis or thrombolysis in myocardial infarction (TIMI) flow grade between the two groups.

Clinical endpoints

The unadjusted 30 day mortality rate in patients with prior PCI was 2.0% compared with 3.8% for those without prior PCI, and the rates of composite death or MI at 30 days were 11.4 and 12.0%, respectively. The rate of MI at 30 days was 10.8% in patients with prior PCI and 9.2% for those without prior PCI. Prior-PCI patients also had a lower mortality rate at 180 days (4.7 vs. 6.3%), but no difference in death or MI at 180 days (14.5 vs. 14.6%). There was no difference in mortality from day 30 to day 180 for patients with or without a prior PCI (2.69 vs. 2.65%; $P = 0.89$). However, patients with a prior PCI had a higher MI rate at 180 days compared with patients without a prior PCI (13.3 vs. 12.0%). The Kaplan–Meier probability of 180 day survival was higher in prior-PCI patients ($P = 0.0003$) (*Figure 1A*), but there was no difference in the probability of survival without re-infarction at 180 days ($P = 0.82$) (*Figure 1B*). The Kaplan–Meier probability of freedom from MI at 180 days was higher in the prior-PCI patients ($P = 0.045$) (*Figure 1C*).

After adjusting for differences in baseline characteristics and treatment, we found that prior-PCI patients had a lower mortality rate at 30 days (HR, 0.60; 95% CI, 0.45–0.80; $P = 0.0006$) and 180 days (HR, 0.81; 95% CI, 0.66–0.98; $P = 0.029$) (*Table 4*). After adjusting for treatment and baseline characteristics, no difference was observed with respect to death or MI at 30 days (HR, 0.95; 95% CI, 0.83–1.08; $P = 0.42$) or 180 days (HR, 1.01; 95% CI, 0.90–1.13; $P = 0.90$).

Patients with a prior PCI underwent more repeat PCIs during the index hospitalization and through the 180 day follow-up period compared with patients with no prior PCI (*Table 5*). Stenting was performed with equal frequency in both groups (47 vs. 47%). Although CABG was performed more often in the prior-PCI group during the in-hospital period, no difference was seen between the two groups in the total number of CABG operations performed during the 180 days following randomization. The incidence of in-hospital complications was lower in patients with prior PCI (*Table 5*). Specifically, there was less cardiogenic shock, CHF, and atrial fibrillation in patients with a prior PCI. Interestingly, there was more acute mitral regurgitation in patients with a prior PCI.

Discussion

Our study is the largest to date to analyse the outcome of patients with prior PCI who subsequently presented with

Table 1 Baseline characteristics

	No prior PCI ($n = 21\,154$)	Prior PCI ($n = 3012$)	*P*
Age, years	65 (55, 72)	63 (54, 71)	<0.001
Female	7421 (35)	883 (29)	<0.001
Race			
White	19 119 (91)	2691 (89)	<0.001
Non-white	2014 (9)	320 (11)	
Region			
Western Europe	9262 (44)	944 (31)	<0.001
North America	7458 (35)	1844 (61)	
Australia	1316 (6)	88 (3)	
South America	734 (4)	59 (2)	
Eastern Europe	2285 (11)	63 (2)	
Blood pressure, mmHg			
Systolic	135 (120, 150)	131 (119, 150)	<0.001
Diastolic	80 (70, 90)	75 (66, 84)	<0.001
Heart rate, beats/min	74 (64, 84)	70 (61, 82)	<0.001
Height, cm	170 (163, 175)	170 (164, 178)	<0.001
Diabetes mellitus	4315 (20)	826 (27)	<0.001
Prior MI	5783 (27)	1878 (62)	<0.001
Current smoker	6082 (29)	690 (23)	<0.001
MI at enrolment	10 329 (49)	1099 (37)	<0.001
Prior stroke	889 (4)	154 (5)	0.02
Hypercholesterolaemia	8632 (41)	1772 (59)	<0.001
Hypertension	10 952 (52)	1860 (62)	<0.001
Peripheral vascular disease	1694 (8)	319 (11)	<0.001
Family history of CAD	7701 (37)	1451 (49)	<0.001
History of angina	13 323 (63)	2310 (77)	<0.001
Time from symptom onset to randomization, hours	7.8 (4.3, 13.4)	7.8 (4.2, 13.5)	0.55
ST-segment depression	9990 (52)	1230 (44)	0.001
T-wave inversion	9057 (47)	1366 (49)	0.09
Transient ST-segment elevation	2781 (14)	395 (14)	0.63
Killip Class III or IV	329 (2)	40 (1)	0.64
Weight, kg	77 (68, 87)	80 (70, 91)	<0.001
Prior CABG	2043 (10)	882 (29)	<0.001
History of CHF	1956 (9)	385 (13)	<0.001

Data are presented as the median (25th, 75th percentile) or number (%) of subjects.

Table 2 Baseline medications

Medications	No prior PCI (%) ($n = 21\,154$)	Prior PCI (%) ($n = 3012$)	*P*
Aspirin	10 746 (51)	1918 (64)	<0.001
Beta-blockers	6257 (30)	1237 (41)	<0.001
Calcium channel blockers	5152 (24)	1150 (38)	<0.001
ACE-inhibitors	3347 (16)	580 (19)	<0.001
Nitrates	13 095 (62)	2101 (70)	<0.001
Lipid-lowering	1885 (9)	753 (25)	<0.001
Anti-arrhythmic agents	648 (3)	96 (3)	0.71

non-ST-segment elevation ACS. In our analysis, patients with prior PCI had significantly more adverse clinical and angiographic baseline characteristics than did patients without prior PCI. However, after adjusting for differences in baseline characteristics using Cox proportional hazard models, the mortality rate for prior-PCI patients was significantly lower at 30 and 180 days following presentation. In addition, patients with prior PCI had significantly fewer in-hospital adverse outcomes.

Other studies

The association between a prior PCI and outcome following a non-ST-segment elevation ACS has not been previously examined in detail. Results from a *post hoc*

Table 3 Baseline angiographic data

	No prior PCI ($n = 12043$)	Prior PCI ($n = 2255$)	P
Number of diseased vessels			<0.001
1	3312 (29)	633 (30)	
2	2904 (26)	620 (30)	
3	3475 (31)	674 (32)	
No significant CAD	1597 (14)	155 (7)	
Unknown	755	173	
EF <50%	2010 (27)	505 (37)	<0.001
Unknown	4666	922	
Culprit vessel			<0.001
LAD	3875 (33)	620 (28)	
LCX	1885 (16)	449 (20)	
RCA	2289 (19)	470 (21)	
Left main	309 (3)	31 (1)	
Bypass graft	421 (4)	202 (9)	
Unknown	1889 (16)	327 (15)	
None	1230 (10)	131 (6)	
Culprit vessels, % stenosis	90 (80, 99)	90 (80, 99)	0.603
Unknown	3773	699	
Culprit vessel, TIMI flow			0.396
0	1175 (16)	199 (14)	
1	1233 (16)	241 (17)	
2	1446 (19)	268 (19)	
3	3689 (49)	704 (50)	
Unknown	4500	843	

Data are presented as the number (%) of subjects or median (25th, 75th percentile).
LAD, left anterior descending; LCX, circumflex artery; RCA, right coronary artery.

analysis of data from the Long-term Intervention with Pravastatin in Ischemic Disease (LIPID) study showed that patients who underwent a coronary revascularization procedure (PCI or CABG) prior to presenting with ACS had a 24% relative increase in the composite of death or non-fatal MI.[13] Another study reported that patients with prior PCI who presented with an acute ST-segment elevation MI had significantly fewer in-hospital complications and lower 30 day mortality compared with patients without prior PCI,[8] which is similar to the findings in this study. The specific effect of prior CABG on outcomes in patients with ACS has also been examined.[4–7] Some studies have suggested that prior CABG does not have an independent effect on outcomes after ACS, while one study did suggest that a prior CABG has a significant independent detrimental impact on survival following an ACS. It is likely that the worse outcomes seen with prior-CABG patients are due to the more extensive coronary disease and left ventricular dysfunction present in these patients compared with prior-PCI patients. Recent studies have not demonstrated any difference in short-term mortality in patients with multi-vessel coronary artery disease (CAD) treated with PCI or CABG.[14–16]

Effect of prior PCI on outcomes in patients with ACS

Our study suggests that a prior PCI may have an important independent effect on mortality following ACS. Compared with patients without prior PCI, patients with prior PCI also had significantly more multi-vessel coronary disease and worse left ventricular function and were taking significantly more cardiac medications. These findings suggest that the underlying disease in prior-PCI patients is more extensive; therefore, the lower mortality seen in this group is particularly surprising because numerous studies have reported an inverse correlation between death and both ejection fraction and the extent of CAD.[17–20]

Factors other than extent of disease may impact prognosis. Collateral circulation may be enhanced in patients with prior PCI due to ischaemia produced by the initial lesion. This 'pre-conditioning' may allow for collaterals to be recruited with a subsequent ACS, and this may help sustain the viability of the threatened myocardium and allow the patient to tolerate the acute ischaemic event better.[21] Patients with a prior PCI and recurrent ischaemic symptoms may be more likely to seek medical attention. These patients may also receive more prompt medical attention and closer surveillance due to their coronary history. Finally, although speculative, the biology of ACS in patients with a prior PCI may be different. For example, the prior PCI may have been performed in a proximal coronary segment causing fibrotic changes in the lesion with subsequent arterial passivation. Therefore, future ACS may be due to plaque rupture in more distal arterial segments and may involve fewer areas of the coronary arteries.

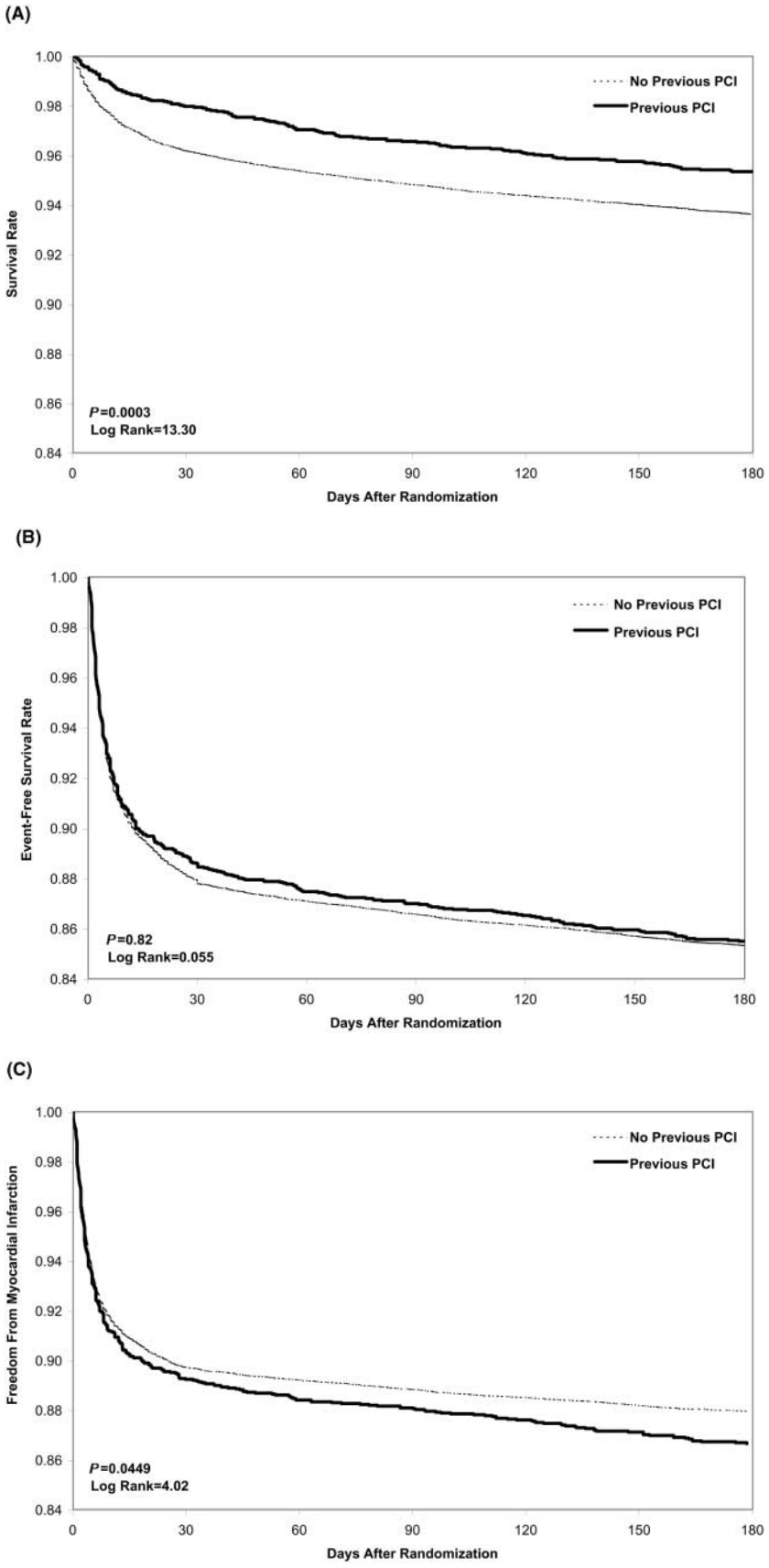

Figure 1 Kaplan–Meier estimates of survival (*A*), survival without infarction (*B*), and freedom from infarction (*C*) for patients with and without prior PCI up to 180 days following randomization.

Table 4 Unadjusted and adjusted hazard ratios in patients with prior PCI versus no prior PCI

	Unadjusted hazard ratio (95% CI)	*P*	Adjusted hazard ratio (95% CI)	*P*
Death (30 days)	0.53 (0.40–0.69)	<0.0001	0.60 (0.45–0.80)	0.0006
Death (180 days)	0.72 (0.61–0.86)	0.0003	0.81 (0.66–0.98)	0.029
Death/MI (30 days)	0.95 (0.85–1.06)	0.37	0.95 (0.83–1.08)	0.42
Death/MI (180 days)	0.99 (0.89–1.09)	0.82	1.01 (0.90–1.13)	0.90

Table 5 Complications and procedures

	No prior PCI (%) ($n = 21\,154$)	Prior PCI (%) ($n = 3012$)	*P*
Cardiac catheterization	12 030 (57)	2252 (75)	<0.001
PCI, post-enrolment			
In-hospital	4433 (21)	1111 (37)	<0.001
<180 days	5356 (25)	1266 (42)	<0.001
CABG			
In-hospital	2859 (14)	459 (15)	0.01
<180 days	4297 (20)	650 (22)	0.10
Cardiogenic shock	523 (3)	48 (2)	0.003
CHF[a]	823 (5)	71 (3)	0.0002
Stroke, in-hospital	129 (0.6)	11 (0.4)	0.10
Sustained VT	238 (1)	45 (2)	0.08
Ventricular fibrillation	292 (1)	43 (1)	0.83
Atrioventricular block[a]	256 (1)	30 (1)	0.46
Atrial fibrillation[a]	1141 (7)	119 (5)	0.006
Acute MR	2664 (14)	552 (20)	<0.001

VT, ventricular tachycardia; MR, mitral regurgitation; VSD, ventricular septal defect.
[a]These complications were not collected in PARAGON-B.

Several studies have highlighted the impact of prior medications on survival in patients presenting with ACS. The previous use of aspirin, beta-blockers, and lipid-lowering agents has been shown to significantly improve early outcomes in patients with ACS.[22–24] In our study, the proportion of patients receiving these medications was significantly higher in the prior-PCI group, but even after adjusting for these important differences in prior medication use, patients with prior PCI had a lower mortality rate than patients without prior PCI. Patients with prior PCI, who have documented CAD, were medically undertreated; for these patients, the use of aspirin, beta-blockers, ACE-inhibitors, and lipid-lowering agents was relatively low.

Repeat revascularization procedures

The rate of in-hospital cardiac catheterization was significantly higher in prior-PCI patients compared with other patients. Paralleling the increased catheterization rate was a significantly greater rate of repeat PCI, but there was no difference with respect to the overall incidence of CABG. This difference in catheterization and PCI may contribute to the difference in outcomes. Several studies have now demonstrated significantly better outcomes with a routine invasive strategy followed by revascularization for ACS.[1–3] For example, based on long-term follow-up data from the FRagmin and fast revascularization during InStability in Coronary artery disease (FRISC II) study, ACS patients treated with a routine invasive strategy have a significantly lower mortality rate than those treated with a conservative, non-invasive strategy. Because the decision to perform cardiac catheterization was at the discretion of the treating physician, it is difficult to ascertain the rationale for the higher rates of invasive procedures. Many ACS patients with a prior PCI were likely treated in a tertiary care hospital with onsite interventional facilities, likely the same hospital where the initial PCI was performed, and this may have led to the increased rate of cardiac catheterization. Other plausible explanations include the presence of more adverse baseline clinical characteristics in patients with prior PCI, inherent physician or patient bias, or a biological difference in coronary disease in patients with prior PCI. For example, the culprit lesions in these patients may be more focal and therefore more amenable to PCI.

Patients with a prior PCI experienced a greater incidence of MI. The higher rate of revascularization procedures could explain the difference. Also, the majority of procedures were performed without glycoprotein IIb/IIIa blockade, which reduces periprocedural MIs. The overall occurrence of death and MI appears to be similar between patients with or without prior PCI.

Therefore, patients experiencing ACS with a prior PCI may simply shift from dying from the ischaemic event to having an MI because of the higher number of revascularization procedures and cardioprotective medications they receive.

Limitations

The current study was a *post hoc* analysis of prospectively collected data. The patients in these three clinical trials may be different from patients encountered in other clinical trials of ACS and in everyday clinical practice. Despite using previously validated statistical models, unmeasured confounders may be responsible for some of the differences in outcome between patients with and without prior PCI. The decision to perform coronary angiography and revascularization procedures was at the discretion of treating physicians and not subject to randomization. Therefore, we are unable to make meaningful conclusions regarding the role of repeat revascularization among prior-PCI patients. Although some angiographic data were available, other important data such as the site of the prior PCI, indication for the prior PCI, and whether the culprit vessel had been previously treated with PCI were unknown. Although some of the patients with ACS in the prior-PCI group may have had re-stenosis, the proportion of these patients is likely to be small. Re-stenosis occurs clinically within 6 months, yet the median time interval between the prior PCI and index ACS was more than 1.5 years.

Conclusions

In a pooled analysis of 24 166 patients, those with prior PCI who presented with a non-ST-segment elevation ACS had a lower mortality rate at both 30 and 180 days compared with patients without prior PCI. However, patients with prior PCI had a higher incidence of MI compared with patients without prior PCI. Furthermore, patients with prior PCI had fewer in-hospital adverse outcomes, despite having more CAD and worse left ventricular function than patients without prior PCI.

Acknowledgements

The authors thank Jennifer King for her outstanding editorial work in preparing the manuscript. Millennium Pharmaceuticals, Inc. generously provided financial assistance to support preparation of the manuscript.

Data used in this analysis were generated from trials funded by the following companies: COR Therapeutics (now Millennium Pharmaceuticals, Inc.) and Schering-Plough Research Institute (PURSUIT); F. Hoffman-La Roche Ltd (now Roche) (PARAGON-B); and Ciba-Geigy (now Novartis), Boehringer Mannheim, and Guidant (GUSTO IIb).

References

1. Cannon CP, Weintraub WS, Demopoulos LA *et al*. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med* 2001;**344**:1879–1887.
2. Lagerqvist B, Husted S, Kontny F *et al*. A long-term perspective on the protective effects of an early invasive strategy in unstable coronary artery disease: two-year follow-up of the FRISC-II invasive study. *J Am Coll Cardiol* 2002;**40**:1902–1914.
3. FRagmin and Fast Revascularisation during InStability in Coronary artery disease Investigators. Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. *Lancet* 1999;**354**:708–715.
4. Labinaz M, Kilaru R, Pieper K *et al*. for the PURSUIT Investigators. Outcomes of patients with acute coronary syndromes and prior coronary artery bypass grafting: results from the platelet glycoprotein IIb/IIIa in unstable angina: receptor suppression using integrilin therapy (PURSUIT) trial. *Circulation* 2002;**105**:322–327.
5. Kleiman NS, Anderson HV, Rogers WJ *et al*. Comparison of outcome of patients with unstable angina and non-Q-wave acute myocardial infarction with and without prior coronary artery bypass grafting (Thrombolysis in Myocardial Ischemia III Registry). *Am J Cardiol* 1996;**77**:227–231.
6. Waters DD, Walling A, Roy D *et al*. Previous coronary artery bypass grafting as an adverse prognostic factor in unstable angina pectoris. *Am J Cardiol* 1986;**58**:465–469.
7. Wiseman A, Waters DD, Walling A *et al*. Long-term prognosis after myocardial infarction in patients with previous coronary artery bypass surgery. *J Am Coll Cardiol* 1988;**12**:873–880.
8. Labinaz M, Sketch MH Jr, Stebbins AL *et al*. for the GUSTO-I Investigators. Thrombolytic therapy for patients with prior percutaneous transluminal coronary angioplasty and subsequent acute myocardial infarction. Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries. *Am J Cardiol* 1996;**78**:1338–1344.
9. GUSTO-IIb Investigators. The Global Use of Strategies To Open Occluded Coronary Arteries: A comparison of recombinant hirudin with heparin for the treatment of acute coronary syndromes. *N Engl J Med* 1996;**335**:775–782.
10. The Platelet IIb/IIIa Antagonist for the Reduction of Acute coronary syndrome events in a Global Organization Network (PARAGON)-B Investigators. Randomized, placebo-controlled trial of titrated intravenous lamifiban for acute coronary syndromes. *Circulation* 2002;**105**:316–321.
11. The PURSUIT Investigators. Inhibition of platelet glycoprotein IIb/IIIa with eptifibatide in patients with acute coronary syndromes. Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin Therapy. *N Engl J Med* 1998;**339**:436–443.
12. Boersma E, Pieper KS, Steyerberg EW *et al*. for the PURSUIT Investigators. Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation. Results from an international trial of 9461 patients. *Circulation* 2000;**101**:2557–2567.
13. Marschner IC, Colquhoun C, Simes RJ *et al*. on behalf of the LIPID Study Investigators. Long-term risk stratification for survivors of acute coronary syndromes. Results from the Long-term Intervention with Pravastatin in Ischemic Disease (LIPID) Study. *J Am Coll Cardiol* 2001;**38**:56–63.
14. Rodriguez A, Bernardi V, Navia J *et al*. for the ERACI II Investigators. Argentine randomized study: coronary angioplasty with stenting versus coronary bypass surgery in patients with multiple-vessel disease (ERACI II): 30 day and one-year follow-up results. *J Am Coll Cardiol* 2001;**37**:51–58.
15. Serruys PW, Unger F, Sousa JE *et al*. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. *N Engl J Med* 2001;**344**:1117–1124.
16. The SoS Investigators. Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the Stent or Surgery trial): a randomised controlled trial. *Lancet* 2002;**360**:965–970.
17. The Multicenter Postinfarction Research Group. Risk stratifaction and survival after myocardial infarction. *N Engl J Med* 1983;**309**:331–336.

18. Schulman SP, Achuff SC, Griffith LS *et al*. Prognostic cardiac catheterization variables in survivors of acute myocardial infarction: a five-year prospective study. *J Am Coll Cardiol* 1988;**11**:1164–1172.
19. Taylor GJ, Humphries JO, Mellits ED *et al*. Predictors of clinical course, coronary anatomy and left ventricular function after recovery from acute myocardial infarction. *Circulation* 1980;**62**:960–970.
20. Topol EJ, Holmes DR, Rogers WJ. Coronary angiography after thrombolytic therapy for acute myocardial infarction. *Ann Intern Med* 1991;**114**:877–885.
21. Williams DO, Amsterdam EA, Miller RR *et al*. Functional significance of coronary collateral vessels in patients with acute myocardial infarction: relation to pump performance, cardiogenic shock and survival. *Am J Cardiol* 1976;**37**:345–351.
22. Garcia-Dorado D, Theroux P, Tornos P *et al*. Previous aspirin use may attenuate the severity of the manifestation of acute ischemic syndromes. *Circulation* 1995;**92**:1743–1748.
23. Harjai KJ, Stone GW, Boura J *et al*. Effects of prior beta-blocker therapy on clinical outcomes after primary coronary angioplasty for acute myocardial infarction. *Am J Cardiol* 2003;**91**:655–660.
24. Stenestrand U, Wallentin L, for the Swedish Register of Cardiac Intensive Care. Early statin treatment following acute myocardial infarction and 1-year survival. *JAMA* 2001;**285**:430–436.