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Reinfarction Following PCI or Medical Management using the Universal Definition in Patients With Total Occlusion After Myocardial Infarction: Results from Long Term Follow up of the OAT Cohort

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Abstract

Background—The Occluded Artery Trial (OAT) randomized 2201 patients with a totally occluded infarct-related artery on days 3–28 (>24 hours) following myocardial infarction (MI) to percutaneous coronary intervention (PCI) or medical treatment (MED). There was no difference in the primary endpoint of death, reinfarction or heart failure at 2.9 year or 6-year mean follow-up. However in patients randomized to PCI there was a trend for an increase in reinfarction.

Methods—We analyzed the characteristics and types of reinfarction according to the universal definition. Independent predictors of reinfarction were determined using Cox proportional hazard models with follow up to 9 years.

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Conflict of interest statement

Drs White, Reynolds, Carvalho, Liu, Martin, Pearte, Knatterud, Kruk, Cantor, Menon and Hochman report having no conflict of interest.

Results—There were 169 reinfarctions; 9.4% PCI vs 8.0% MED, HR 1.31, 95% CI 0.97 – 1.77, $p=0.08$. Spontaneous reinfarction (type 1) occurred with similar frequency in the groups; 4.9% PCI vs 6.7% MED, HR 0.78, 95% CI 0.53 – 1.15, $p=0.21$. Rates of type 2 (secondary) and 3 (sudden death) MI were similar in both groups. There was an increase in type 4a reinfarctions (related to protocol or repeat PCI), 0.8% PCI vs 0.1% MED, $p=0.01$ and type 4b reinfarctions (stent thrombosis); 2.7% PCI vs 0.6% MED, $p<0.001$.

Multivariate predictors of reinfarction were history of PCI prior to study entry ($p=0.001$), diabetes ($p=0.005$), and absence of new Q waves with the index infarction ($p=0.01$).

Conclusions—There was a trend for reMI to be more frequent with PCI. Opening an occluded infarct-related artery in stable patients late post-MI exposes them to a risk of subsequent reinfarction related to reocclusion and stent thrombosis.

Keywords

reinfarction; universal definition; occluded infarct artery

Introduction

In the Occluded Artery Trial (OAT) 2201 patients with a total occlusion of the infarct-related artery (IRA) were randomized 3 (>24 hours) to 28 days after myocardial infarction (MI) to percutaneous coronary intervention (PCI), or optimal medical treatment alone (MED). There was no difference in the 4-year event rate (mean 2.9 years) between the groups in respect of a composite endpoint of death, MI or New York Heart Association (NYHA) Class IV heart failure.¹ However there was a trend toward excess reinfarction at 2.9 years in patients randomized to PCI. Patients in OAT have been followed for up to 9 years (mean 6 years).²

Since the design of the OAT trial³ the universal definition of MI has defined 5 types of MI.⁴ Types of reinfarctions, their characteristics and predictors are unknown in patients with totally occluded infarct-related arteries, whether managed with PCI or MED alone. In order to understand the contribution of spontaneous reinfarctions as opposed to other types, we analyzed the characteristics and predictors for reinfarction by type using the universal definition in an extended follow-up phase of the OAT trial. This analysis was prospectively predefined.

Methods

Patient Population

The design of the OAT study has been described in detail.^{3,5} In summary, between February 2000 and June 2006, 2201 patients were enrolled. Eligible patients had a totally occluded IRA on angiography on calendar days 3–28 (> 24 hours) after MI, met an additional high-risk criterion (ejection fraction below 50% or proximal occlusion) and were clinically stable. Exclusion criteria included NYHA class III or IV heart failure, shock, serum creatinine >2.5 mg per deciliter (221 μ mol per liter), significant left main or three-vessel coronary artery disease, rest angina, and severe ischemia on stress testing.

Eligible patients were randomized to PCI with stenting (1101 patients) or optimal medical therapy (1100 patients), including aspirin, anticoagulation if indicated, angiotensin-converting enzyme inhibition, beta-blockade, and lipid-lowering therapy, unless contraindicated. Thienopyridine therapy was recommended to be initiated prior to PCI and to be continued for 2 to 4 weeks after stent deployment. After the publication of CURE⁶ and CREDO⁷ clopidogrel was recommended for at least 1 year after stent placement.

Protocol PCI angiograms were reviewed at a core laboratory.¹ Cardiac biomarkers (preferably creatine kinase MB [CK-MB] or, if not available, troponin I or T, or creatine kinase) were to be measured routinely in both groups three times during the first 48 hours after randomization and within 24 hours after PCI in patients assigned to PCI. There were forms for the collection of biomarker information during follow up, but sites were not queried about results after PCI or coronary artery bypass grafting (CABG).

Study endpoints

The primary end point was a composite of death, reinfarction, or NYHA class IV heart failure with hospitalization or admission to a short-stay unit. In this analysis, the universal definition of myocardial infarction was used. All reinfarctions were reviewed by 5 investigators and classified; type 1 spontaneous; type 2 secondary to supply and demand imbalance; type 3 sudden death; type 4 related to PCI and type 5 related to CABG.⁴ Two reviewers, blinded to treatment, reviewed hospital records and case report forms. Disagreements were adjudicated by the group. See Figure 1 for flow of the review process. The universal definition of stent thrombosis MI is similar to the Academic Research Consortium (ARC) definite stent thrombosis criteria.⁸ Cases that met criteria for probable or possible stent thrombosis by the ARC criteria were classified according to the universal definition (usually as type 1 or type 3). Unlike the OAT definition, which required two out of three criteria (symptoms, ECG, biomarkers) with at least two-fold biomarker elevation for type 1 MI, the universal definition requires biomarker elevation to be any value above the upper limit of normal (ULN). For type 4 (3× ULN) and type 5 (5× ULN) infarction the biomarker criteria for the universal definition is similar to the OAT definition.^{3,4} When baseline biomarker levels were stable or falling, re-elevation had to be >20% and if levels were rising no interpretation was made. Fatal reinfarction was defined as death within 24 hours of MI.

Statistical Analysis

Baseline characteristics of patients were summarized as frequencies and percentages for categorical variables and as median (interquartile range) for continuous variables and compared within the risk strata with chi-square test, Fisher's exact test or ANOVA respectively. Estimates of the cumulative event rates were calculated by the Kaplan-Meier product-limit method⁹ and groups were compared by the log-rank test.¹⁰ Hazard ratio and 95% confidence intervals were calculated by Cox proportional hazards regression models.¹¹ The 7-year event rates are presented because numbers of patients followed for more than 7 years was small.

Univariable and multivariable Cox proportional hazards models were developed to evaluate the relations between the baseline characteristics and the occurrence of reinfarction. All baseline variables entered the multivariable stage. Angiographic factors included presence of multivessel disease, the collateral flow to the IRA, left ventricular ejection fraction, and whether the left anterior descending artery was the IRA. The prognostic discriminatory capacity of the resulting risk model was measured with the c-statistic representing the agreement between predicted with observed event.¹²

To control for type I error, it was pre-specified by the study protocol that a p-value of <0.01 would be considered as showing evidence of differences in secondary analyses. SAS version 9.1.3 (SAS Institute, Cary, NC) was used for statistical analyses.

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Results

Review of all suspected reinfarctions submitted by sites resulted in an additional 29 events according to the universal definition that were not confirmed by the Mortality and Morbidity Classification Committee (MMCC) because they did not meet OAT criteria defined in the original protocol, Figure 1, Table 1. Of these 29 events, 9 were classified as spontaneous MI, 4 as secondary, 10 as sudden death, 4 as PCI related, 1 as stent related and 1 as CABG related.

There were 169 reinfarctions that met the universal definition. Baseline demographics of patients who did and did not have reinfarctions are shown in Table 2. Prior history of MI, heart failure, diabetes, PCI, CABG prior to study end, and rates at randomization all occurred more frequently in patients who had reinfarction. Reinfarction occurred in 9.4% of the PCI group and 8.0% of the MED group; HR 1.31; 95% CI 0.97 – 1.77, p=0.08. Figure 2 shows the reinfarction rates over time in the two randomized groups.

Most reinfarctions were type 1 (62.7%), with similar rates in both groups; 4.9% PCI vs 6.7% MED, HR 0.78, 95% CI 0.53–1.15, p=0.21 (Table 3). Reinfarction related to either protocol or repeat PCI (type 4a) or stent thrombosis (type 4b) was more common in the PCI group: 3.5% PCI vs 0.7% MED, HR 5.22, 95% CI 2.32–11.74, p<0.001 (Figure 3a); PCI related: 0.8% PCI vs 0.1 % MED, HR 9.03, 95% CI 1.14–71.28, p=0.01, and stent thrombosis, 2.7% PCI vs 0.6% MED, HR 4.59, 95% CI 1.89–11.11, p<0.001 (Figure 3b). Most stent thromboses in the PCI group occurred in the IRA for the OAT qualifying MI (84.6%) while in the MED group only 2 out of 6 (33.33%) stent thromboses were in the OAT IRA.

Information as to stent type was collected in the 944 patients (86.6%) who had stents inserted at the protocol assigned PCI procedure. Drug eluting stents were inserted in 79

patients. In patients with stent information reinfarctions with definite stent thrombosis occurred in 5.1%.

Table 4 shows the clinical, biomarker and angiographic features of the reinfarctions. Most reinfarctions in the PCI group were in the OAT- qualifying territory; 59.5% vs 37.7% in the MED group, $p = 0.01$ and most (61.2%) were ST elevation reinfarctions in the PCI group and about half in the MED group. In the subgroup (54.4%) of patients who had a wall motion study performed after the reinfarction, new wall motion abnormality occurred in 45.5% in both PCI and MED groups. Of the 70 patients in the PCI group with angiograms stent restenosis occurred in the qualifying IRA in half of the reinfarctions (Table 4). There were 11/95 (11.6%) fatal reinfarctions in the PCI group and 8/74 (10.8%) in the MED group. Of the 29 patients with reinfarction that met the universal but not the OAT definition, 16 died during the follow-up period.

Additional recurrent nonfatal reinfarction data after the first re-MI were collected but these events were not adjudicated. In the PCI group, 8 patients had 2 reinfarctions and 7 had 3 reinfarctions. In the MED group, 6 patients had 2 reinfarctions and 1 had 3 reinfarctions.

Table 5 shows the multivariate model with the risk factors and hazard ratios for reinfarction. History of PCI prior to study entry, $p=0.001$, lack of development of Q waves on the qualifying MI ECG, $p=0.011$, and diabetes, $p=0.005$, were significant predictors. There were trends for a shorter time from the index MI to randomization to be associated with a higher rate of reinfarction, $p=0.02$ and for randomization to PCI to be associated with a higher rate of reinfarction, $p=0.07$. There were no angiographic or post PCI predictors. The C-statistics for this model is 0.73, 95% CI 0.59 – 0.86. There were six predictors for reinfarction for the MMCC adjudication multivariate model compared with the seven predictors in this model with the additional factor being lower ejection fraction.

Table 6 shows the percentage of patients in the PCI and MED group who continued to smoke, or who stopped their aspirin or thienopyridine prior to their reinfarction. Rates of smoking and cessation of aspirin and thienopyridine were high in both groups and not significantly different between the groups.

Discussion

In this trial of 2201 stable patients with occluded IRAs treated medically or with the PCI in the subacute phase post MI, we found a low rate of reinfarction that continued to accrue over 9 years of follow up. The low rates of reinfarction illustrate the stable ischemic substrate of these patients when treated with current medical therapy. There was a trend for more reinfarctions in patients randomized to PCI, $p=0.08$. The reinfarctions in the PCI group were similar to those in the MED group as judged by biomarker elevation, new Q waves, or new wall motion abnormality.

The reinfarctions were clinically significant as most were associated with a new wall motion abnormality, half with ST-segment elevation, greater than a quarter developed new Q waves and approximately 10% were fatal within 24 hours. In addition, reinfarctions were

independently associated with increased late mortality regardless of randomized management strategy and MI type.¹³

Patients with a prior history of PCI, diabetes and no new Q waves, were more likely to have reinfarction. The known risk factors entered into the models were able to predict only 73% of events indicating that there are also important unknown factors.

Over half of the reinfarctions occurred in patients enrolled following a Q wave MI. The finding that patients who did not have new Q waves during their index MI had more frequent reinfarction may reflect the possibility that an area of ischemic myocardium which had not necrosed could be threatened with reinfarction if the IRA was opened and it subsequently occluded. The development of a Q wave infarction may be evidence of a “completed” full thickness infarction in the territory of an occluded artery which may not present clinically with reinfarction if the opened artery subsequently occluded. However, the presence of Q waves does not necessarily indicate transmural or mean lack of viability, and the OAT viability substudy demonstrated at least moderately preserved infarct zone viability in 70% of patients.¹⁴ Thus these patients could have reinfarction in the territory of the previously occluded IRA either related to reocclusion or other mechanisms such as imbalance in supply and demand.

Most reinfarctions were spontaneous (type 1), which occurred at a similar frequency in both randomized groups. The increase in reinfarctions in the PCI group was largely driven by excess stent thrombosis and not by peri-procedural reinfarctions. The stent thrombosis (type 4b), rate does not include sudden death, (type 3) which would have been ascribed as probable stent thromboses with the ARC definition⁸ if it occurred within 30 days and possible stent thrombosis if it occurred after 30 days of stent implantation. The rate of stent thrombosis (2.7%) in the PCI group may seem high, but this was over 6 years. It is possible that modification of stent deployment techniques, newer stent designs, and prolonged thienopyridine therapy, or the use of different P2Y₁₂ inhibitors¹⁵ may decrease reinfarction rates after PCI for occluded IRA.¹⁶

Peri-procedural infarction has been shown to occur as defined by delayed enhancement magnetic resonance imaging (MRI) in 23% of patients undergoing PCI¹⁷ with distal embolization of plaque material and occlusive thrombi being an important mechanism. Another mechanism of infarction following PCI of an occluded IRA is plaque shifting (or “snow ploughing”) at the site of the occlusion.¹⁷ Both these mechanisms potentially may compromise collateral blood flow resulting in the loss of rapidly recruitable collateral vessels if reocclusion subsequently occurs in another coronary artery territory.^{18,19} Reocclusion occurred in ~ 11% of occluded IRAs which had been opened with PCI in TOSCA 2, a substudy of OAT.²⁰ Interestingly in OAT the presence of angiographic collaterals at the time of the presenting MI angiogram was not independently associated with better outcomes in patients undergoing PCI.²¹

The trend for a shorter time from the OAT qualifying MI to randomization to be associated with a higher rate of reinfarction is likely related to the confounding of diagnosing reinfarction when biomarkers may still be elevated from the index MI. It could also be

related to higher rates of viability in the patients randomized earlier after the qualifying MI. However in the OAT nuclear ancillary study there was no relation of time to randomization and viability.¹⁴

Use of Evidence Based Treatments

It may have been expected that use of evidence based medications would have been related to the frequency of reinfarction. However, in OAT there was a high rate of discharge use of these therapies in both groups; aspirin 96%, beta-blockers 88%, lipid-lowering agents 81%, and ACE inhibitors 80%.³ Thienopyridines were infrequently prescribed in the MED group through one year,^{1,5} which may have resulted in higher reinfarction rates compared to contemporary practice.

Limitations

There are a number of limitations to this study. Data on the release of biomarkers following uncomplicated PCI were not systematically collected and reviewed. The rates of type 4a reinfarction may therefore be underestimated. The number of reinfarctions limits the power of our multivariate analysis of predictors of reinfarction. Although we collected data on thienopyridine and aspirin discontinuation, the data were incomplete with respect to reasons for discontinuation and timing of discontinuation in relation to reinfarction.

Conclusions

In the OAT trial there was an ongoing low rate of reinfarction over 9 years of follow up. Reinfarction tended to occur at a higher rate in patients randomized to PCI. Most reinfarctions were spontaneous (type 1) which occurred at a similar frequency in both randomized treatment groups. However, in the PCI group there were more type 4a (both protocol PCI-related and other PCI-related reinfarctions), and type 4b (stent thrombosis) reinfarctions. The reinfarctions were clinically significant with approximately 10% of reinfarctions being rapidly fatal.

A number of non-modifiable predictors of reinfarction were identified. No single angiographic predictive factor was identified. A routine strategy of PCI of the occluded IRA in the subacute phase post MI not only fails to decrease ischemic events, but by creating a substrate for target vessel reocclusion, occlusive restenosis and stent thrombosis, may potentially expose the stable patient to a higher risk of future reinfarction.

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The paper is not under consideration elsewhere and none of the paper's contents have been previously published. All authors have contributed to, and have read and approved the current manuscript. The Corresponding Author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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Figure 1.
Process for adjudication of reinfarction in OAT.
reMI = reinfarction; MI = myocardial infarction

Figure 2.

Frequency of reinfarction according to Universal Definition and randomized treatment.

PCI = percutaneous coronary intervention group; MED = medical group; reMI = reinfarction

a

Figure 3.

a Frequency of occurrence of type 4a and type 4b reMI according to randomized treatment.

PCI = percutaneous coronary intervention group; MED = medical group; reMI = reinfarction

b Frequency of type 4b (stent thrombosis) reMI according to randomized treatment.

PCI = percutaneous coronary intervention group; MED = medical group; reMI = reinfarction

Table 1

Comparison of reinfarctions using universal and OAT trial definitions.

Type of reMIs by Universal Definition	Number of reMIs by Universal Definition	Number of additional reMIs picked-up by Universal Definition
Type 1: Spontaneous	106	9
Type 2: Secondary	7	4
Type 3: Sudden death	12	10
Type 4a: PCI related	10	4
Type 4b: Stent related	33	1
Type 5: CABG related	1	1
Total	169	29

Two reinfarction cases identified by the Mortality and Morbidity Classification Committee using the OAT trial definition were not considered as reinfarctions by reviewers using the universal definition.⁴ These were both PCI related.

Table 2

Baseline Characteristics

	No Reinfarction N = 2032	Reinfarction N = 169	P value *
Age – years (mean)	58.7	57.3	0.112
Sex (%)			
Male	78.2	75.7	0.46
Female	21.8	24.3	
Race or ethnic group (%)			
White	80.2	79.3	
Black	3.1	4.1	0.12
Hispanic	12.8	9.5	
Other	3.9	7.1	
History (%)			
Angina	22.1	27.8	0.09
Myocardial infarction	10.4	20.7	<0.001
Cerebrovascular disease	3.6	4.7	0.47
Peripheral-vessel disease	3.5	7.1	0.2
Heart failure**	2.0	6.5	<0.001
PCI	4.1	13.0	<0.001
CABG	0.3	1.8	0.004
Diabetes	19.9	29.0	0.005
Insulin use	5.3	10.1	0.009
Hypertension	48.6	49.1	0.90
Current smoker (%)	38.6	43.8	0.19
Highest Killip class II through IV during index MI (%)	18.9	20.8	0.53
NYHA classification at randomization (%)			
I	83.5	80.4	0.23
II	16.5	19.6	
ECG (%)			
ST-segment elevation	66.5	64.5	0.60
New Q-waves	68.0	55.6	0.001
R wave loss	41.9	37.9	0.31
New Q waves, ST elevation or R wave loss	86.6	87.6	0.71
Glomerular filtration rate – mL/min/m²	80.7	80.03	0.71
Thrombolytic therapy during first 24 hrs after onset of index MI (%)	19.1	21.3	0.49
Interval between MI and randomization – days			

	No Reinfarction N = 2032	Reinfarction N = 169	P value *
Mean	11.1	9.5	0.01
Stress test performed (%)	27.3	25.4	0.60
Ischemia in infarct-related artery territory (%)			
Severe (ineligible)	0.1	0.0	0.18
Moderate	9.6	13.9	
Mild	29.2	41.9	
None	61.1	44.2	
Infarct –related artery (%)			
Left anterior descending	36.3	33.1	0.35
Circumflex	14.9	18.9	
Right coronary artery	48.8	47.9	
Collateral vessels present (%)	88.6	86.4	0.38
Multi-vessel disease (%)	17.2	18.9	0.57
Ejection fraction (%)	47.8	46.3	0.09
Blood pressure mmHg			
Systolic	120.8	120.5	0.82
Diastolic	72.4	70.8	0.07
Rales present (%)	5.6	13.7	<0.001

* p value from a Chi-square, Fisher exact, or F-test statistic comparing distributions among the 2 groups;

** CHF at baseline: CHF condition at baseline that includes any of the following conditions:

CHF = chronic heart failure

MI = myocardial infarction

NYHA = New York Heart Association

Table 3
Types of reinfarction and estimated 7-year event rates according to randomized groups

	PCI (N = 1101)		Medical (N = 1100)		HR (95%CI)	p-value
	n	7-year rate	n	7-year rate		
Type 1: Spontaneous	46	4.9%	60	6.7%	0.78 (0.53–1.15)	0.21
Type 2: Secondary	6	0.6%	1	0.1%	6.16 (0.74–51.17)	0.05
Type 3: Sudden death	7	0.7%	5	0.5%	1.43 (0.46–4.52)	0.54
Type 4a and 4b	36	3.5%	7	0.7%	5.22 (2.32–11.74)	<0.001
Type 4a: PCI related	9	0.8%	6	0.1%	9.03 (1.14–71.28)	0.01
Type 4b: Stent thrombosis	27	2.7%	1	0.6%	4.59 (1.89–11.1)	<0.001
Type 5: CABG related	0	...	1	...	...	...
Total	95	9.4%	74	8.0%	1.31 (0.97–1.77)	0.08
MMCC adjudicated	77	7.7%	65	7.2%	1.20 0.86–1.67	0.27

CI = Confidence Intervals

HR = Hazard ratio

PCI = Percutaneous Coronary Intervention

CABG = Coronary Artery Bypass Graft Surgery

MMCC = Mortality and Morbidity Classification Committee

Table 4

Clinical, biomarker and angiographic features of the reinfarctions

	PCI Occur/avail	PCI (%) N = 95	MED Occur/avail	MED (%) N = 74	P Value
Same territory as qualifying infarction					
Overall	44/74	59.5	23/61	37.7	0.01
Type 1 MI subset	15/39	38.5	19/52	36.5	0.85
ST elevation					
Overall	52/85	61.2	33/67	49.3	0.14
In qualifying territory	36/85	42.4	21/67	31.3	0.16
LBBB present					
Overall	1/87	1.2	4/67	6.0	0.09
New LBBB *	1/87	1.2	1/67	1.5	0.85
New Q waves					
Overall	12/82	14.6	12/68	17.7	0.62
Biomarker elevation ** (1)	81/83	97.6	58/61	95.1	0.426
Biomarker elevation >2×ULN	79/83	95.2	57/61	93.4	0.72
Biomarker elevation >3×ULN	76/83	91.6	54/61	88.5	0.54
Biomarker elevation >5×ULN	63/83	75.9	41/61	67.2	0.25
Biomarker elevation >10×ULN	54/83	65.1	33/61	54.1	0.18
Wall motion abnormality					
Overall	36/46	78.3	38/46	82.6	0.60
New wall motion abnormality	21/46	45.5	21/46	45.5	1.00
Location of culprit ***					
Overall	62		46		0.23 ***
LAD	26/62	41.9	19/46	41.3	
Circumflex	11/62	17.8	14/46	30.4	
RCA	25/62	40.3	13/46	28.3	
In stent restenosis in qualifying IRA ****					
Overall	35/70	50.0	5/48	10.4	<0.001
In stent restenosis in another artery	8/70	11.4	7/48	14.6	0.61
Stent thrombosis in qualifying IRA	22/70	31.4	2/48	4.2	<0.001

	PCI Occur/avail	PCI (%) N = 95	MED Occur/avail	MED (%) N = 74	P Value
Stent thrombosis in another artery	4/70	5.7	4/48	8.3	0.58

There are missing values for some of the items listed. The percentages and p-values are based on only the cases with valid values for each item.

* New LBBB: only 4 of 169 patients have valid values for new LBBB

** Biomarker elevation (1): Defined as any peak CK>ULN or CKMB>ULN or Troponin>ULN.

*** p-value for location of culprit: Excluding one patient with bypass grafting.

**** Instant restenosis in another artery, stent thrombosis in qualifying IRA and stent thrombosis in another artery use the data from the patients who had an angiogram available. Any possible or probable thrombosis identified by the ARC definition ⁸ were not included.

Avail = available

LBBB = left bundle branch block

LAD = left anterior descending artery

MED = medical

Occu = occurred

PCI = percutaneous coronary intervention

RCA = right coronary artery

IRA = infarct related artery

Table 5

Multivariate predictors of reinfarction

Parameter	Parameter Estimate	Standard Error	P Value	HR	95% HR CI
Treatment group	0.296	0.16	0.07	1.33	0.98 1.81
Prior MI	0.45	0.21	0.03	1.57	1.04 2.39
Prior PCI	0.82	0.26	0.001	2.28	1.38 3.77
Diabetes	0.49	0.17	0.005	1.63	1.16 2.28
Lower age *	0.15	0.07	0.03	1.16	1.01 1.34
No new Q waves	0.41	0.16	0.01	1.51	1.10 2.06
Shorter time from MI **	0.03	0.01	0.02	1.03	1.01 1.05
Lower ejection fraction ***	0.16	0.07	0.03	1.17	1.02 1.34

* By 10 year intervals

** Time from MI to randomization

*** By 10 percent intervals

CI = Confidence Intervals

HR = Hazard ratio

MI = Myocardial Infarction

PCI = Percutaneous Coronary Intervention

Table 6

Smoking and antiplatelet therapy at time of reinfarction

	PCI Occur./avail.	PCI (%) n = 95	MED Occur./avail.	MED (%) n = 74	P value
Current smoker	22/44	50.0	20/35	57.1	0.53
Not on aspirin	13/51	25.5	8/48	16.7	0.28
Not on thienopyridine	37/57	64.9	38/46	82.6	0.05

Occur – no of patients with condition

Avail – no of patients with information available

MED = medical

PCI = Percutaneous Coronary Intervention