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Impact of Left Ventricular Ejection Fraction on Clinical Outcomes Over Five Years After Infarct-Related Coronary Artery Recanalization (from the Occluded Artery Trial [OAT])

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Abstract

In the Occluded Artery Trial (OAT), percutaneous coronary intervention (PCI) of an infarct-related artery on days 3 to 28 after acute myocardial infarction was of no benefit compared to medical therapy alone. The present analysis was conducted to determine whether PCI might provide benefit to the subgroup of higher risk patients with a depressed ejection fraction (EF). Of 2,185 analyzed patients (age 58.6 ± 11.0 years) with infarct-related artery occlusion on days 3 to 28 after acute myocardial infarction in the Occluded Artery Trial, 1,094 were assigned to PCI and 1,091 to medical therapy. The primary end point was a composite of death, reinfarction, and New York Heart Association class IV heart failure. The outcomes were analyzed by EF (first tertile, $EF \leq 44\%$, vs second and third tertiles combined, $EF > 44\%$). Interaction of the treatment effect with EF on the study outcomes were examined using the Cox survival model. The five-year rates of the primary end point (death, reinfarction, or New York Heart Association class IV heart failure) were not different in either subgroup (PCI vs medical therapy, hazard ratio 1.25, 99% confidence interval 0.83 to 1.88, for $EF \leq 44\%$; hazard ratio 0.98, 99% confidence interval 0.64 to 1.50, for $EF > 44\%$). However, in patients with an $EF > 44\%$, PCI reduced the rate of subsequent revascularization ($p = 0.004$, interaction $p = 0.05$). In conclusion, optimal medical therapy remains the overall treatment of choice for stable patients with a persistent total occlusion of the infarct-related artery after acute myocardial infarction, irrespective of the baseline EF. In patients with normal or moderately impaired left ventricular contractility, PCI reduced the need for subsequent revascularization but did not otherwise improve outcomes.

After acute myocardial infarction (AMI), left ventricular (LV) systolic dysfunction is a key predictor of subsequent morbidity and mortality.¹ Because of the progressive nature of LV

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remodeling, it remains a hazard during long-term follow-up. Previous reports have suggested that delayed percutaneous coronary intervention (PCI) of the infarct-related artery (IRA) might preserve LV function and improve the clinical outcomes in patients with impaired LV systolic function.^{2,3} The benefits of PCI might be expected to be greater in those with poor LV function. The Occluded Artery Trial (OAT) was a controlled, randomized study of PCI of the IRA versus medical therapy alone after AMI.⁴ Although an ancillary study did demonstrate modest improvements in LV geometry in patients assigned to PCI, no reduction in death, reinfarction, or heart failure was identified during an average of 3 years of follow-up for PCI relative to a conservative medical approach.^{4,5} We hypothesized that a clinical benefit attributable to PCI might be more apparent in patients with a depressed baseline ejection fraction (EF). Therefore, we incorporated this as a prespecified analysis in the OAT protocol.⁴ In the present analysis, we examined whether the clinical effects of the study intervention (PCI of IRA vs medical therapy alone) were related to the baseline EF.

Methods

The design and methods of the OAT have been previously described.⁶ In brief, OAT was a randomized multi-center, controlled, unblinded study of patients sustaining an AMI who were found to have a persistently occluded infarct artery at diagnostic cardiac catheterization on calendar days 3 to 28 (minimum of 24 hours after symptom onset) after the index event. To be eligible, patients had to be clinically stable with either a large area of affected myocardium (i.e., proximal occlusion of a major epicardial vessel) or a baseline EF of <50%. Of the 2,201 patients, 1,101 were randomly assigned to PCI with stent placement and optimal medical therapy (PCI group) and 1,100 were randomly assigned to optimal medical therapy alone (medical group). These patients included 2,166 who were enrolled between February 2000 and December 2005 in the main OAT and 35 patients who were enrolled in the extension phase of the OAT-Nuclear (NUC) substudy in 2006. All patients were to receive optimal medical therapy, including aspirin, anticoagulation, if clinically indicated, an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, a β blocker, and lipid-lowering therapy, unless contraindicated. Thienopyridine therapy was to be initiated before PCI and continued for ≥ 2 to 4 weeks in patients undergoing PCI, with consideration of 1 year of therapy for both groups beginning in 2003. The Agency for Healthcare Research and Quality guidelines were to be followed for treating patients in heart failure with LV systolic dysfunction.⁷ The major exclusion criteria included New York Heart Association class III or IV heart failure, shock, serum creatinine concentration ≥ 2.5 mg/dl (221 μ mol/L), angiographically significant left main or 3-vessel coronary artery disease, angina at rest, and severe ischemia on stress testing.

The baseline EF was available for 1,094 patients in the PCI group and 1,091 in the medical group. Left ventriculography was to be performed during baseline angiography unless contraindicated or if a qualifying coronary angiogram was obtained without LV angiography before transfer to the OAT Center. The EF was assessed by the Angiography Core Laboratory on a routine basis for 1,723 patients. In the cases for which no core laboratory data were available, the site-determined LVEF (as determined by echocardiography radionuclide ventriculography or LV angiogram) was used ($n = 462$) for the present analysis.

The institutional review boards at the participating centers approved the study protocol. All patients provided written informed consent.

The primary end point was the first occurrence of death from any cause, reinfarction, or New York Heart Association class IV heart failure resulting in hospitalization or admission to a short-stay unit. The secondary end points included the incidence of the individual components of the primary end point (i.e., New York Heart Association class III or IV heart failure, death, or reinfarction), stroke, revascularization, and the presence of angina symptoms. In addition

to these prespecified end points, we analyzed the composite of death or New York Heart Association class IV heart failure, which was of particular interest in relation to the EF.

The study end points were adjudicated by an independent committee unaware of the treatment assignments. The definition of reinfarction has been previously provided.⁴

The intent of the present analysis was to evaluate the relationships among the EF, PCI, and outcomes. Patients were divided by baseline EF into 2 groups, one group consisted of patients in the lowest tertile of EF ("low EF," defined as EF of $\leq 44\%$) and the second consisted of patients in the second and third tertiles ("higher EF," defined as EF $> 44\%$). Analyses of the interactions between the study treatment and EF were prespecified in the OAT protocol, and the tertile-based thresholds of EF were prespecified before the present analyses. Continuous variables are presented as the median with the interquartile ranges and were compared using the Wilcoxon nonparametric test. Categorical variables were compared using the chi-square test. The association of the EF and the study outcomes was analyzed using Cox regression models. Multivariate Cox models included all baseline clinical and angiographic characteristics with $< 10\%$ missing data. The interaction of the study treatment and the outcomes was assessed with the EF stratified into the 2 EF subgroups, as described. In addition, the interaction between the study treatment and outcomes was modeled with LVEF as a continuous function. Hazard ratios for the study treatment within the EF-based subgroups were adjusted for the baseline variables predictive of the primary outcome on multivariate analysis. All α values are 2 sided, and all analyses were by intention to treat. To control for the type I error rate, it was prespecified by the study protocol that a p value of ≤ 0.01 would be considered evidence of differences in the secondary analyses, and a p value > 0.01 to < 0.05 would be evidence of a trend toward a difference.⁴ The Statistical Analysis Systems, version 9.1.3 (SAS Institute, Cary, NC) software, was used for the statistical analyses.

Results

The baseline EF was available for 2,185 (99.3%) of the 2,201 patients enrolled in the OAT. Of these patients, 1,170 (53.5%) had an EF $< 50\%$. For 92 of these 1,170 patients, the sole high-risk criterion of an EF $< 50\%$ (and no proximal occlusion of a large vessel) was sufficient for enrollment in the study. The EF ranged from 10% to 82%. The median EF was 48% (interquartile range 40% to 55%); 449 patients (20.6%) had an EF $< 40\%$ and 134 (6.1%) had an EF $< 30\%$.

A comparison between the low ($\leq 44\%$) and higher ($> 44\%$) EF groups with respect to the baseline clinical and angiographic characteristics, medications, and procedural outcomes for those treated invasively is provided in Tables 1 and 2. Clopidogrel use at 1 year did not differ between the low and higher EF groups (14.9% vs 14.8%, respectively, $p = 0.95$), nor did it differ between those randomized to PCI in the low and higher EF groups (18.1% vs 17.6%, respectively, $p = 0.86$).

Periprocedural complications were uncommon. A total of 7 reinfarctions and 5 deaths occurred, with a similar distribution between the EF subgroups.

Overall, the cumulative 5-year composite primary event rate was 17.5%. The rates of the components of the primary end point were as follows: death 11.7%, repeat myocardial infarction 6.0%, and New York Heart Association class IV heart failure 4.6%. The rates of the primary outcome and each of its components were greater among patients with a lower baseline EF. Detailed data on the frequency of the study end points within the lower and higher EF subgroups are listed in Table 3.

In the multivariate models adjusting for independent predictors of the primary outcome (glomerular filtration rate, days from qualifying AMI to randomization, history of peripheral vascular disease, congestive heart failure, diabetes, rales on examination) or death (glomerular filtration rate, days from qualifying AMI to randomization, history of angina, cerebrovascular disease, congestive heart failure, Killip class 2 to 4 at presentation), a low EF was independently associated with excess risk of the primary outcome, death and heart failure (Table 3).⁸

No interaction was found between the baseline EF and treatment effect for the composite outcome or any of its components, using either EF modeled as a continuous function or when EF was divided into low versus higher subgroups (Table 4 and Figure 1).

The outcomes were similar for the PCI and medical groups for all EF subgroups, before (Table 4) and after adjustment for variables that were not balanced in the EF subgroups and for the independent predictors of the primary outcome and death. A numeric surplus of reinfarctions was observed in the patients with a low EF assigned to PCI, but it did not reach the prespecified level of statistical significance ($p = 0.04$), and no interaction was seen between the EF and treatment assignment on reinfarction or any other outcome (Table 4). However, the greater rate of events among the patients with a low EF treated with PCI contributed to the trend observed in the main OAT analysis toward more reinfarctions in patients assigned to PCI.⁴

Consistent with the overall trial findings,⁴ randomization to PCI was associated with longer intervals to the first occurrence of angina during the follow-up period. Although this effect was only statistically significant in the larger higher EF group, we observed no formal statistical interaction between the EF and treatment assignment on angina (Table 4). A trend toward an interaction between the EF and treatment assignment was seen for revascularization through 5 years, with a greater reduction in revascularization seen in those with higher EF assigned PCI ($p = 0.004$).

Discussion

This prespecified analysis of the OAT was conducted to explore whether the high-risk subgroup of patients with decreased EF might derive benefit from delayed PCI of the IRA, when such a benefit was not seen in the overall study population. Although our analysis reaffirmed low EF as a powerful predictor of increased risk among patients with persistent total occlusion of the IRA, we observed no signal favoring a routine PCI approach in the higher risk (low EF) group. In fact, the trend toward a greater rate of reinfarction in the PCI-assigned subjects described in the primary OAT report⁴ appeared to be mainly attributable to patients with lower EF. Our results also suggest that lower subsequent revascularization rates observed in the PCI arm of the OAT in the overall trial were driven by the patients with higher baseline EF, albeit without clear-cut statistical significance for an interaction between this outcome and EF group.

The present analysis has important clinical implications and addresses one of the fundamental issues underlying the late open artery hypothesis on which the OAT was based. The study selection criteria reflected a straightforward concept that the high risk associated with significant LV jeopardy or injury resulting from recent occlusion of the responsible vessel could be alleviated by mechanically opening this artery, albeit outside the standard reperfusion window. In OAT, it was hypothesized that establishing late infarct artery patency would prevent infarct expansion and adverse ventricular remodeling, as well as increase electrical stability. The purported beneficial effects would be most important in patients with a lower EF. These theoretical assumptions were partially supported by the Total Occlusion Study of Canada 2 (TOSCA-2) substudy of OAT, in which a lower EF was an independent predictor of LV remodeling and in which randomization to PCI was associated with modest attenuation of the increase in LV volume during follow-up compared to medical therapy alone.⁵ However,

although another OAT substudy (OAT-NUC) confirmed the presence of viable myocardium within the infarct zone in 69% of the patients, it did not show a benefit of PCI on LV remodeling.⁹ The present analysis has extended these observations in suggesting that regardless of a potential benefit of PCI on LV remodeling in the OAT, this did not translate into better outcomes, including lower rates of heart failure, even in the low EF cohort.

In light of the prognostic significance of LV dilation and reinfarction, the potential gain from PCI of the IRA in terms of reperfusion of the stunned myocardium or decreased infarct expansion might have been offset by an increased risk of reinfarction, which was unexpectedly observed predominantly in the patients with a low EF and might have been due to IRA reocclusion. Of note, the EF itself was not significantly associated with reinfarction. The pathologic background for the observation remains speculative. One possibility is that the trend toward more reinfarction among the patients with a low EF was related to an increased rate of stent thrombosis, which has been reported previously for patients with a decreased EF.¹⁰ Our observations of no benefit and of potential harm from PCI of the occluded IRA in OAT patients with a low EF build on the main trial's findings and their clinical implications. Previous revascularization experience in patients with a low EF was based largely on surgical studies performed >2 decades ago. Data from the Coronary Artery Surgery Study registry and Duke University cardiovascular database showed the greatest clinical benefits from revascularization were derived by patients with an EF of <25%, extensive coronary artery disease, and severe angina.^{2,11} A meta-analysis of studies of revascularization in patients with a depressed EF stressed the value of confirmation of preintervention viability as a determinant of clinical benefit¹²; however, this issue remains controversial and is currently being tested in the Surgical Treatment for Ischemic Heart Failure (STICH) trial.¹³ Importantly, these studies tested (as will STICH) surgical, rather than percutaneous, revascularization. Percutaneous revascularization might be complicated by downstream embolization of thrombus and atherosclerotic material, which might be more likely in patients with total occlusion after an acute coronary syndrome.¹⁴ However, this mechanism is unlikely to pertain to the OAT, because most patients undergoing PCI had good myocardial perfusion after the procedure.¹⁵

The OAT patients with lower EF more often had a history of AMI, preceding the index event, which might support an alternative hypothesis that patients with a lower EF had pre-existing LV damage that would not improve with PCI of the recently occluded vessel. However, only 14% of those with a low EF had previously experienced myocardial infarction. Also, patients with lower EF more often had the left anterior descending coronary artery as the IRA (59% vs 24%), and it has been hypothesized that patients with anterior infarcts derive the greatest potential benefit from the re-establishment of flow.¹⁶ The underlying pathophysiologic mechanisms accounting for the disparity between the results of the OAT in patients with a low EF with the results of the surgical data regarding those with a low EF remain unclear.

Major advances in medical therapy for coronary artery disease and LV dysfunction have been made during the period since these trials were conducted. In particular, angiotensin-converting enzyme inhibition and β blockade are associated with significant improvement in survival,^{17–20} and a high proportion of OAT patients received these medications. It is therefore possible that revascularization is less important with a low EF in a background of intensive medical therapy. In patients with a higher EF, PCI of the IRA resulted in lower rates of angina and less need for subsequent revascularization; however, no statistically significant interaction was found between PCI and EF on angina, and the interaction between PCI and EF on subsequent revascularizations (likely angina driven) was statistically borderline. The lack of benefit of PCI compared to optimal medical therapy in the subset of 406 patients with an EF <50% in the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial²¹ is consistent with the results of the present analysis, although it must be recognized in both cases that the number of patients with severely decreased EF was relatively small. Whether

a revascularization benefit will emerge after 5 years is unknown and awaits the completion of the long-term follow-up phase of the OAT.

We found a numeric trend toward greater benefit related to a reduction of subsequent coronary revascularization derived from PCI in patients with a higher EF. These findings are in contrast to the hypothesis that patients with the lowest EF would derive the greatest benefit. These observations would support a hypothesis that restoration of direct blood flow in the IRA late after AMI is more often required in patients with more viable myocardium.

Although prespecified, the main limitations of the present analysis were those related to all secondary analyses, including multiplicity, smaller size, and confounding. To compensate for these limitations, the OAT protocol predefined the statistical models with careful control for the type I error rate to be applied in the secondary analyses, and multivariate adjustment was performed. Although the number of patients with a low EF was far larger than in many previous studies,^{22–26} 743 patients afforded only modest power to detect differences. These results are only applicable to patients who would have qualified for inclusion into the OAT. Thus, the results do not apply to patients with severe heart failure, electrical instability, angina at rest, severe inducible ischemia after myocardial infarction or patients undergoing revascularization for chronic total occlusion.

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Figure 1.

Occurrence of study outcomes as function of LVEF (Cox regression analysis) for 5 years of follow-up for patients treated with mechanical recanalization of IRA (PCI) or medical treatment alone (MED). (A) Primary composite event of death, myocardial infarction, and New York Heart Association class IV heart failure, (B) death, (C) myocardial infarction, (D) congestive heart failure class IV. PCI group versus medical group hazard ratio and 99% confidence interval determined using model adjusting for EF.

Table 1Baseline clinical characteristics by low ($\leq 44\%$) and higher ($>44\%$) left ventricular (LV) ejection fraction (EF)

Variable	Low EF ($\leq 44\%$; n = 743)	Higher EF ($>44\%$; n = 1,442)	p Value
Ejection fraction (%)	37.0 (31–41)	53.0 (49–58)	
Age (10 years)	5.9 (5.1–6.7)	5.8 (5–6.7)	0.07
Men	577 (77.7%)	1,125 (78.0%)	0.85
White	574 (77.3%)	1,175 (81.5%)	0.02
Diabetes mellitus	204 (27.5%)	247 (17.1%)	<0.0001
Angina pectoris	174 (23.4%)	317 (22.0%)	0.45
Myocardial infarction	106 (14.3%)	137 (9.5%)	0.0008
Hypertension	373 (50.2%)	689 (47.8%)	0.28
New York Heart Association >I before index acute myocardial infarction or at randomization	213 (28.7%)	243/1,441 (16.9%)	<0.0001
Cerebrovascular disease	20 (2.7%)	61 (4.2%)	0.07
Peripheral vascular disease	30 (4.0%)	53/1,440 (3.7%)	0.68
Renal insufficiency	12 (1.6%)	17 (1.2%)	0.40
Congestive heart failure	34 (4.6%)	18/1,440 (1.3%)	<0.0001
Percutaneous coronary revascularization	47 (6.3%)	58 (4.0%)	0.02
Hypercholesterolemia*	372/742 (50.1%)	758 (52.6%)	0.28
Family history of coronary disease before age 55 in first-degree relative	280 (37.7%)	599 (41.5%)	0.08
Current cigarette smoker	275 (37.0%)	578 (40.1%)	0.16
Killip class >I	213/741 (28.7%)	200/1,435 (13.9%)	<0.0001
Heart rate $\dot{f}$ (10 beats/min)	7.5 (6.7–8.2)	7.0 (6.2–7.7)	<0.0001
Systolic blood pressure $\dot{f}$ (10 mm Hg)	11.8 (10.6–13)	12.0 (11–13)	0.0003
Diastolic blood pressure $\dot{f}$ (10 mm Hg)	7.0 (6.2–8)	7.0 (6.4–8)	0.12
Pulse pressure $\dot{f}$ (10 mm Hg)	4.5 (4.0–5.5)	5.0 (4–5.8)	0.0003
Glomerular filtration rate $\dot{f}$ (10 ml/min/1.73 m ²)	7.8 (6.5–9.1)	7.9 (6.7–9.3)	0.03
Glucose $\dot{f}$ (10 mg/dl)	11.2 (9.7–14.2)	10.5 (9.4–12.4)	<0.0001
Body mass index $\dot{f}$ (10 kg/m ²)	2.8 (2.5–3.1)	2.8 (2.5–3.1)	0.88
Index event			
Rales	77 (10.4%)	59/1,438 (4.1%)	<0.0001
New Q waves	526 (70.8%)	941 (65.3%)	0.009
ST elevation	555/723 (76.8%)	843/1,387 (60.8%)	<0.0001
ST elevation or new Q waves	659 (88.7%)	1,171 (81.2%)	<0.0001
Thrombolytic in first 24 hours	169 (22.7%)	248/1,441 (17.2%)	0.002
Interval to index acute myocardial infarction (days)	9 (5–17)	8.0 (5–16)	0.43
Culprit left anterior descending artery	436 (58.7%)	351 (24.3%)	<0.0001
Any collaterals	623/734 (84.9%)	1,287/1,423 (90.4%)	0.0001
Multivessel coronary disease	162/737 (22.0%)	212/1,430 (14.8%)	<0.0001
Medications at hospital discharge			

Variable	Low EF ($\leq 44\%$; n = 743)	Higher EF ($> 44\%$; n = 1,442)	p Value
Long-acting nitrate	159 (21.4%)	338 (23.4%)	0.28
Sublingual nitrate	197 (26.5%)	450 (31.2%)	0.02
β Blocker	655 (88.2%)	1,263 (87.6%)	0.70
Calcium channel blocker	40 (5.4%)	89 (6.2%)	0.46
Aspirin	706 (95.0%)	1,384 (96.0%)	0.30
Ticlopidine or clopidogrel	454 (61.1%)	866 (60.1%)	0.64
Warfarin (Coumadin)	139 (18.7%)	75 (5.2%)	<0.0001
Digoxin	51 (6.9%)	10 (0.7%)	<0.0001
Diuretics	216 (29.1%)	153 (10.6%)	<0.0001
Spironolactone	78 (10.5%)	46 (3.2%)	<0.0001
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker	662 (89.1)	1,096 (76.0)	<0.0001
Insulin	71 (9.6%)	66 (4.6%)	<0.0001
Oral hypoglycemic	136 (18.3%)	160 (11.1%)	<0.0001
Lipid-lowering agent	572 (77.0%)	1,202 (83.4%)	0.0003
Antiarrhythmic agent	51 (6.9%)	31 (2.1%)	<0.0001

Data are presented as frequencies (%) for categorical variables and as median (interquartile range) for continuous variables.

Denominators less than full subgroup indicate missing values for categorical variables.

* Hypercholesterolemia defined as previous diagnosis of hypercholesterolemia or previously treated with lipid-lowering agent or having fasting low-density lipoprotein cholesterol ≤ 130 mg/dl or total cholesterol ≥ 200 mg/dl.

[†] Missing values for continuous variables include glomerular filtration rate, 40 patients; glucose, 67 patients; heart rate, 3 patients; systolic blood pressure, 2 patients; diastolic blood pressure, 2 patients; pulse pressure, 2 patients; body mass index, 16 patients.

EF = ejection fraction.

Table 2

Assigned PCI procedural variables and outcomes stratified by low ($\leq 44\%$) and higher ($>44\%$) left ventricular (LV) ejection fraction (EF)

Variable	EF		p Value
	$\leq 44\%$ (n = 390)	$>44\%$ (n = 704)	
Infarct-related artery			<0.0001
Left anterior descending	215 (55.1%)	168 (23.9%)	
Circumflex	57 (14.6%)	118 (16.8%)	
Right	118 (30.3%)	418 (59.4%)	
Pre-PCI TIMI grade flow			0.18
0	317/386 (82.1%)	578/698 (82.8%)	
1	64/386 (16.6%)	118/698 (16.9%)	
2	3/386 (0.8%)	2/698 (0.3%)	
3	2/386 (0.5%)	0/698 (0.0%)	
Post-PCI TIMI grade flow			0.0002
0	54/379 (14.2%)	50/690 (7.2%)	
1	12/379 (3.2%)	16/690 (2.3%)	
2	27/379 (7.1%)	30/690 (4.3%)	
3	286/379 (75.5%)	594/690 (86.1%)	
2 or 3	313/379 (82.6%)	624/690 (90.4%)	0.0002
Collaterals			
Any collaterals	320/385 (83.1%)	628/695 (90.4%)	0.0005
0	65/385 (16.9%)	67/695 (9.6%)	<0.0001
1	280/385 (72.7%)	494/695 (71.1%)	
2	40/385 (10.4%)	134/695 (19.3%)	

Denominators less than full subgroup indicate missing values for categorical variables.

PCI = percutaneous coronary intervention; TIMI = thrombolysis in myocardial infarction; other abbreviations as in Table 1.

Table 3

Life table for 5-year outcomes in low ($\leq 44\%$) and higher ($> 44\%$) left ventricular (LV) ejection fraction (EF)

Variable	EF		Hazard Ratio (99% Confidence Interval)		
	$\leq 44\%$ (n = 743)	$> 44\%$ (n = 1,442)	Unadjusted	Adjusted*	p Value
Composite (primary) outcome	26.3%	13.2%	2.33 (1.74–3.13)	1.97 (1.46–2.67)	<0.0001
Death	18.4%	8.5%	2.44 (1.66–3.57)	2.00 (1.35–2.97)	<0.0001
Fatal or nonfatal reinfarction	6.7%	5.7%	1.33 (0.80–2.23)	1.18 (0.69–2.00)	0.42
NYHA IV heart failure	8.9%	2.6%	3.86 (2.17–6.86)	3.0 (1.66–5.42)	<0.0001
NYHA III/IV HF	11.8%	3.1%	3.99 (2.42–6.55)	3.21 (1.93–5.35)	<0.0001
Death or nonfatal reinfarction	23.1%	12.7%	2.05 (1.49–2.81)	1.72 (1.24–2.39)	<0.0001
Death or NYHA IV HF	22.2%	9.7%	2.68 (1.91–3.74)	2.19 (1.55–3.09)	<0.0001
Stroke	1.9%	1.8%	1.06 (0.42–2.64)	0.99 (0.39–2.53)	0.98
Revascularization	20.7%	20.6%	1.04 (0.79–1.38)	1.03 (0.77–1.36)	0.82
Angina pectoris	43.7%	39.6%	1.11 (0.91–1.35)	1.08 (0.88–1.32)	0.32

* Adjusted for variables predictive of primary outcome.

HF = congestive heart failure; other abbreviations as in Table 1.

Table 4

Life table for 5-year outcomes by study treatment assignment for low ($\leq 44\%$) and higher ($>44\%$) left ventricular (LV) ejection fraction (EF)

Variable	Low EF ($\leq 44\%$)				Higher EF ($>44\%$)				Interaction p Value
	PCI (n = 390)	MED (n = 353)	HR (99% CI)	p Value	PCI (n = 704)	MED (n = 738)	HR (99% CI)	P Value	
Composite (primary) outcome	28.8%	23.5%	1.25 (0.83–1.88)	0.17	13.7%	12.9%	0.98 (0.64–1.50)	0.92	0.30
Death	19.3%	17.5%	1.11 (0.66–1.87)	0.62	7.6%	9.3%	0.81 (0.46–1.43)	0.35	0.30
Fatal or nonfatal reinfarction	8.8%	4.5%	2.02 (0.85–4.80)	0.04	6.1%	5.4%	1.06 (0.56–2.01)	0.82	0.12
NYHA IV HF	9.5%	8.1%	1.10 (0.55–2.18)	0.73	2.5%	2.6%	0.75 (0.29–1.92)	0.43	0.40
NYHA III/IV HF	12.9%	10.5%	1.19 (0.66–2.15)	0.44	2.2%	4.0%	0.54 (0.23–1.26)	0.06	0.05
Death or nonfatal reinfarction	25.3%	20.6%	1.33 (0.84–2.10)	0.11	12.8%	12.6%	0.98 (0.63–1.54)	0.93	0.23
Death or NYHA IV HF	23.7%	20.5%	1.11 (0.71–1.74)	0.55	9.5%	9.9%	0.85 (0.51–1.40)	0.40	0.38
Stroke	1.2%	2.7%	0.46 (0.09–2.21)	0.20	1.9%	1.6%	1.14 (0.39–3.35)	0.75	0.22
Revascularization	22.3%	19.1%	1.05 (0.67–1.66)	0.77	17.8%	23.3%	0.69 (0.50–0.96)	0.004	0.05
Angina pectoris	41.5%	46.0%	0.83 (0.60–1.14)	0.12	35.2%	43.9%	0.74 (0.59–0.93)	<0.001	0.46

CI = confidence interval; HF = congestive heart failure; HR = hazard ratio; other abbreviations as in Table 1.