

ORIGINAL ARTICLE

Quality of Life after Late Invasive Therapy for Occluded Arteries

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ABSTRACT

BACKGROUND

From the Outcomes Research Group (D.B.M., W.P., N.E.C.-C., K.J.A., P.A.C., L.D.R.), Duke Clinical Research Institute, and the Departments of Medicine (D.B.M.) and Biostatistics and Bioinformatics (W.P., K.J.A.) — all at Duke University Medical Center, Durham, NC; the University Health Network, University of Toronto (J.R.R.), and the Sunnybrook Health Sciences Centre (E.A.C.) — both in Toronto; Vancouver General Hospital, Vancouver, BC, Canada (R.S.F.); Waikato Hospital, Hamilton, New Zealand (G.P.D.); Cardiac Diagnostic Associates, York, PA (C.E.M.); the Department of Internal Medicine II, Medical University of Vienna, Vienna (C.A.); the Columbia University Division of Cardiology, Mt. Sinai Medical Center, Miami Beach, FL (G.A.L.); and the New York University School of Medicine, New York (J.S.H.).

The open-artery hypothesis postulates that late opening of an infarct-related artery after myocardial infarction will improve clinical outcomes. We evaluated the quality-of-life and economic outcomes associated with the use of this strategy.

METHODS

We compared percutaneous coronary intervention (PCI) plus stenting with medical therapy alone in high-risk patients in stable condition who had a totally occluded infarct-related artery 3 to 28 days after myocardial infarction. In 951 patients (44% of those eligible), we assessed quality of life by means of a battery of tests that included two principal outcome measures, the Duke Activity Status Index (DASI) (which measures cardiac physical function on a scale from 0 to 58, with higher scores indicating better function) and the Medical Outcomes Study 36-Item Short-Form Mental Health Inventory 5 (which measures psychological well-being). Structured quality-of-life interviews were performed at baseline and at 4, 12, and 24 months. Costs of treatment were assessed for 458 of 469 patients in the United States (98%), and 2-year cost-effectiveness was estimated.

RESULTS

At 4 months, the medical-therapy group, as compared with the PCI group, had a clinically marginal decrease of 3.4 points in the DASI score ($P=0.007$). At 1 and 2 years, the differences were smaller. No significant differences in psychological well-being were observed. For the 469 patients in the United States, cumulative 2-year costs were approximately \$7,000 higher in the PCI group ($P<0.001$), and the quality-adjusted survival was marginally longer in the medical-therapy group.

CONCLUSIONS

PCI was associated with a marginal advantage in cardiac physical function at 4 months but not thereafter. At 2 years, medical therapy remained significantly less expensive than routine PCI and was associated with marginally longer quality-adjusted survival. (ClinicalTrials.gov number, NCT00004562.)

N Engl J Med 2009;360:774-83.

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DESPITE THE WIDESPREAD AVAILABILITY of several effective reperfusion strategies, at least one third of hospitalized patients with acute myocardial infarction have persistent occlusion of the infarct-related artery after 72 hours. Consequently, clinicians and researchers have had great interest in the possibility that some of the benefits seen with early opening of the infarct-related artery could be achieved with later opening. Data from experimental studies, observational studies, and small clinical trials have provided support for the open-artery hypothesis, which postulates that late opening of occluded infarct-related arteries after acute myocardial infarction may improve survival (because of lower risks of heart failure and sudden death from cardiac causes), ventricular function (through both revascularization of hibernating myocardium and improved remodeling after myocardial infarction), and quality of life.¹

To assess this hypothesis, we conducted the Occluded Artery Trial (OAT), which compared PCI with medical therapy alone in 2166 patients who had an occluded infarct-related artery 3 to 28 days after a myocardial infarction. Eligible patients were in stable condition and had occlusion of the proximal portion of an infarct-related artery with a large region at risk, an ejection fraction below 50%, or both.² Patients were randomly assigned to optimal medical therapy alone or to optimal medical therapy plus percutaneous coronary intervention (PCI) with coronary stenting. We previously reported that the rate of the primary outcome of the trial — the composite of death, reinfarction, or hospital treatment for class IV heart failure — did not differ significantly between the PCI and medical-therapy groups at 4 years (17.2% and 15.6%, respectively; hazard ratio with PCI, 1.16; $P=0.20$).² Significantly fewer patients in the PCI group had angina (a secondary end point) at 4 months and 1 year; by 3 years, the rates of angina in the two groups were similar. In this article, we describe the effects of the two treatment strategies on the economic and quality-of-life outcomes for patients in OAT.

METHODS

QUALITY-OF-LIFE DATA COLLECTION

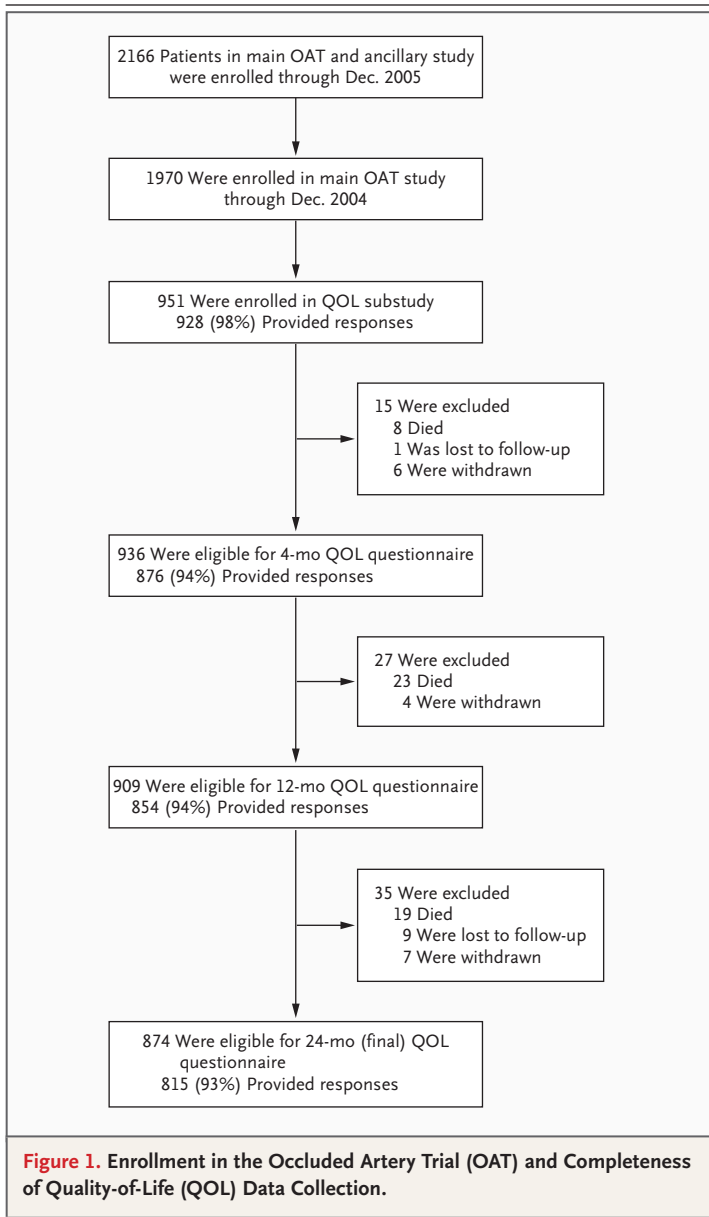
The initial study plan was for all patients to be enrolled in North America; all U.S. patients were to be included in the economic substudy, and both

U.S. and Canadian patients were to be included in the quality-of-life substudy. Of the countries subsequently added to meet enrollment goals, four (Latvia, New Zealand, Poland, and Russia) agreed to participate in the quality-of-life substudy. Because of funding issues, enrollment in the economic and quality-of-life substudies ended as planned in December 2004, when enrollment in OAT had reached 1970 patients (Fig. 1). Of those 1970 patients, 951 were enrolled in the quality-of-life substudy. Enrollment in the parent trial continued for 1 additional year, with a total sample of 2166 patients.²

The trial was supported by the National Heart, Lung, and Blood Institute. Companies that provided financial support, products, or both had no role in the study design, analysis, or interpretation of the results or in the decision to submit the manuscript for publication. All patients provided written informed consent. The institutional review board or ethics committee at each site approved the study protocol. Baseline quality-of-life questionnaires were administered after written informed consent had been obtained and before randomization and treatment. Follow-up structured interviews were administered 4 months, 12 months, and 24 months after randomization. Site coordinators, who had been trained by the coordinating center, conducted all interviews during a clinic visit or by telephone if a clinic visit was missed. From a total of 3670 expected patient contacts over four interviews, 3473 quality-of-life questionnaires (95%) were collected; 1% of the questionnaires collected were incomplete, and 4% of the questionnaires were shortened proxy forms used for patients who were unable to participate in the full interview (e.g., because of illness or incapacity).

QUALITY-OF-LIFE MEASURES

Two principal quality-of-life measures were prespecified: the Duke Activity Status Index (DASI)³ and the Medical Outcomes Study 36-Item Short-Form (SF-36) Mental Health Inventory 5 (MHI-5).⁴ The DASI is a questionnaire-based analogue of the cardiopulmonary exercise test and is used to assess cardiac-related functional status.³ Scores range from 0 to 58, with higher scores indicating better function and greater ability to perform physical activities in 12 domains without difficulty or assistance. A difference of 4 points or more is considered to be clinically significant.⁵



The inclusion in the study of 40 non-English-speaking patients outside North America made it necessary to identify a quality-of-life instrument that already had validated translations; the SF-36 physical-function scale was used for these patients rather than the DASIS.⁴ This generic scale assesses the ability to engage in 10 sets of physical activities; these activities overlap substantially with those assessed in the DASIS, although the scoring method is different. One-to-one imputation methods were used to transform the SF-36 physical-function subscales into corresponding

DASIS values. Since comparisons according to treatment were unaffected by whether these imputed values were included or excluded, the imputed values are included in this article.

The MHI-5 assesses psychological well-being, including both depression and anxiety.⁴ It is scored from 0 to 100, with higher scores indicating better function. A clinically significant difference in the MHI-5 score is approximated as one quarter of 1 SD, or approximately 5 points in this study.

Seven additional scales from the SF-36 were used to assess role function (both physical and emotional limitations), general health perceptions, bodily pain, social function, vitality, and health transitions (changes in health status). Each scale is scored separately and is customarily transposed to a scale from 0 to 100, with higher scores indicating better function and differences of 5 points or more considered to be clinically significant.

We assessed cardiac symptoms with the use of the Rose angina and dyspnea questionnaires.⁶ The Rose angina questionnaire consists of seven questions about the presence of chest pain and whether it is provoked by walking and relieved by rest. We classified angina as being present when patients reported symptoms consistent with the classic features of this condition. The Rose dyspnea questionnaire consists of four questions about dyspnea induced by progressively lower levels of exertion. We classified exertional dyspnea as being present when patients reported any effort-related dyspnea.

We used a short set of questions adapted from a previous randomized trial, the Bypass Angioplasty Revascularization Investigation, to assess employment status at baseline and during follow-up.⁷

The relative desirability (utility) of each patient's health status was assessed with the use of the time-trade-off method. Patients were asked in a series of questions how much of a postulated life expectancy of 10 years in their current state of health they would be willing to trade in order to live the remaining years in excellent health.⁸ We also asked patients to rate their health on a scale of 0 to 100, with 0 indicating a state of health equivalent to being dead and 100 indicating excellent health; a difference of 5 points or more was considered to be clinically significant.

COST AND COST-EFFECTIVENESS ANALYSES

The economic substudy used data on the 469 patients in the trial who were enrolled in the United

States. For these patients, medical costs for up to 2 years were estimated with the use of a combination of hospital bills (for inpatient care) and Medicare fees (for physicians' fees and outpatient care). Data on hospital bills were collected for 458 U.S. patients (98%). Hospital charges on the UB92 hospital bill forms were converted to average hospital costs with the use of the Medicare conversion factors reported each year in each hospital's Medicare cost report.^{9,10} Physicians' fees were estimated from counts of major services provided by physicians and the Medicare fee schedule, as previously described.^{11,12} Costs were expressed in 2005 U.S. dollars. Follow-up costs after the first year were discounted at a 3% annual rate.

Costs incurred at non-OAT hospitals before randomization were presumed to be balanced by random assignments to the treatment groups, and data on these costs were not collected. By protocol, all enrolled patients underwent a diagnostic catheterization to confirm eligibility for the study.

Because the final results of OAT showed that PCI was not superior to medical therapy alone in reducing major cardiac events but that it had a small advantage with regard to freedom from angina in the early follow-up period, we performed a prespecified 2-year cost-effectiveness analysis to examine the relationship between incremental net health benefits (expressed in quality-adjusted life-years [QALYs]) and incremental costs associated with PCI. In each group, the observed survival was weighted with a utility or preference weight derived from empirically assessed time-trade-off data.

For a sensitivity analysis, we used the mean time-trade-off weights for angina according to the Canadian Cardiovascular Society (CCS) classification to assign utilities over the first 2 years of the study to surviving patients. Utility values were assigned at baseline and carried forward until the next available CCS reclassification (at 4, 12, or 24 months).

Cumulative 2-year QALYs and 2-year medical costs were aggregated according to treatment assignment, and the difference between treatments was calculated. The ratio of these two incremental quantities constituted the cost-effectiveness ratio. Bootstrap analysis of 1000 samples was used to generate a 95% confidence interval for the incremental 2-year costs and QALYs. Because there were no clear trends in the 2-year data and there was no evidence that PCI reduced major events, analyses of lifetime cost-effectiveness were not performed.

STATISTICAL ANALYSIS

Descriptive statistics included percentages for discrete variables and medians with interquartile ranges, means with standard deviations, or both for continuous variables. Comparisons were performed according to randomized treatment assignments. Univariate comparisons were performed with the use of the chi-square test for discrete variables and the Wilcoxon rank-sum test for continuous variables.

P values are reported without adjustment for multiple comparisons. We also calculated 95% confidence intervals for outcomes at each time point in the PCI group as compared with the medical-therapy group on the basis of the t distribution.

RESULTS

STUDY POPULATION

Of the 2166 patients enrolled in OAT, 1970 were enrolled by the end of 2004, and 951 of these patients (48%) were enrolled in the quality-of-life substudy (Fig. 1). Although the patients in the substudy were generally representative of the overall OAT population, the quality-of-life sample had slightly higher proportions of minorities and patients with a history of infarction, heart failure, or hypercholesterolemia (Table 1). Within the quality-of-life substudy, the two treatment groups were well balanced; only 1 of 18 baseline comparisons (history of cerebrovascular disease) had a nominally significant P value (Table 2).

QUALITY-OF-LIFE OUTCOMES

The comparison of cardiac-related physical function according to treatment group (Table 3) showed similar scores at baseline and a 3.4-point lower DASI score (indicating more functional impairment) in the medical-therapy group than in the PCI group at 4 months (P=0.008). The mean between-group difference in the DASI score was 1.0 (P=0.36) at 12 months and 1.7 (P=0.29) at 24 months, with higher scores in the PCI group at both time points. Comparison of the SF-36 MHI-5 scores did not show either statistically or clinically significant differences at any follow-up point (Table 3). No significant differences according to treatment were found in the other SF-36 subscale measurements (see Appendix A in the Supplementary Appendix, available with the full text of this article at NEJM.org).

Table 1. Baseline Characteristics of the Patients.*

Variable	Patients in Overall Study (N=1970)	Patients Not Participating in QOL Substudy (N=1019)	Patients Participating in QOL Substudy (N=951)	P Value†
Age — yr				
Mean	58.8±11.0	58.3±10.9	59.2±11.1	0.06
Median (interquartile range)	59.0 (51.0–67.0)	59.0 (51.0–68.0)	58.0 (50.0–67.0)	
Female sex — %	21.9	22.2	21.7	0.78
Nonwhite race — %‡	14.6	12.2	17.25	<0.001
Medical history — %				
Angina	23.0	23.4	22.6	0.66
Myocardial infarction	11.7	9.8	13.8	0.006
Cerebrovascular disease	3.6	3.0	4.3	0.11
Stroke	3.0	2.6	3.4	0.33
Peripheral vascular disease	3.9	3.4	4.5	0.21
Renal insufficiency	1.4	1.6	1.2	0.42
ICD	0.4	0.3	0.5	0.43
Congestive heart failure	2.5	1.4	3.6	0.002
PCI	4.9	4.0	5.9	0.06
Coronary-artery bypass grafting	0.4	0.1	0.7	0.03
Cardiac risk factors — %				
Diabetes	20.8	19.2	22.6	0.06
Hypercholesterolemia	55.8	52.6	59.4	0.004
Hypertension	48.8	47.8	49.8	0.37
Current smoker	39.3	41.5	36.9	0.001
NYHA class — %				<0.001
I	83.3	89.0	85.3	0.02
II	16.8	10.2	14.7	0.02

* Plus-minus values are means ±SD. ICD denotes implantable cardioverter-defibrillator, NYHA New York Heart Association, PCI percutaneous coronary intervention, and QOL quality of life.

† P values are for the comparison of the patients who participated in the QOL substudy with those who did not participate in the substudy.

‡ Race was self-reported.

At baseline, 26.3% of the patients in the medical-therapy group and 26.9% of those in the PCI group reported exertional angina in the month preceding the index myocardial infarction. At 4 months, 16.5% of the patients in the medical-therapy group and 10.3% of those in the PCI group reported angina ($P=0.01$), but the absolute difference in the percentages of patients reporting angina at 24 months was smaller (11.9% of patients in the medical-therapy group and 7.1% in the PCI group, $P=0.03$). At baseline, 46.7% of the patients in the medical-therapy group and 48.0% of those in the PCI group reported exertional

dyspnea; the respective proportions were 39.6% and 32.4% at 4 months ($P=0.04$), 40.2% and 30.7% at 12 months ($P=0.006$), and 35.3% and 28.5% at 24 months ($P=0.05$).

RESOURCE USE AND COSTS

Medical billing data were collected for 458 of the 469 patients in OAT who were enrolled in the United States (98%). Baseline characteristics were well balanced according to treatment assignment (data not shown). In the first 30 days after enrollment, patients in the PCI group stayed in the hospital on average 1.2 days longer than patients in

Table 2. Baseline Characteristics of the Patients in the Quality-of-Life Substudy According to the Intention-to-Treat Analysis.*

Variable	PCI Group (N=477)	Medical-Therapy Group (N=474)	P Value
Age — yr			0.50
Mean	59.5±10.9	59.0±11.3	
Median (interquartile range)	59.0 (52.0–68.0)	59.0 (51.0–68.0)	
Female sex — %	20.6	22.8	0.40
Nonwhite race — %†	16.8	17.7	0.13
Medical history — %			
Angina	22.3	22.8	0.86
Myocardial infarction	15.8	11.7	0.07
Cerebrovascular disease	5.7	3.0	0.04
Stroke	4.5	2.4	0.09
Peripheral vascular disease	5.7	3.2	0.07
Renal insufficiency	1.7	0.6	0.13
ICD	0.8	0.2	0.18
Congestive heart failure	4.0	3.2	0.51
PCI	5.9	5.9	1.00
Coronary-artery bypass grafting	0.8	0.6	0.71
Cardiac risk factors — %			
Diabetes	20.6	24.6	0.14
Hypercholesterolemia	59.8	58.9	0.78
Hypertension	50.4	49.3	0.72
Current smoker	35.1	38.8	0.36
NYHA class — %			0.53
I	88.2	86.7	
II	8.7	9.1	
III	1.3	2.5	
IV	1.9	1.7	

* Plus–minus values are means ±SD. ICD denotes implantable cardioverter–defibrillator, NYHA New York Heart Association, and PCI percutaneous coronary intervention.

† Race was self-reported.

the medical-therapy group (5.8 days vs. 4.6 days) (Table 4), with the difference reflecting differential stays in the intensive care unit (3.4 days vs. 2.6 days). In the U.S. cohort, 98% of patients assigned to PCI underwent the procedure, and 14% of patients in the medical-therapy group underwent PCI before discharge from the index hospital (the rate includes PCI for both infarct-related arteries and other vessels). The mean initial cost (total cost of hospital care and physicians' services for the first 30 days) was \$22,859 for the PCI group

as compared with \$12,683 for the medical-therapy group ($P<0.001$).

During the period from 31 days to 1 year after enrollment, 7% of patients in the PCI group and 10% of patients in the medical-therapy group underwent PCI. The mean number of hospital days during this period was 1.1 days in the PCI group and 1.9 days in the medical-therapy group, and the mean cost was \$3,414 in the PCI group and \$5,289 in the medical-therapy group ($P<0.001$). Discounted costs during year 2 were \$1,515 in the

PCI group and \$2,727 in the medical-therapy group (P=0.01).

COST-EFFECTIVENESS

The mean 2-year net cost in the PCI group was \$7,089. With the use of utility weights at 4, 12,

and 24 months (Appendix A in the Supplementary Appendix), the 2-year quality-adjusted survival was 1.42 years in the PCI group and 1.45 years in the medical-therapy group. In 1000 bootstrap repetitions, 89% of the samples had either lower costs and higher QALYs for medical therapy (62%) or a

Table 3. Selected Quality-of-Life Measures.*

Measure	PCI Group	Medical-Therapy Group	Difference, PCI vs. Medical Therapy (95% CI)
Score on Duke Activity Status Index			
Baseline			
No. of patients	429	436	
Median (interquartile range)	42 (18 to 58)	43 (19 to 58)	
Mean	36.3±19.7	37.3±19.6	-1.0 (-3.6 to 1.6)
4 mo			
No. of patients	407	412	
Median (interquartile range)	41 (19 to 58)	35 (16 to 51)	
Mean	36.8±19.3	33.3±19.2	3.4 (0.8 to 6.1)
12 mo			
No. of patients	400	409	
Median (interquartile range)	42 (19 to 58)	41 (17 to 58)	
Mean	37.0±20.0	36.0±20.1	1.0 (-1.8 to 3.8)
24 mo			
No. of patients	384	392	
Median (interquartile range)	42 (20 to 58)	40 (17 to 58)	
Mean	37.1±19.5	35.4±20.2	1.7 (-1.1 to 4.5)
Score on Mental Health Inventory 5			
Baseline			
No. of patients	443	446	
Median (interquartile range)	80 (64 to 88)	76 (60 to 88)	
Mean	74.7±18.6	72.6±19.3	2.1 (-0.4 to 4.6)
4 mo			
No. of patients	413	420	
Median (interquartile range)	84 (64 to 92)	80 (64 to 92)	
Mean	77.2±18.5	75.7±18.9	1.5 (-1.0 to 4.1)
12 mo			
No. of patients	408	406	
Median (interquartile range)	80 (68 to 92)	84 (64 to 92)	
Mean	77.4±18.5	77.0±18.9	0.4 (-2.2 to 3.0)
24 mo			
No. of patients	386	387	
Median (interquartile range)	84 (68 to 92)	80 (65 to 92)	
Mean	78.7±17.5	76.9±17.6	1.8 (-0.7 to 4.3)

Table 3. (Continued.)

Measure	PCI Group	Medical-Therapy Group	Difference, PCI vs. Medical Therapy (95% CI)
Exertional angina, Rose questionnaire			
Baseline			
Patients — no.	400	405	
Patients with angina — %	26.3	26.9	-0.7 (-6.8 to 5.4)
4 mo			
Patients — no.	398	405	
Patients with angina — %	10.3	16.5	-6.2 (-10.9 to -1.6)
12 mo			
Patients — no.	395	393	
Patients with angina — %	10.4	12.5	-2.1 (-6.5 to 2.4)
24 mo			
Patients — no.	379	379	
Patients with angina — %	7.1	11.9	-4.8 (-8.9 to -0.6)
Exertional dyspnea, Rose questionnaire			
Baseline			
Patients — no.	422	423	
Patients with dyspnea — %	46.7	48.0	-1.3 (-8.0 to 5.4)
4 mo			
Patients — no.	395	394	
Patients with dyspnea — %	32.4	39.6	-7.2 (-13.9 to -0.5)
12 mo			
Patients — no.	388	383	
Patients with dyspnea — %	30.7	40.2	-9.5 (-16.3 to -2.8)
24 mo			
Patients — no.	369	368	
Patients with dyspnea — %	28.5	35.3	-6.9 (-13.6 to -0.2)

* Plus-minus values are means ±SD. Primary quality-of-life measures were the score on the Duke Activity Status Index (on a scale from 0 to 58, with higher scores indicating better function) and the score on the Medical Outcomes Study 36-Item Short-Form Mental Health Inventory 5 (on a scale from 0 to 100, with higher scores indicating better function). Cardiac symptoms were assessed with the use of the Rose angina and dyspnea questionnaires, which consisted of questions that have yes-or-no answers.⁶ PCI denotes percutaneous coronary intervention.

cost-effectiveness ratio of more than \$100,000 per QALY for PCI versus medical therapy (27%). When we applied time-trade-off weights to the CCS empirical data for each treatment group and time point and recalculated the cost-effectiveness ratios, 94% of the bootstrap samples had either both lower costs and higher QALYs for medical therapy (70%) or a cost-effectiveness ratio of more than \$100,000 per QALY for PCI (24%).

For the sensitivity analysis, we used a regression model to develop cost weights from the U.S.

cost data for the entire cohort of 1970 patients in OAT. On the basis of this analysis, the estimated 2-year incremental cost of PCI was \$9,945, and only 1 of 1000 bootstrap cost-effectiveness ratios for PCI as compared with medical therapy was less than \$100,000 per QALY.

DISCUSSION

Our study showed that, as compared with medical therapy alone, late PCI of occluded infarct-

Table 4. Resource Use in the U.S. Economic Substudy Cohort.*

Variable	PCI (N=232)	Medical Therapy (N=226)
0–30 days		
Mean length of stay — days	5.8	4.6
Procedure — %		
CABG	0.4	0.0
ICD	2.6	0.9
Cardiac catheterization	100.0	92.0
PCI	97.8	14.2
31 days–4 mo		
Mean length of stay — days	0.6	0.7
Procedure — %		
CABG	1.3	0.9
ICD	1.7	1.3
Cardiac catheterization	5.2	5.8
PCI	2.6	5.3
4 mo, 1 day–12 mo		
Mean length of stay — days	0.5	1.2
Procedure — %		
CABG	1.7	0.9
ICD	0.9	0.0
Cardiac catheterization	7.8	6.6
PCI	3.9	4.4
12 mo, 1 day–24 mo		
Mean length of stay — days	0.5	0.8
Procedure — %		
CABG	0.9	1.8
ICD	0.9	0.9
Cardiac catheterization	4.3	4.4
PCI	1.3	1.8

* CABG denotes coronary-artery bypass grafting, ICD implantable cardioverter-defibrillator, and PCI percutaneous coronary intervention.

related arteries provided a marginal clinical advantage with regard to cardiac physical function at 4 months that was not sustained. In addition, medical therapy alone resulted in both lower cumulative medical costs and higher quality-adjusted life expectancy at 2 years, with no empirical trends suggesting that longer-term follow-up might reveal a reversal of these patterns. Combined with the previously reported lack of advantage of PCI with respect to the primary end point of the OAT, these data do not provide support for the com-

mon practice of routine PCI in patients in stable condition after myocardial infarction with an occluded infarct-related artery.²

Additional quality-of-life comparisons showed only that fewer patients who underwent PCI had exertional angina and dyspnea at 4 months and that the between-group difference in the proportion of patients reporting angina was attenuated by 12 months, whereas the difference in the proportion of patients reporting dyspnea was sustained through 24 months. The clinical significance of these subjective differences in angina and dyspnea is unclear since, except at the 4-month follow-up, they did not affect the activities that patients reported they were able to perform.

Comparison of our results with those of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial is instructive.¹³ In the COURAGE trial, which enrolled patients with stable coronary disease, routine PCI resulted in small incremental benefits with regard to both angina and physical limitations at 3 months, as compared with medical therapy alone. By 12 months, the difference in physical limitations was no longer significant, and the difference in angina was about 50% smaller. In the Trial of Invasive versus Medical Therapy in Elderly Patients (TIME), which enrolled elderly patients (mean age, 80 years) with refractory angina,¹⁴ there was improvement in both treatment groups during the first 6 months, but the group of patients who received invasive treatment had greater improvements with regard to angina and general health perceptions. At a median of 3.1 years, however, the advantage of the invasive treatment had disappeared.¹⁵

Thus, our study adds to the evidence that in a variety of clinical situations involving patients with coronary artery disease in stable condition, a strategy of routine revascularization adds only a modest early advantage with regard to symptoms and functional status, and this advantage is not maintained. Given that this modest quality-of-life benefit was obtained at a cost of more than \$7,000 per patient, our cost-effectiveness analysis showed that this strategy was not economically attractive. The analysis of lifetime cost-effectiveness in the COURAGE trial had similar results, with an estimated cost per additional QALY with PCI as compared with medical therapy alone of approximately \$168,000.¹⁶

Several caveats apply to our work. First, samples in both the quality-of-life and economic substudies were considerably smaller than initially planned because of the enrollment of patients outside North America in the parent study. Although the sample in the quality-of-life substudy differed from the main OAT population with regard to some baseline measures, the differences were clinically small and unlikely to have affected our conclusions. A sensitivity analysis for the economic substudy suggested that a substantively different result would have been unlikely even if we had included all patients in the OAT in the analysis. Because treatment was not blinded, we cannot rule out biases in quality-of-life responses and changes in patterns of care resulting from knowledge of the treatment assignment.

In summary, PCI of a persistently occluded infarct-related artery 3 to 28 days after infarction provided clinically marginal improvement in physical function, as compared with medical therapy alone, but this effect was not sustained at 1 year or later. In addition, PCI was more expensive than medical therapy alone at 2 years, and the small benefits observed with regard to symptoms were insufficient to make PCI an economically attrac-

tive strategy for patients who were eligible for this study.

Supported by grants from the National Heart, Lung, and Blood Institute (U01-HL062257, to Dr. Mark; and U01-HL062509, to Dr. Hochman). Eli Lilly donated replacement doses of abciximab (ReoPro) and funding for meetings (in 2001, 2002, and 2006); Guidant donated stent reimbursement for one site and stents for OAT sites; Medtronic (Canada) donated stents for the Canadian sites; Merck donated funding for training meetings; and Millennium Pharmaceuticals and Schering-Plough donated replacement doses of eptifibatid (Integrilin).

Dr. Mark reports receiving lecture fees and grant support from Medtronic; Dr. Anstrom, grant support from Eli Lilly, Pfizer, and Medtronic Vascular; Dr. Cowper, grant support from CV Therapeutics, Eli Lilly, United Healthcare, and Pfizer; and Dr. Hochman, grant support from Eli Lilly and Bristol-Myers Squibb Medical Imaging product donations from Millennium Pharmaceuticals, Schering-Plough, Guidant, and Merck, consulting fees from Bristol-Myers Squibb, and honoraria from CV Therapeutics, Eli Lilly, GlaxoSmithKline, and Schering-Plough. No other potential conflict of interest relevant to this article was reported.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National, Heart, Lung, and Blood Institute or the National Institute of Health. We thank Jason Blevins for coordinating the economic and quality-of-life outcomes study; Heather Read for collecting the economic data; Judith Stafford for preparing the data for analysis; Melanie R. Daniels for editing an earlier version of the manuscript; the OAT site coordinators, who worked to collect the data for this study; and the OAT patients who volunteered to participate in the study.

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