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Impact of National Clinical Guideline Recommendations for Revascularization of Persistently Occluded Infarct-Related Arteries on Clinical Practice in the United States

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Background: The Occluded Artery Trial (OAT) was a large, randomized controlled trial published in 2006 that demonstrated no benefit to routine percutaneous coronary intervention (PCI) of persistently totally occluded infarct-related arteries (IRA) identified a minimum of 24 hours (on calendar days 3-28) after myocardial infarction (MI). The purpose of this study was to determine the impact of OAT results and consequent change in guideline recommendations for PCI for treatment of persistently occluded IRAs.

Methods: We identified all patients enrolled in the CathPCI Registry, from 2005 to 2008, undergoing catheterization more than 24 hours after MI with a totally occluded native coronary artery and no major OAT exclusion criteria. We examined trends in monthly rates of PCI for occlusions after OAT publication and after guideline revisions. Because reporting of diagnostic catheterizations was not mandatory, we examined trends among hospitals in the highest quartile for reporting of diagnostic procedures.

Results: A total of 28 780 patient visits from 896 hospitals were included. Overall, we found no significant decline in the adjusted monthly rate of PCI of occlusions after publication of OAT (odds ratio [OR], 0.997; 95% confidence interval [CI], 0.989-1.006) or after guideline revisions (OR, 1.007; 95% CI, 0.992-1.022). Among hospitals consistently reporting diagnostic catheterizations, there was no significant decline after OAT publication (OR, 1.018; 95% CI, 0.995-1.042), and there was a trend toward decline after guideline revisions (OR, 0.963; 95% CI, 0.920-1.000).

Conclusion: These findings suggest that the results of OAT and consequent guideline revisions have not, to date, been fully incorporated into clinical practice in a large cross-section of hospitals in the United States.

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THE PURPOSE OF MAJOR CLINICAL trials is to establish a scientific basis for clinical practice. However, few trials are subjected to rigorous impact analyses. The Occluded Artery Trial (OAT) was a large, randomized controlled trial funded by the National Heart, Lung, and Blood Institute testing routine percutaneous recanalization of persistently totally occluded infarct-related arteries (IRAs) identified a minimum of 24 hours (on calendar days 3-28) after myocardial infarction (MI).¹ No reduction in death, reinfarction, or class IV heart failure was observed. These primary results

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informed 2007 updates of 3 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines (unstable angina and non-ST elevation MI [NSTEMI],

ST elevation MI [STEMI], and percutaneous coronary intervention [PCI]).²⁻⁴

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A bias favoring PCI for persistent IRA occlusion drove practice prior to the OAT and was supported by experimental and observational data.^{5,6} The OAT results provided

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objective evidence that the use of PCI did not lead to a reduction in clinical events and that the beneficial effect on angina and quality of life was small and not durable. Percutaneous coronary intervention was more

costly than optimal medical therapy alone; hence, these findings should have discouraged routine PCI in this setting.

The National Cardiovascular Data Registry (NCDR), Washington, DC, and its CathPCI Registry (version 3.0) offers an opportunity to measure the degree to which clinical trials affect US cardiology practice.⁷ The registry collected data on all PCI procedures at participating centers in 2004. We used these data to examine whether publication of OAT in December 2006, and the resultant change in the STEMI and NSTEMI guideline updates (published from August through December 2007) reduced the application of PCI for treatment of occluded IRAs identified at least 24 hours after MI.

METHODS

STUDY POPULATION AND DATA SOURCES

The cohort for this study was identified using the CathPCI Registry, version 3.0, data from 1042 hospitals across the US. Patients undergoing cardiac catheterization following an admission for STEMI or NSTEMI from January 1, 2005, through December 31, 2008, were eligible. We applied additional clinical criteria to define a population that reflected OAT eligibility.⁸ Patients were included if the interval from symptom onset to admission was greater than 24 hours or at least 2 calendar days separated admission from catheterization. The following exclusion criteria were applied: (1) congestive heart failure (CHF) on presentation, (2) cardiogenic shock or intra-aortic balloon pump placement prior to catheterization, (3) emergent or salvage catheterization, (4) facilitated or rescue PCI for STEMI, (5) coronary artery bypass grafting (CABG) during the catheterization admission, and (6) at least 50% left main stenosis or severe 3-vessel disease ($\geq 70\%$ stenosis in the left anterior descending, right, and either ramus or circumflex arteries).

Details of the CathPCI registry have been described previously.⁹ Systematic data entry, quality assurance, and auditing programs are used to ensure that only data meeting predetermined criteria for completeness and accuracy are entered into the database. The overall rate of missing data was less than 0.5% across all collected data elements, except for baseline creatinine (approximately 10% missing) and lesion length (approximately 2% missing).

The CathPCI Registry does not code specifically for the IRA. To identify all persistently occluded IRAs, all patients with a 100% native stenosis were initially captured. To minimize the capture of occlusions unrelated to the admission MI, we excluded those with prior CABG. To estimate the remaining number of included patients with occlusions unrelated to the acute MI, we examined the proportion of patients undergoing PCI of nonoccluded targets as well as temporal changes in the rate of nonoccluded PCI. The registry also does not specifically code for angina at rest or severe ischemia on noninvasive testing. We attempted to capture these OAT exclusion criteria by excluding patients who underwent emergent or salvage catheterization. The proportion of remaining patients with severe ischemia would not be expected to change dramatically over the time course of this study.

PRIMARY ANALYSIS

We examined trends in the monthly rate of PCI for occlusions after MI within and among all participating hospitals across the following time periods of interest: (1) prior to publication of the OAT (January 1, 2005, to November 30, 2006), (2) after simultaneous presentation and publication of the OAT but before revision of practice guidelines (December 1, 2006, to No-

vember 30, 2007), and (3) after revision of guidelines reflecting the OAT (December 1, 2007, to December 31, 2008). We adjusted for baseline differences between the time periods using covariates adapted from the validated mortality risk factors for the CathPCI database, which were also predictors of undergoing PCI for an occlusion.

PRINCIPAL SECONDARY ANALYSIS

Reporting of diagnostic-only cardiac catheterizations (ie, without PCI) is not mandatory in the CathPCI Registry, and incomplete reporting would lead to overestimation of PCI rates. In a prespecified secondary analysis, we examined trends in the monthly rate of PCI for occlusions among hospitals that consistently reported at least 3 times as many diagnostic catheterizations as catheterizations leading to PCI, corresponding to the top quartile among participating sites.

ADDITIONAL SECONDARY ANALYSES

Most patients enrolled in the OAT had STEMI/Q wave MI, and results may have been incorporated into practice differentially for patients with STEMI vs NSTEMI. Incorporation of the OAT results may also have been influenced by the type of hospital (university, government, or private) or insurance provider (government, commercial, health maintenance organization, or other). We examined trends in the rate of PCI for persistent occlusions among these additional subgroups.

The OAT excluded patients with severe heart failure (New York Heart Association [NYHA] Functional classifications 3 and 4).⁸ Since the registry does not reliably code for severity of heart failure on presentation, our primary analysis excluded patients presenting with any heart failure symptoms. In a supplementary analysis, however, we examined trends in the rate of PCI for occlusions among patients with CHF at presentation. All secondary analyses were prespecified.

STATISTICAL METHODS

Baseline characteristics across the time periods were compared using the χ^2 rank-based group means score test for categorical variables and the χ^2 rank correlation test for continuous or ordinal variables.

The crude proportion of PCI for occlusions identified after MI was compared across the 3 time periods of interest using the χ^2 rank-based group means score test. The additive spline transformation was used to fit the rate of occluded PCI over the procedure date based on the logistic model. Four knots were selected according to the 5%, 35%, 65%, and 95% quantiles. Evaluation of the trends in the monthly rate of PCI for occlusion within the time periods of interest and comparisons of trends between time periods was performed using a generalized estimating equation model that adjusted for differences in patient characteristics across time as well as for within-hospital clustering. Wald χ^2 tests were used to test the significance of time trends. The final model was adjusted for age, sex, insurance payer, prior MI, prior CHF, prior renal failure, cerebrovascular disease, prior PCI, peripheral vascular disease, chronic lung disease, STEMI at presentation, time from symptom onset to presentation, and number of diseased vessels. All statistical analyses were performed using SAS software (version 9.2; SAS Institute Inc, Cary, North Carolina).

RESULTS

From January 1, 2005, through December 31, 2008, the CathPCI Registry captured 670 043 laboratory visits, from

Table 1. Baseline Characteristics^a

Characteristic	No. (%)				P Value
	Total Cohort (n=28 780)	Catheterization Prior to OAT (n=11 083)	Catheterization Between OAT and Guidelines (n=7838)	Catheterization After Guidelines (n=9859)	
Baseline Characteristic					
Demographic					
Age, mean (SD), y	61.64 (13.34)	61.66 (13.26)	61.50 (13.43)	61.73 (13.37)	.96
Female sex	9268 (32.20)	3615 (32.62)	2503 (31.93)	3150 (31.95)	.29
BMI, mean (SD)	29.90 (6.64)	29.82 (6.60)	29.90 (6.66)	29.99 (6.66)	.04
Insurance payer					
Government	12 704 (44.14)	4964 (44.79)	3374 (43.05)	4366 (44.28)	<.001
Commercial	8649 (30.05)	3333 (30.07)	2407 (30.71)	2909 (29.51)	
HMO	3692 (12.83)	1495 (13.49)	990 (12.63)	1207 (12.24)	
Other	2696 (9.37)	933 (8.41)	782 (9.97)	981 (9.95)	
History					
MI	6719 (23.35)	2663 (24.03)	1787 (22.80)	2269 (23.01)	.17
PCI	6589 (22.89)	2311 (20.85)	1827 (23.31)	2451 (24.86)	<.001
CHF	1817 (6.31)	702 (6.33)	484 (6.18)	631 (6.40)	.71
Diabetes mellitus	8151 (28.32)	3117 (28.12)	2187 (27.90)	2847 (28.88)	.18
Presenting Characteristics					
ACS type					
NSTEMI	26 096 (90.67)	9854 (88.91)	7112 (90.74)	9130 (92.61)	<.001
STEMI	2684 (9.33)	1229 (11.09)	726 (9.26)	729 (7.39)	
STEMI receiving fibrinolysis	561 (1.95)	278 (2.51)	136 (1.74)	147 (1.49)	<.001
Ejection fraction, mean (SD)	49.21 (11.85)	49.25 (11.91)	49.25 (11.90)	49.14 (11.76)	.81
Positive results from noninvasive testing	15 731 (54.66)	6132 (55.33)	4250 (54.22)	5349 (54.25)	.11
Angiography					
Diseased vessels, No.					
1	12 621 (43.85)	4850 (43.76)	3466 (44.22)	4305 (43.67)	.19
2	14 351 (49.86)	5574 (50.29)	3865 (49.31)	4912 (49.82)	
3	1803 (6.26)	656 (5.92)	505 (6.44)	642 (6.51)	
Site of occlusion					
Proximal LAD	3159 (10.98)	1251 (11.29)	834 (10.64)	1074 (10.89)	.90
Mid/distal LAD	4647 (16.15)	1780 (16.06)	1289 (16.45)	1578 (16.01)	.50
Circumflex	8310 (28.87)	3155 (28.47)	2253 (28.74)	2902 (29.44)	.46
RCA	14 372 (49.94)	5570 (50.26)	3930 (50.14)	4872 (49.42)	.12
Ramus	555 (1.93)	201 (1.81)	154 (1.96)	200 (2.03)	<.001

Abbreviations: ACS, acute coronary syndrome; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CHF, congestive heart failure; HMO, health maintenance organization; LAD, left anterior descending; MI, myocardial infarction; NSTEMI, non-ST elevation MI; OAT, occluded artery trial; PCI, percutaneous coronary intervention; RCA, right coronary artery; STEMI, ST elevation MI.

^aPatients with missing data were excluded from this table; therefore, column numbers may not sum up to the total group number.

996 sites, of patients undergoing angiography at least 24 hours after MI. Of these, 28 780 patient visits from 896 hospitals met all inclusion and exclusion criteria (eFigure; <http://www.archinternmed.com>). Among the 896 hospitals, 631 (70.4%) contributed patients over the entire study period. Cardiac catheterization was performed prior to the OAT publication in 11 083 patients, after publication of the OAT but before the guideline revisions in 7838 patients, and after the guideline revisions in 9859 patients.

Comparison of the demographic and clinical characteristics of patients across the 3 time periods is presented in **Table 1**. The mean age of patients (range, 61.5-61.7 years) and the proportion of women (range, 31.9%-32.6%) were similar across the 3 time periods. Most patients presented with NSTEMI (90.7% overall), and this proportion increased over time ($P < .001$). Most patients had either 1-vessel disease (43.9%) or 2-vessel disease (49.9%).

The procedural characteristics among those patients undergoing PCI for total occlusion are presented in **Table 2**.

All patients undergoing PCI had thrombolysis in MI flows of 0 or 1. Multivessel PCI was performed in 12.5% of patients, and this rate decreased steadily over time ($P = .002$). Almost half the patients (48.9%) received 1 stent only, and 64.2% of patients received at least 1 drug-eluting stent (DES). The proportion of patients receiving DES decreased markedly over time, corresponding to a widely recognized reduction in DES use generally that followed reports of late and very late DES thrombosis.¹⁰ There were less procedural complications in the latter time periods, driven by decreased general and bleeding complications.

PRIMARY ANALYSIS

Overall, just over half of all patients with qualifying coronary occlusions (53.0%) underwent PCI targeting a total occlusion identified after MI. Overall, 25.3% of patients did not undergo PCI while 21.7% underwent PCI of nonoccluded targets only. There was no change in the rate of PCI for non-

Table 2. Procedural Characteristics of Percutaneous Coronary Intervention (PCI) for Persistent Total Occlusion After Myocardial Infarction (MI)

Procedural Characteristic	No. (%)				P Value
	Total Cohort (n=6231)	Catheterization Prior to OAT (n=2438)	Catheterization After OAT (n=1673)	Catheterization After Guidelines (n=2120)	
PCI characteristics					
Multivessel PCI	1903 (12.47)	800 (13.32)	525 (12.69)	578 (11.29)	.002
Stents, No.					
0	1806 (11.83)	634 (10.55)	503 (12.16)	669 (13.07)	<.001
1	7470 (48.94)	2900 (48.27)	2006 (48.50)	2564 (50.09)	
≥2	5987 (39.23)	2474 (41.18)	1627 (39.34)	1886 (36.84)	
Any DES implanted	9805 (64.24)	4778 (79.53)	2244 (54.26)	2783 (54.37)	<.001
Site of occlusion PCI					
Proximal LAD	1460 (9.57)	561 (9.34)	423 (10.23)	476 (9.30)	.43
Other LAD	2306 (14.67)	884 (14.71)	621 (15.01)	801 (15.65)	
RCA	6692 (42.83)	2707 (45.06)	1796 (43.42)	2189 (42.76)	
Left circumflex	4560 (29.19)	1766 (29.39)	1230 (29.74)	1564 (30.55)	
Ramus	245 (1.57)	90 (1.50)	66 (1.60)	89 (1.74)	
Lesion risk high ^a	8484 (55.59)	3338 (55.56)	2356 (56.96)	2790 (54.50)	.31
Postprocedural TIMI 3 flow	13 728 (89.94)	5376 (89.48)	3728 (90.14)	4624 (90.33)	.43
PCI complications					
General complication ^b	823 (2.86)	341 (3.08)	245 (3.13)	237 (2.41)	.005
Bleeding complication	594 (2.07)	262 (2.37)	161 (2.06)	171 (1.74)	.001
Vascular complication	160 (0.56)	68 (0.61)	46 (0.59)	46 (0.47)	.16
Any complication	1423 (4.95)	616 (5.97)	398 (5.08)	409 (4.15)	<.001
Death same day as procedure	31 (0.15)	15 (0.19)	7 (0.12)	9 (0.13)	.36

Abbreviations: DES, drug-eluting stent; LAD, left anterior descending; OAT, occluded artery trial; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction.

^aHigh-risk lesions had at least 1 of the following characteristics: length greater than 20 mm, excessive tortuosity of the proximal segment, extremely angulated segments, and inability to protect major side branches.

^bGeneral complications included periprocedural myocardial infarction, cardiogenic shock, congestive heart failure, cerebrovascular accident, tamponade, thrombocytopenia, contrast reaction, or renal failure.

occluded targets over the study period ($P=.18$). Changes in the unadjusted rate of PCI for occlusions identified after MI over time are depicted in **Figure 1**. The time from symptom onset to admission was less than 24 hours in 47.6% and greater than 24 hours in 47.5%. Those presenting within 24 hours had an interval between admission to angiography of at least 2 days, as per the inclusion criteria.

The crude rate of PCI for total occlusions was slightly but significantly lower after the publication of the OAT (52.8% vs 54.2% before publication) and dropped again after the guideline revisions (51.9%; $P<.001$ for comparison across all 3 groups). However, there was an unexpected peak in the rate of PCI for occlusions in March, 2006, 8 months prior to the presentation and publication of the OAT results. This peak substantially accounted for the observed decline in the crude rate of PCI in subsequent time periods.

To account for this peak in the examination of trends in PCI within the time periods, the first time period was divided into 2 at the peak rate of PCI for occlusions (January 2005 to March 2006 and April 2006 to November 2006). There was a significant decline in the adjusted rate of PCI for occlusions from the peak in March 2006 to the OAT publication (odds ratio [OR] for occluded PCI per 30-day increase in time, 0.976; 95% confidence interval [CI], 0.964-0.987). However, there was no significant further decline after publication of the OAT (OR, 0.997; 95% CI, 0.989-1.006) or after the guideline revisions (OR, 1.007; 95% CI, 0.992-1.022). There was no

difference in the adjusted monthly trends of occluded PCI between the time period after publication of the OAT and the time period after the guideline revisions ($P=.40$ for comparison of slopes) (**Table 3**).

PRINCIPAL SECONDARY ANALYSIS

Among hospitals with the highest quartile for reporting of diagnostic catheterizations (a ratio of diagnostic to PCI catheterizations of $\geq 3:1$), a total of 5542 patients with qualifying occlusions were included, of whom 41.9% did not receive PCI, 17.7% underwent PCI of a nonoccluded target only, and the remaining 40.4% underwent PCI of an occlusion. The crude rate of PCI for total occlusions declined significantly from 42.4% prior to the OAT to 39.9% after the OAT but before the guideline revisions, and to 38.5% after the guideline revisions ($P=.01$). After adjustment using the generalized estimating equation, there was no difference in the monthly rate of PCI for occlusions after publication of the OAT (OR, 1.018; 95% CI, 0.995-1.042). There was, however, a trend towards decline in the adjusted monthly rate of occluded PCI after the guideline revisions (OR, 0.963; 95% CI, 0.928-1.000).

ADDITIONAL SECONDARY ANALYSES

Overall, patients presenting with STEMI and NSTEMI were equally likely to undergo PCI for an occlusion (53.5% vs 53.0%, respectively; $P=.61$). Among the subgroup of

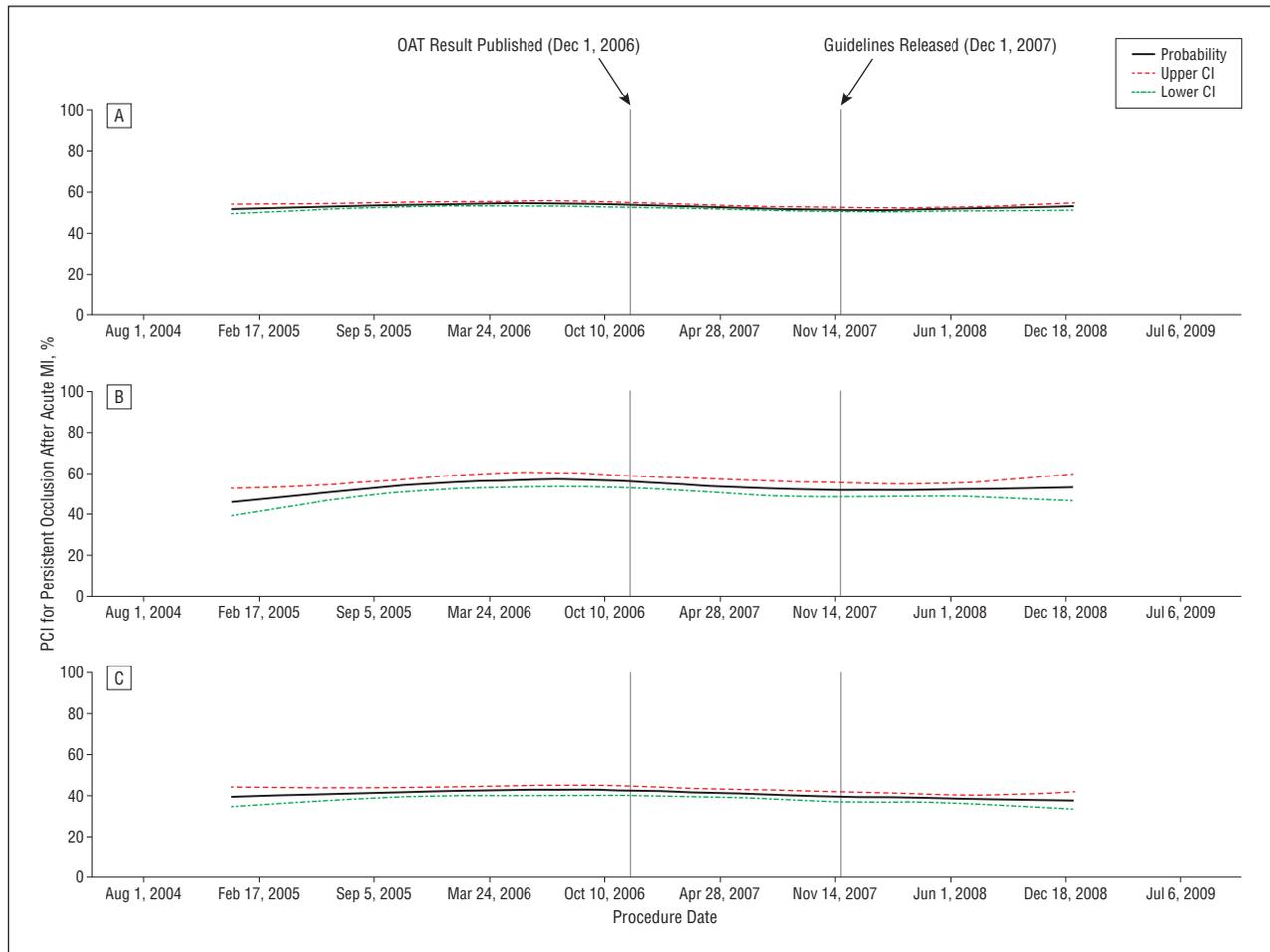


Figure 1. Unadjusted rates of percutaneous coronary intervention (PCI) for occlusions identified after myocardial infarction (MI) over time. The unadjusted rate of PCI for persistent total coronary artery occlusions after acute MI over the study period is shown, along with 95% confidence intervals, for the overall study population (A), for patients presenting with an ST elevation MI (B), and only those patients treated in hospitals in the highest quartile for reporting of diagnostic catheterizations (C). CI indicates confidence interval; OAT, the Occluded Artery Trial.

Table 3. Odds Ratios (ORs) for Change in the Rate of Percutaneous Coronary Intervention (PCI) for Persistent Occlusions After Myocardial Infarction, per 30-Day Period

Time Period	Total, No.	Adjusted Analysis ^a	
		OR (95% CI)	P Value
Overall study population			
Before the OAT publication (Mar-Dec 2006)	4893	0.976 (0.964-0.987)	<.001
After the OAT publication (Dec 2006–Nov 2007)	7812	0.997 (0.988-1.006)	.54
After guideline revisions (Dec 2007–Mar 2009)	9859	1.007 (0.992-1.022)	.34
Hospitals reporting a ratio of ≥ 3:1 for diagnostic to PCI procedures			
Before OAT publication (Mar-Dec 2006)	981	0.977 (0.954-1.001)	.06
After the OAT publication	1467	1.018 (0.995-1.042)	.12
After guideline revisions	1906	0.963 (0.928-1.000)	.047
STEMI at presentation			
Before OAT publication (Mar-Dec 2006)	533	0.980 (0.949-1.012)	.21
After the OAT publication	725	0.999 (0.972-1.027)	.96
After guideline revisions	729	0.997 (0.950-1.046)	.91

Abbreviations: CI, confidence interval; OAT, occluded artery trial; STEMI, ST elevation myocardial infarction.

^aThe final model was adjusted for age, sex, insurance payer, prior myocardial infarction, prior congestive heart failure, prior renal failure, cerebrovascular disease, prior PCI, peripheral vascular disease, chronic lung disease, STEMI at presentation, time from symptom onset to presentation, and number of diseased vessels.

patients presenting with STEMI (2684 patients), there was no difference in the adjusted monthly rate of PCI for occlusions after publication of the OAT (OR, 0.999; 95%

CI, 0.972-1.027) or after the guideline revisions (OR, 0.997; 95% CI, 0.950-1.046). These findings are summarized in Table 3.

Patients with symptoms of CHF at presentation were less likely to receive PCI for occlusions identified after MI than those without (34.0% vs 55.4%, respectively; $P < .001$). There was no change in the rate of PCI for occlusions after publication of the OAT or after guideline publication when subgroups were analyzed on the basis of heart failure symptoms at presentation, insurance payer, geographical region, or hospital type (**Figure 2**).

COMMENT

Overall, we found no change in the adjusted rate of PCI for total occlusions identified at least 24 hours after MI following the publication of the OAT or the revision of the major guidelines. Although there was a trend toward a decrease in the PCI rate in the subset of hospitals in the highest quartile of diagnostic catheterization reporting, the magnitude of the decline was small, especially in comparison with reported rates of decline in PCI following the COURAGE trial.¹¹ Despite more than 2 years of follow-up since the publication of the OAT and over 1 year of follow-up since the guideline revisions, PCI for total occlusions identified after MI among patients similar to those enrolled in the OAT continues to be performed in a considerable proportion of patients. These findings suggest that the evidence provided by the OAT and other small studies^{12,13} and the resultant class III guideline recommendations²⁻⁴ (“should not be performed”) for PCI in clinically stable patients with persistently occluded IRAs more than 24 hours after STEMI or NSTEMI have not, to date, been widely incorporated into clinical practice in a large cross-section of hospitals in the United States.

The reasons for the lack of impact of the ACC/AHA guideline recommendations on clinical practice in the United States are likely multifactorial. The OAT was a negative trial overall, but it did not demonstrate excessive harm from PCI apart from a trend toward increased reinfarction.¹ Cardiologists and interventionalists have been quick to incorporate the results of positive clinical device trials and related guideline recommendations in the past¹⁴ and to respond to trials reporting clinically significant safety concerns.^{15,16} However, there has been substantial lag in the impact of recommendations regarding medical therapy such as β blockers and angiotensin-converting enzyme inhibitor use in acute coronary syndrome.¹⁵⁻¹⁸ To our knowledge, the impact of a negative trial demonstrating lack of efficacy and excess cost of a procedure and subsequent guideline revisions has not been previously assessed. Physicians may be less likely to alter their practice based on negative results, especially when there are important competing factors. Barriers preventing physician adoption of clinical practice guidelines are incompletely understood.^{19,20} Analysis of physician behaviors suggest a wide spectrum of factors contributing to this clinical inertia, including lack of agreement regarding interpretation of data, especially when it contradicts long-held beliefs and external influences, such as conflicting patient expectations and financial incentives to perform the unindicated procedure and fear of litigation.^{21,22} In addition, the incentives to move clinicians toward evidence-based practice are unclear, although enhanced payment through the pay-for-performance initiatives will test the effect of financial incentives.

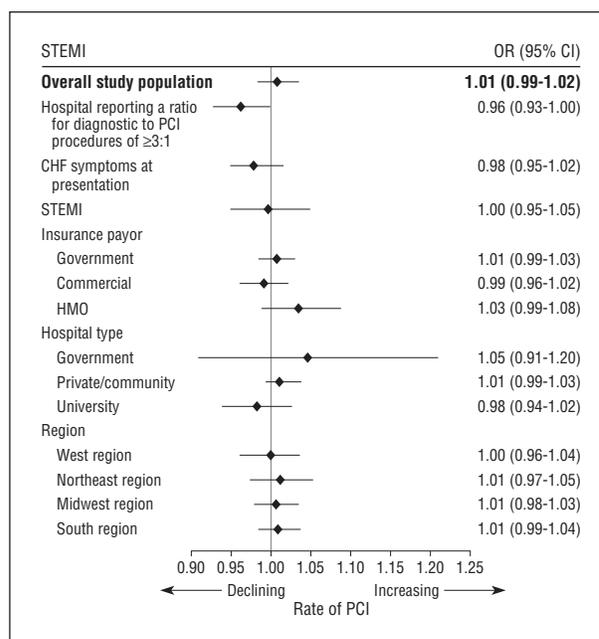


Figure 2. Adjusted trends in the rate of percutaneous coronary intervention (PCI) for occlusions identified after myocardial infarction among selected subgroups following guideline revisions. The odds ratios presented here refer to the adjusted odds of receiving PCI for a persistent occlusion, per 30-day increase in time, during the specified time period. They reflect overall trends in the use of PCI for total occlusions during the period from December 2007 to December 2008. CHF indicates congestive heart failure; CI, confidence interval; HMO, health maintenance organization; OR, odds ratio; STEMI, ST elevation myocardial infarction.

Most of the patients in our cohort presented with NSTEMI. Aggregate clinical trial data and guidelines currently support routine invasive management following NSTEMI,² and very early post-NSTEMI angiography is now commonplace. In the post-NSTEMI setting where persistent occlusion of the infarct-related artery is identified, this apparent incongruity of evidence may lead to continued equipoise among clinicians. Physicians may elect to perform PCI at that sitting, even in the absence of functional testing demonstrating severe ischemia. Nonetheless, the findings of the OAT were consistent across the STEMI and NSTEMI subgroups, and this is reflected in the current guidelines.²

There were important limitations to our study. While we strived to define a population within the CathPCI registry that reflected the OAT inclusion and exclusion criteria, there are considerable differences between the cohort in this study and that of the OAT. The population in this study consisted predominantly of NSTEMI; however, the rate of PCI for occlusions was not different from that seen in patients with STEMI. The OAT also excluded patients with angina at rest and those with severe ischemia on non-invasive testing. The CathPCI Registry does not collect information on either of these variables; however, we did attempt to capture these patients by excluding those undergoing emergency or salvage PCI.

The absolute rates of PCI for persistent occlusions reported in this study should be interpreted with caution. The CathPCI Registry does not code for the IRA, and our angiographic inclusion criteria may have resulted in the inclusion of some patients with coronary occlusions un-

related to their recent MI, leading to underestimation of the actual rate of PCI for persistent total occlusions. Conversely, nonmandatory reporting of diagnostic catheterizations in the registry may have led to overestimation of the rate of PCI for total occlusions. Nonetheless, these limitations would have had no influence on the ability to detect trends in use of PCI for total occlusions identified after MI.

We were not able to assess whether the new guideline recommendations resulted in a change in the rate of referral for cardiac catheterization among patients presenting at least 24 hours after MI. However, the OAT did not test the need for angiography in these patients, and the class III recommendation in the guidelines address only patients with total occlusion identified at coronary angiography. However, most patients with NSTEMI or STEMI treated with thrombolysis in the United States eventually undergo cardiac catheterization.⁶ The proportion of patients who did not undergo angiography is likely small and would not influence the overall findings of this study.

Finally, the generalizability of the CathPCI registry population to that of the entire United States has not been formally evaluated. However, the registry is the single largest clinical catheterization database in the country, with participating centers from every geographic region and includes both academic and community practices. The results of this study cannot be generalized to practice outside the United States. The impact of the OAT and major society guideline recommendations in countries with different models of health care delivery and practice environments has not been assessed.

In conclusion, among this large cross-section of hospitals in the United States we found only modest evidence that the results of the OAT and its incorporation into major guideline revisions have influenced cardiology and interventional cardiology practice over the subsequent 1 to 2 years. Percutaneous coronary intervention of total occlusions identified greater than 24 hours after MI remains commonplace despite little evidence to support its use in stable patients and new clinical practice guidelines recommending against it. The results of this study are a cause for concern on 2 levels. First, they imply that many stable patients with recent MI and persistent infarct artery occlusion continue to undergo a costly and ineffective procedure. Second, a large public, scientific, and human patient investment in the generation of robust clinical evidence has yet to broadly influence US practice. The factors accounting for this incomplete knowledge transfer over this time period remain uncertain.

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INVITED COMMENTARY

ONLINE FIRST

Medical Reversal, Clinical Trials, and the “Late” Open Artery Hypothesis in Acute Myocardial Infarction

Since the initial reports of a beneficial effect of reperfusion therapy in the management of acute myocardial infarction (MI), the open artery hypothesis and the benefits of timely reperfusion have been confirmed in numerous clinical trials investigating either pharmacological or mechanical reperfusion with percutaneous coronary intervention (PCI). Clinical trials have shown the importance of time to reperfusion. However, while the “early” open artery hypothesis has been consistently confirmed, the “late” open artery hypothesis (ie, reperfusion of an occluded infarct-related artery at a time too late for myocardial salvage and in patients without continuous symptoms) has been controversial for years. The rationale is that patency of the infarct vessel can improve left ventricular systolic function, and prevent ventricular remodeling and the late development of arrhythmias. It is important to note that, while late reperfusion with thrombolytic therapy has been found to be potentially harmful because it is associated with the added risk of myocardial rupture, with PCI, neither harm nor any definitive benefit has been reported in limited registry-based analysis and small clinical trials.

More recently, the Occluded Artery Trial (OAT)¹ showed that in stable patients with occlusion of the in-

farct related artery 3 to 28 calendar days after MI (with day 1 the day of symptom onset), reperfusion with PCI did not reduce the occurrence of death, reinfarction, or heart failure during 4 years of follow-up. On the basis of these results, and according to the research letter by Prasad and Cifu² in this issue of the *Archives*, the OAT can be classified as a medical “reversal” trial (ie, a new trial superior to the predecessors and contradicting current medical practice). Indeed, the results of the OAT were incorporated in 2007 in the revised American College of Cardiology/American Heart Association guidelines for the management of ST-segment elevation myocardial infarction and in the revised PCI guidelines,^{3,4} which now include late reperfusion (>24 hours) with PCI of the infarct artery in asymptomatic patients who are hemodynamically and electrically stable as a class III indication (ie, not indicated and inappropriate).

In this issue of the *Archives*, Deyell et al⁵ report the results of a retrospective analysis of 2005 to 2008 data from the American College of Cardiology CathPCI Registry. They evaluated patterns of care for 28 780 patients undergoing catheterization more than 24 hours after MI and examined trends of PCI for occluded artery before and after the publication of OAT and the revised guide-