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Incomplete Revascularization Is Associated With an Increased Risk for Major Adverse Cardiovascular Events Among Patients Undergoing Noncardiac Surgery

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ABSTRACT

OBJECTIVES The aim of this study was to determine whether incomplete revascularization is associated with a higher risk for major adverse cardiovascular events (MACE) and myocardial infarction (MI) among patients undergoing noncardiac surgery.

BACKGROUND Patients with coronary artery disease and prior percutaneous coronary intervention (PCI) frequently undergo noncardiac surgery. These patients may have had PCI either on all obstructive lesions (i.e., complete revascularization) or only on some (i.e., incomplete revascularization).

METHODS Patients were identified using the Veterans Affairs Clinical Assessment, Reporting, and Tracking program. Veterans Affairs and non–Veterans Affairs surgical records were used to link patients who underwent noncardiac surgery within 2 years after stent placement. Incomplete revascularization was defined as a residual stenosis of ≥50% in the left main coronary artery or ≥70% in another major epicardial coronary artery on the basis of operator visual estimate.

RESULTS In total, 4,332 patients (34.7%) had incomplete revascularization. A total of 567 MACE occurred within 1 month post-operatively. Patients with incomplete revascularization had an unadjusted 19% increased odds of post-operative MACE, compared with those with complete revascularization (odds ratio: 1.19; 95% confidence interval [CI]: 1.00 to 1.41). Among the MACE components, post-operative MI appears to contribute the most, with a 37% increased risk for post-operative MI among patients with incomplete revascularization (odds ratio: 1.37; 95% CI: 1.10 to 1.70). After adjustment, there was a significant interaction between time from PCI and outcomes after noncardiac surgery; incomplete revascularization was associated with significantly increased risk for post-operative MI primarily if surgery was performed within 6 weeks after PCI (adjusted odds ratio: 1.84; 95% CI: 1.04 to 2.38). The number of vessels with incomplete revascularization was also associated with an increased risk for post-operative MI: for each additional vessel with incomplete revascularization, there was a 17% increased odds of post-operative MI.

CONCLUSIONS Incomplete revascularization among patients with coronary artery disease is associated with an increased risk for MI after noncardiac surgery. (J Am Coll Cardiol Intv 2017;10:329–38) Published by Elsevier on behalf of the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CART = Clinical Assessment, Reporting, and Tracking

CI = confidence interval

MACE = major adverse cardiovascular event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

VA = Veterans Affairs

Approximately 20% of patients who undergo percutaneous coronary intervention (PCI) require noncardiac surgery in the subsequent 2 years (1–3). Optimal risk stratification of these patients is crucial, as they represent a high-risk subset of patients who are more likely to experience adverse post-operative events compared with the overall population of patients undergoing noncardiac surgery (4–7). Current guidelines for perioperative management have suggested optimal control of risk factors and delaying surgery for 1 year among patients with drug-eluting stents but deemphasize the need for stress testing or evaluation for underlying ischemia in the absence of symptoms (8,9).

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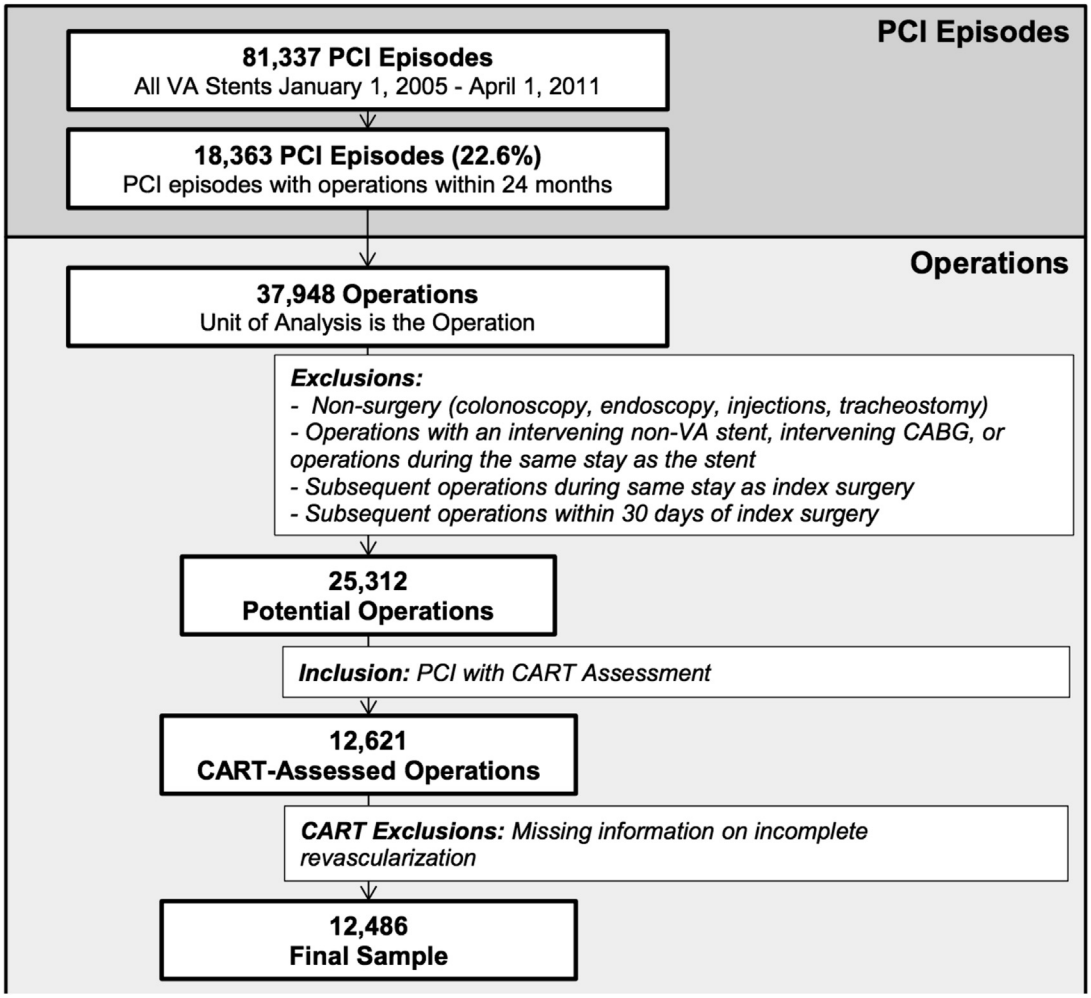
Although both patient- and lesion-related factors contribute to the risk for noncardiac surgery among patients with prior PCI, the attributable risk from incomplete revascularization and presumed residual ischemia remains uncertain (10). It is known that residual ischemia in patients with stable coronary artery disease is a risk factor for long-term adverse cardiovascular events and that patients treated with anatomic complete revascularization (either surgically or percutaneously) have lower cardiovascular event rates (11–14). More recently, anatomic scoring systems

FIGURE 1 Patient Flowchart



The total cohort consisted of 12,486 patients who underwent percutaneous coronary intervention (PCI) and then noncardiac surgery within 2 years. CABG = coronary artery bypass grafting; CART = Clinical Assessment, Reporting, and Tracking; VA = Veterans Affairs.

have also suggested an association between incomplete anatomic revascularization after PCI and major adverse cardiovascular event(s) (MACE) (15,16). Residual ischemia and incomplete revascularization may similarly represent significant risk factors for patients undergoing surgery, but the prevalence and outcomes of patients with incomplete revascularization undergoing noncardiac surgery is not well described.

We hypothesized that patients who had incomplete revascularization and presumed residual ischemia would be at increased risk for MACE when undergoing subsequent noncardiac surgery and that this risk would be independent of other established risk factors. We studied this question in a national cohort of veterans undergoing noncardiac surgery within 2 years after PCI.

METHODS

STUDY DESIGN AND STUDY POPULATION. This was a retrospective cohort study of patients who underwent noncardiac surgery within 2 years after coronary stent placement. Patients with histories of coronary artery bypass grafting were excluded from the cohort. Coronary artery stent placement was identified using the Veterans Affairs (VA) Clinical Assessment, Reporting, and Tracking (CART) system. All coronary stents implanted at VA facilities between 2005 and 2010 were identified using data elements derived directly from the CART database, which includes prespecified fields for bare-metal stents as well as the type of drug-eluting stent.

Subsequent noncardiac surgery occurring up to 24 months after coronary stent placement was identified using the VA Surgical Quality Improvement Program database; noncardiac surgery outside the VA was identified using the Centers for Medicare and Medicaid Services database, as previously described (2). Surgery performed during the same hospitalization as the initial PCI or after intervening cardiac surgery or placement of a stent at a non-VA facility were excluded. The type of noncardiac surgery performed was identified using Current Procedural Terminology codes 10000 through 32999 and 34000 through 69999. Minor procedures, including endoscopy and outpatient musculoskeletal injections, were excluded. Surgery types were also grouped by organ system and by elective versus nonelective status.

The study protocol was reviewed and approved by the local VA Institutional Review Board of each coauthor with a waiver of the requirement to obtain informed consent.

STUDY VARIABLES. The primary outcome was a composite outcome of MACE within 30 days after

TABLE 1 Baseline Demographics of the Study Population

	Overall	Complete Revascularization	Incomplete Revascularization	p Value
Overall	12,486	8,154 (65.3)	4,332 (34.7)	
Age (yrs)				
<60	2,017 (16.2)	1,422 (17.4)	595 (13.7)	<0.001
≥60	10,469 (83.8)	6,732 (82.6)	3,737 (86.3)	
Race				
White	10,823 (88.4)	7,046 (88.3)	3,777 (88.6)	<0.001
Black	1,246 (10.2)	845 (10.6)	401 (9.4)	
Other	177 (1.4)	93 (1.2)	84 (2.0)	
Sex				
Male	12,304 (98.5)	8,017 (98.3)	4,287 (99.0)	0.004
Female	182 (1.5)	137 (1.7)	45 (1.0)	
Revised cardiac risk index				
1	5,190 (46.5)	3,519 (48.6)	1,671 (42.6)	<0.001
2	3,845 (34.5)	2,404 (33.2)	1,441 (36.8)	
≥3	2,124 (19.0)	1,316 (18.2)	808 (20.6)	
Myocardial infarction in past 6 months				
No	11,032 (88.4)	7,300 (89.5)	3,732 (86.2)	<0.001
Yes	1,454 (11.6)	854 (10.5)	600 (13.9)	
History of CHF				
No	8,116 (65.0)	5,479 (67.2)	2,637 (60.9)	<0.001
Yes	4,370 (35.0)	2,675 (32.8)	1,695 (39.1)	
History of cerebrovascular disease				
No	12,298 (98.5)	8,033 (98.5)	4,265 (98.5)	0.78
Yes	188 (1.5)	121 (1.5)	67 (1.6)	
Hypertension in past year				
No	891 (7.1)	619 (7.6)	272 (6.3)	0.01
Yes	11,595 (92.9)	7,535 (92.4)	4,060 (93.7)	
Diabetes				
No	5,670 (45.4)	3,845 (47.2)	1,825 (42.1)	<0.001
Non-insulin-dependent	4,705 (37.7)	3,018 (37.0)	1,687 (38.9)	
Insulin-dependent	2,111 (16.9)	1,291 (15.8)	820 (18.9)	
Chronic kidney disease				
No	10,464 (83.8)	6,864 (84.2)	3,600 (83.1)	0.12
Stages 1–5	1,084 (8.7)	677 (8.3)	407 (9.4)	
Dialysis	938 (7.5)	613 (7.5)	325 (7.5)	
Stress testing within 3 months				
No	11,101 (88.9)	7,234 (88.7)	3,867 (89.3)	0.35
Yes	1,385 (11.1)	920 (11.3)	465 (10.7)	
Previous PCI within 1 yr				0.03
No	8,798 (70.5)	5,692 (69.8)	3,106 (71.7)	
Yes	3,688 (29.5)	2,462 (30.2)	1,226 (28.3)	
Subsequent operation type				
Digestive	1,303 (10.4)	853 (10.5)	450 (10.4)	0.01
Eye/ear	2,249 (18.0)	1,430 (17.5)	819 (18.9)	
Genital/urinary	1,886 (15.1)	1,228 (15.1)	658 (15.2)	
Integumentary	1,989 (15.9)	1,309 (16.1)	680 (15.7)	
Musculoskeletal	1,911 (15.3)	1,301 (16.0)	610 (14.1)	
Nervous	619 (5.0)	417 (5.1)	202 (4.7)	
Other	148 (1.2)	106 (1.3)	42 (1.0)	
Respiratory	600 (4.8)	396 (4.9)	204 (4.7)	
Vascular	1,781 (14.3)	1,114 (13.7)	667 (15.4)	
Subsequent operation admission				
Outpatient	8,029 (64.3)	5,244 (64.3)	2,785 (64.3)	0.98
Elective inpatient	3,919 (31.4)	2,561 (31.4)	1,358 (31.4)	
Nonelective inpatient	538 (4.3)	349 (4.3)	189 (4.4)	

Values are n (%).
CHF = congestive heart failure; PCI = percutaneous coronary intervention.

TABLE 2 Procedural Characteristics of Percutaneous Coronary Intervention

	Complete Revascularization	Incomplete Revascularization	p Value
Indication for intervention			
ACS with MI	859 (10.6)	459 (10.6)	<0.001
ACS without MI	4,314 (53.0)	2,614 (60.4)	
Non-ACS	2,965 (36.4)	1,254 (29.0)	
Stent type			
BMS only	2,289 (28.1)	1,126 (26.0)	0.07
Both generation DES	101 (1.2)	66 (1.5)	
First-generation DES	3,734 (45.8)	2,012 (46.5)	
Second-generation DES	1,781 (21.8)	1,001 (23.1)	
Missing	249 (3.1)	127 (2.9)	
Target vessel			
LAD	3,047 (37.4)	1,225 (28.3)	<0.001
Circumflex	1,499 (18.4)	891 (20.6)	0.003
RCA	2,618 (32.1)	1,156 (26.7)	<0.001
Left main	198 (2.4)	187 (4.3)	<0.001
Target vessel location			
Proximal	2,684 (32.9)	1,383 (31.9)	0.26
Mid	3,995 (49.0)	1,649 (38.1)	<0.001
Distal	1,081 (13.3)	548 (12.7)	0.34
Ostial lesion			
No	7,678 (94.2)	3,979 (91.9)	<0.001
Yes	476 (5.8)	353 (8.2)	
Calcified lesion			
No	6,792 (83.3)	3,468 (80.1)	<0.001
Yes	1,362 (16.7)	864 (19.9)	
PCI risk			
Not high	4,853 (59.5)	2,202 (50.8)	<0.001
High	2,058 (25.2)	1,342 (31.0)	
Missing	1,243 (15.2)	788 (18.2)	
Number of target vessels			
1	5,515 (67.6)	2,807 (64.8)	0.001
≥2	2,639 (32.4)	1,525 (35.2)	
Number of stents			
1	5,339 (65.5)	2,659 (61.4)	<0.001
2	1,924 (23.6)	1,140 (26.3)	
≥3	891 (10.9)	533 (12.3)	
Bifurcation			
No	7,552 (92.6)	4,100 (94.6)	<0.001
Yes	602 (7.4)	232 (5.4)	
Pre-procedure stenosis (%)	85 (80.0-90.0)	90 (80.0-95.0)	<0.001
Post-procedure stenosis (%)	0 (0.0-0.0)	0 (0.0-0.0)	0.20
Lesion length (mm)			
≤20	4,922 (60.4)	2,554 (59.0)	0.19
>20	1,085 (13.3)	573 (13.2)	
Missing	2,147 (26.3)	1,205 (27.8)	
Total stent length (mm)			
≤30	5,503 (67.5)	2,773 (64.0)	<0.001
>30	2,183 (26.8)	1,341 (31.0)	
Missing	468 (5.7)	218 (5.0)	

Continued on the next page

noncardiac surgery, defined as the first occurrence of all-cause death, myocardial infarction (MI) (International Classification of Diseases-Ninth Revision-Clinical Modification codes 410.x1 or VA Surgical Quality Improvement Program-abstracted MI), or need for coronary revascularization (International Classification of Diseases-Ninth Revision-Clinical Modification codes 00.66 and 36.01 through 36.09; Current Procedural Terminology codes 33510 through 33519, 33520 through 33523, 33530 through 33536, 92973 through 92984, and 92995 through 92998).

Procedural elements of the initial PCI were derived from CART data entered at the time of the procedure. These variables included the indication for the PCI (acute coronary syndrome with MI, acute coronary syndrome without MI, or stable angina), the stent type implanted (bare-metal stent, drug-eluting stent, or both), target vessel (left main, left anterior descending, right, or circumflex coronary artery), target lesion location (ostial, proximal, mid, or distal within given vessel), presence of significant lesion calcification, presence of lesion at a bifurcation, lesion length, intervention to chronic total occlusion, use of intravascular ultrasound, PCI risk, number of target vessels, stent length, largest stent diameter, and the anticoagulant agent used during PCI. Incomplete anatomic revascularization was defined as the presence of a ≥50% lesion in the left main coronary artery or ≥70% stenosis in another major epicardial coronary artery ≥2 mm in diameter at the conclusion of PCI, on the basis of visual estimate by the operator. All of the procedural variables were entered by the treating physician at the time of the intervention and were based on physician judgment at the time of the procedure.

The patient's cardiac risk at the time of noncardiac surgery using the revised cardiac risk index was estimated using International Classification of Diseases-Ninth Revision codes for congestive heart failure, stroke, MI, and diabetes; Current Procedural Terminology codes associated with high-risk surgery; and laboratory data identifying 1 or more serum creatinine values >2 mg/dl in the year prior to surgery.

STATISTICAL ANALYSIS. For bivariate analyses, chi-square test statistics and Wilcoxon rank sum tests were used to compare categorical and continuous variables, respectively. Backward stepwise selection with an alpha value of 0.05 was used to build the most parsimonious logistic regression model for the association of incomplete revascularization with post-operative MACE and MI. Covariates found to be associated with MACE in bivariate analyses were tested during model selection along with additional variables considered to be clinically significant. The final model included age, history of MI within 6 months of surgery, revised cardiac risk index, procedure type, PCI risk, and time to surgery from PCI. A significant interaction term between time from PCI and outcomes after

noncardiac surgery was identified that persisted even after adjusting for potential confounders. Therefore, the association of incomplete revascularization with post-operative MACE and MI was stratified on the basis of the time from PCI to noncardiac surgery. All analyses were completed using SAS version 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

During the study period, 12,486 patients without histories of coronary artery bypass grafting underwent PCI and subsequent noncardiac surgery (Figure 1). A total of 4,332 patients (34.7%) had incomplete anatomic revascularization. The baseline demographics of patients with and without incomplete revascularization are summarized in Table 1. Patients with incomplete revascularization were more likely to have had MIs in the prior 6 months (13.9% vs. 10.5%; $p < 0.001$), were more likely to have histories of congestive heart failure (39.1% vs. 32.8%, $p < 0.001$), and were more likely to have diabetes (57.9% vs. 52.8%; $p < 0.001$). Patients with incomplete revascularization were also slightly more likely to have undergone PCI within the prior year (71.7% vs. 69.8%; $p = 0.03$).

The angiographic characteristics of the index PCI are detailed in Table 2. Patients with incomplete revascularization were more likely to have been treated for acute coronary syndromes (71% vs. 64.6%; $p < 0.001$) but had a similar distribution of target vessels compared with patients with complete revascularization. Patients with incomplete revascularization were on average treated with more coronary artery stents and were more likely to have an overall treatment length >30 mm, suggesting a greater burden of atherosclerotic disease among the patients who had incomplete revascularization.

Table 3 details the unrevascularized vessels among patients with incomplete revascularization. The right coronary artery (18%) and the left anterior descending coronary artery (17.9%) were the vessels most frequently associated with incomplete revascularization, while the circumflex coronary artery (11.3%) and posterior descending coronary artery (3%) were less frequently associated with incomplete revascularization. The prevalence of any chronic total occlusion in the nontarget vessel among patients with incomplete revascularization was 1.3%.

Pre-operative stress testing was performed in 11.1% of the cohort in the 3 months prior to noncardiac surgery. There was no association between incomplete revascularization and the decision to perform pre-operative stress testing (10.7% vs. 11.3%; $p = 0.40$).

TABLE 2 Continued

	Complete Revascularization	Incomplete Revascularization	p Value
Largest stent diameter (mm)			
≤3	5,139 (63.0)	2,623 (60.6)	0.002
>3	2,672 (32.8)	1,549 (35.8)	
Missing	343 (4.2)	160 (3.7)	
Pre-PCI TIMI flow grade			
3	6,052 (74.2)	2,988 (69.0)	<0.001
<3	1,648 (20.2)	924 (21.3)	
Missing	454 (5.6)	420 (9.7)	
Final TIMI flow grade			
3	7,580 (93.0)	3,864 (89.2)	<0.001
<3	114 (1.4)	47 (1.1)	
Missing	460 (5.6)	421 (9.7)	
Dissection			
No	2,059 (96.0)	976 (93.8)	0.01
Yes	86 (4.0)	65 (6.2)	
Chronic total occlusion			
No	2,010 (88.4)	960 (90.4)	0.09
Yes	263 (11.6)	102 (9.6)	
Intravascular ultrasound			
No	7,343 (90.1)	4,033 (93.1)	<0.001
Yes	811 (10.0)	299 (6.9)	
Anticoagulant			
Heparin	3,128 (54.8)	1,774 (56.2)	0.20
Bivalirudin	2,116 (37.1)	1,086 (34.4)	0.01
Low-molecular weight heparin	142 (2.5)	95 (3.0)	0.14
Access site			
Femoral	7,593 (93.1)	3,945 (91.1)	<0.001
Radial	363 (4.5)	230 (5.3)	
Brachial	52 (0.6)	54 (1.3)	
Other	3 (0.0)	6 (0.1)	
Missing	143 (1.8)	97 (2.2)	
Time to surgery			
<6 weeks	407 (5.0)	265 (6.1)	0.01
6 weeks to <6 months	1,573 (19.3)	887 (20.5)	
6 to <12 months	1,986 (24.4)	1,064 (24.6)	
12 to 24 months	4,185 (51.3)	2,116 (48.9)	

Values are n (%). A total of 357 procedures (2.7%) had both DES and non-DES coded for the PCI. These are included in both the DES and BMS stratified tables.

ACS = acute coronary syndrome; BMS = bare-metal stent(s); DES = drug-eluting stent(s); LAD = left anterior descending coronary artery; MI = myocardial infarction; PCI = percutaneous coronary intervention; RCA = right coronary artery; TIMI = Thrombolysis In Myocardial Infarction.

Tables 4 and 5 demonstrate the unadjusted and adjusted associations of incomplete revascularization with 30-day MACE after noncardiac surgery. Those with incomplete revascularization had a 19% increased odds of MACE in the post-operative period, compared to those with complete revascularization (odds ratio: 1.19; 95% confidence interval [CI]: 1.00 to 1.41). A significant relationship between the number of unrevascularized vessels and the risk for post-operative adverse outcomes was also observed (Figure 2). When examined as a continuous variable, there was a 17% increase in the odds of post-operative

TABLE 3 Angiographic Characteristics of Patients With Incomplete Revascularization

Number of vessels	1 (1-2)
Vessel with incomplete revascularization	
RCA	
No	10,235 (82.0)
Yes	2,251 (18.0)
LAD	
No	10,248 (82.1)
Yes	2,238 (17.9)
Circumflex	
No	11,075 (88.7)
Yes	1,411 (11.3)
PDA	
No	12,116 (97.0)
Yes	370 (3.0)
Other	
No	11,716 (93.8)
Yes	770 (6.2)

Values are median (interquartile range) or n (%).
PDA = patent ductus arteriosus; other abbreviations as in Table 2.

MI for every additional vessel with residual stenosis ($p < 0.001$). Post-operative MI among patients with incomplete revascularization appears to contribute the most to the increased risk for MACE throughout all time periods investigated (3.3% vs. 2.5%; odds ratio: 1.37; 95% CI: 1.10 to 1.70).

After multivariate adjustment for patient and procedural risk factors, a significant interaction term remained between the time from PCI to surgery and the risk for post-operative events. Among patients who underwent noncardiac surgery <6 weeks after PCI, incomplete revascularization was associated with adjusted odds of 1.84 (95% CI: 1.04 to 2.38) for post-operative MI and 1.22 (95% CI: 0.76 to 1.95) for MACE (Figure 3). In comparison, the risk for post-operative MI or MACE was not significant among patients who underwent noncardiac surgery between 6 weeks and 1 year post-PCI. A second increase in post-operative MI risk was also observed if surgery was performed 1 to 2 years post-PCI (adjusted odds ratio: 1.42; 95% CI: 1.08 to 1.89). Consistent with this time-to-surgery interaction, the overall rates of post-operative MI were significantly higher at early and late time points among patients with incomplete revascularization (Figure 4). There was no significant interaction between stent type and the risk for post-operative MACE on the basis of these different time points, suggesting that the early and late risk for post-operative MACE was not dependent on the type of stent implanted (p for interaction = 0.09).

TABLE 4 Thirty-Day Outcomes

	Complete Revascularization	Incomplete Revascularization	OR	95% CI	p Value
MACE	349 (4.3)	218 (5.0)	1.19	1.00–1.41	0.05
MI	200 (2.5)	144 (3.3)	1.37	1.10–1.70	0.01
Revascularization	83 (1.0)	46 (1.1)	1.04	0.73–1.50	0.82
Death	111 (1.4)	68 (1.6)	1.16	0.85–1.57	0.35

Values are n (%).
CI = confidence interval; MACE = major adverse cardiac event(s); MI = myocardial infarction; OR = odds ratio.

DISCUSSION

Patients with coronary artery disease and prior PCI who undergo noncardiac surgery have a significantly increased risk for post-operative adverse events compared with the general population (4,5). In this study, we found that incomplete revascularization among patients with prior PCI was associated with a significantly increased rate of post-operative MACE as a composite outcome and post-operative MI as a component of MACE. We also observed a stepwise association between the number of vessels that were not revascularized and the risk for post-operative MI, suggesting that greater ischemic burden was associated with an increased risk for post-operative MI. There was also a significant interaction between time from PCI and risk for post-operative outcomes, with the greatest attributable risk from incomplete revascularization if the surgery was performed <6 weeks after the initial PCI.

Noncardiac surgery may result in post-operative MI because of numerous mechanisms, including plaque rupture from a proinflammatory state, stent thrombosis as a result of antiplatelet interruption, or a so-called demand event due to hemodynamic stress in the setting of a fixed stenosis (type 2) (17). Although we could not adjudicate the classification of MI category in our cohort, the majority of such events attributable to incomplete revascularization are presumably related to type 2 MIs in the setting of angiographically significant residual stenosis. Recent evidence suggests that type 2 MI is associated with significantly worse adverse outcomes than previously recognized, with a 2-fold increased rate of MACE and cardiovascular death compared with patients without type 2 MI (18,19). These findings suggest that mechanisms to risk-stratify patients at risk for post-operative MI would minimize long-term morbidity among patients with coronary artery disease undergoing noncardiac surgery.

Consistent with our primary finding that incomplete revascularization was associated with an increased risk for post-operative MACE and MI, we

also observed a dose-response effect between the number of unrevascularized vessels and the risk for post-operative MI, with a 17% increased odds of post-operative MI for each additional vessel that was not revascularized. This finding suggests that a greater atherosclerotic and ischemic burden was associated with an increased risk for adverse events. Consistent with this hypothesis, the nuclear substudy of the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial, patients with continued ischemic burden (regardless of PCI or medical therapy) had a significantly increased risk for death or MI during follow-up (20). Recently, the residual SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score after multivessel PCI was also found to be associated with an increased risk for death and major adverse cardiac and cerebrovascular events during 5-year follow-up (21). Importantly, that study also identified a dose-response relationship between the residual SYNTAX score and risk for adverse events, again confirming the relationship between the anatomic extent of residual coronary artery disease and risk for adverse outcomes.

Our analysis also revealed a significant time interaction, with the risk for post-operative MI highest among patients with incomplete revascularization who underwent surgery within 6 weeks post-PCI. Multiple mechanisms may account for this time interaction. First, procedures performed within 6 weeks were presumably urgent and could not be deferred; however, we adjusted for surgical urgency and complexity in multivariate analysis. Second, surgery within 6 weeks is likely associated with a higher risk for stent thrombosis. Patients with incomplete revascularization were also treated with longer stent lengths, suggesting more complex initial PCI and possibly a higher risk for stent-related adverse events in the post-operative period. Third, surgery within 6 weeks may not provide enough time for optimal medical titration to reduce the hemodynamic stress on patients with incomplete revascularization, who might benefit from more intensive medical optimization prior to surgery. Overall, our findings are consistent with those of prior studies, which have recently shown that the majority of the perioperative risk is attributable to the first 6 months post-PCI, regardless of stent type or indication for the initial PCI (7). Patients with incomplete revascularization, who represent a high-risk subgroup of such patients, should also have surgery delayed for at least 6 weeks and ideally 6 months post-PCI on the basis of our findings.

Should patients with incomplete revascularization after PCI who require noncardiac surgery undergo additional risk stratification or possibly revascularization prior to surgery? Although our data support an association between incomplete revascularization and adverse events, they do not prove a causal association between complete revascularization and a reduction in cardiovascular risk, which remains controversial. A recent meta-analysis suggested that complete revascularization was associated with decreased mortality, MI, and repeat coronary revascularization, regardless of revascularization modality (13). Although revascularization has not been shown to definitely reduce perioperative morbidity prior to major surgery, subsequent analysis suggested that patients with complete revascularization (primarily via coronary artery bypass grafting) were less likely to develop post-operative MI (22,23). Current guidelines have de-emphasized a role for routine stress testing or evaluation for underlying ischemia in the absence of symptoms (8,9). However, our data suggest that risk stratification using cardiac stress testing in a select subset of patients with known residual angiographic stenoses may be a way to affect post-operative morbidity. If such patients demonstrate residual ischemia, a decision could be made regarding intensification of medical therapy versus further revascularization prior to surgery.

TABLE 5 Odds of Post-Operative Outcomes for Patients With Incomplete Revascularization Compared With Those With Complete Revascularization

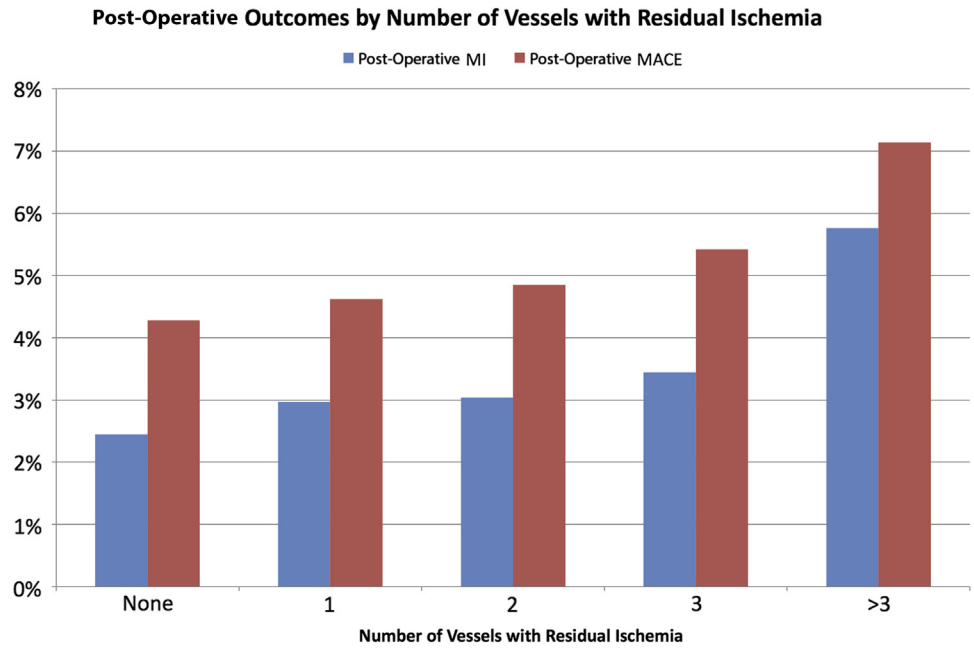
	Post-Operative MI		Post-Operative MACE	
	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
<6 weeks	1.79 (1.07–2.99)	1.84 (1.04–3.28)	1.26 (0.84–1.91)	1.22 (0.76–1.95)
6 weeks to <12 months	1.00 (0.71–1.40)	0.72 (0.50–1.04)	0.90 (0.69–1.19)	0.71 (0.53–0.95)
12 to 24 months	1.60 (1.12–2.28)	1.38 (0.91–2.09)	1.42 (1.08–1.89)	1.26 (0.92–1.73)

*Adjusted for recent MI, age, Revised Cardiac Risk Index, procedure specialty, LAD treated, and PCI risk.
Abbreviations as in Tables 2 and 4.

STUDY LIMITATIONS. This study should be interpreted in light of several aspects of its design. First, the CART data elements allow the identification of additional unrevascularized coronary artery vessels, but current data elements in that dataset do not allow the granular extraction necessary to calculate SYNTAX or residual SYNTAX scores. It is therefore not possible to integrate the overall anatomic details of patients with incomplete anatomic revascularization into a single scoring system.

Second, we were able to identify patients with incomplete anatomic revascularization on the basis of visual estimation of a 70% lesion that was not revascularized but not necessarily residual ischemia.

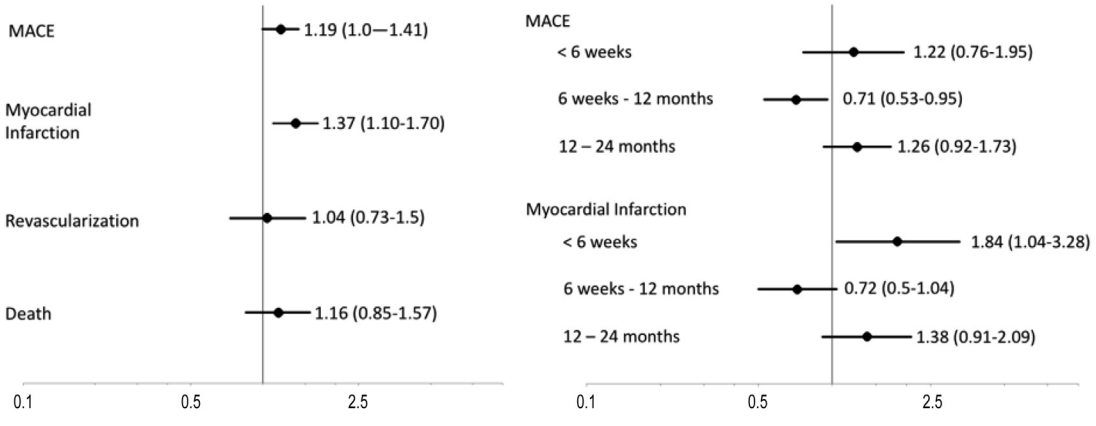
FIGURE 2 Post-Operative Outcomes Within 1 Month After Surgery by Number of Vessels With Incomplete Revascularization



There was a significant relationship between the number of vessels with incomplete revascularization and the risk for post-operative myocardial infarction (MI) or major adverse cardiac event(s) (MACE).

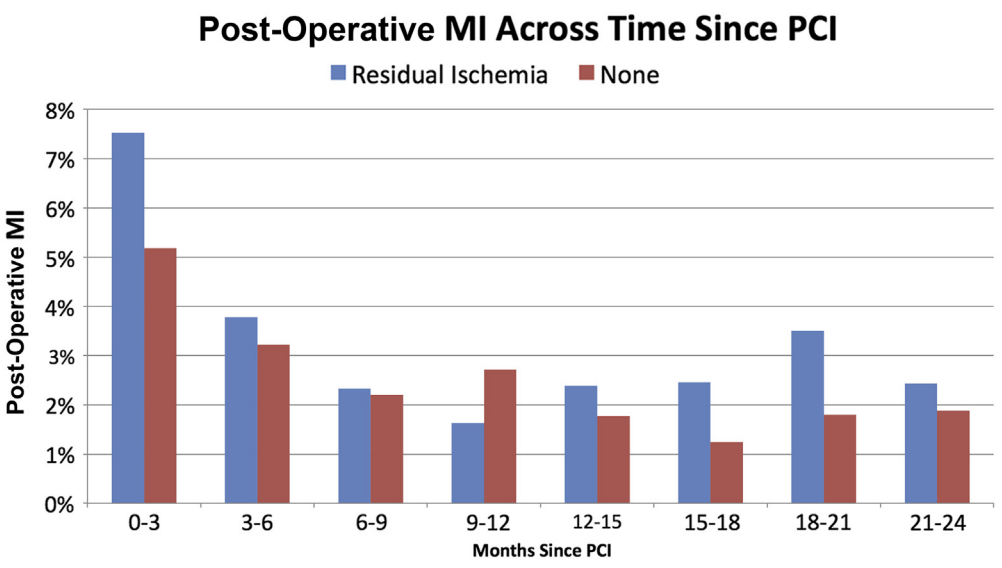
Operator visual assessment is known to potentially overestimate the severity of stenosis compared with more quantitative methods. Additionally, the identification of residual ischemia would require stress imaging or invasive fractional flow reserve technology to determine the extent of jeopardized myocardium. Although incomplete anatomic revascularization is therefore a proxy for residual ischemia,

FIGURE 3 Association of Incomplete Revascularization With Increased Rates of Major Adverse Cardiovascular Events and Myocardial Infarction and Effect of Surgical Timing on the Risk for Myocardial Infarction



Incomplete revascularization was associated with an increased risk for post-operative major adverse cardiac event(s) (MACE) or myocardial infarction. There was also a significant time interaction between incomplete revascularization and the risk for post-operative outcomes, with the risk increased early (<6 weeks) and late (1 to 2 yrs).

FIGURE 4 Association of Incomplete Revascularization With Post-Operative Myocardial Infarction in Relation to Timing From Prior Percutaneous Coronary Intervention



The highest risk for post-operative myocardial infarction occurred early among patients with incomplete revascularization, although there was also a higher risk for adverse events among patients with incomplete revascularization who underwent surgery >1 year post-percutaneous coronary intervention. MACE = major adverse cardiac event(s).

the significant association between the number of vessels with incomplete revascularization and the risk for post-operative MI supports this association between incomplete revascularization and the presumed extent of residual ischemia.

Third, the CART data elements do not provide data on aspirin doing or refills, nor were we able to obtain detailed information on clopidogrel use post-PCI and in the perioperative period. It is therefore possible that other patient-related or prescribing patterns contributed to the some of the observed association between incomplete revascularization and post-operative outcomes.

Fourth, we do not have data on the clinical decision making to perform complete versus incomplete revascularization, patient anginal symptoms prior to surgery, the mechanisms of post-operative MI, and whether such events were primarily type 2 (i.e., demand related), due to plaque rupture, or due to stent thrombosis. However, recent data have suggested that type 2 MIs are associated with similarly poor long-term prognosis, suggesting that this is a clinically important endpoint in this patient population.

Fifth, we do not have data on patients who underwent PCI and for whom surgery was ultimately deferred, as the cohort was defined by patients who underwent PCI and then subsequent noncardiac surgery. It is possible that a group of patients with residual ischemia and who were therefore considered at high risk for post-operative complications had surgery cancelled or delayed beyond 2 years.

Last, we do not have data on whether medical therapy was intensified in the perioperative period among patients with prior PCI and whether this was associated with any change in ischemic burden.

CONCLUSIONS

Incomplete revascularization among patients who have undergone PCI is associated with a significantly increased risk for MACE after noncardiac surgery. Of the MACE components, post-operative MI has the strongest association for patients with multiple unrevascularized vessels. Future studies should investigate the utility of further risk stratification among patients with incomplete revascularization and whether complete revascularization is associated with lower rates of post-operative MACE.

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PERSPECTIVES

WHAT IS KNOWN? Patients with coronary artery disease and prior PCI frequently undergo noncardiac surgery. The contribution of incomplete revascularization to adverse outcomes is unknown.

WHAT IS NEW? In a national cohort of veterans, patients with coronary artery disease and incomplete revascularization who required subsequent noncardiac surgery had higher rates of MACE and MI compared with patients with complete revascularization.

WHAT IS NEXT? Future studies should investigate the contribution of incomplete revascularization to MACE after noncardiac surgery.

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