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Periprocedural Myocardial Injury in Chronic Total Occlusion Percutaneous Interventions

A Systematic Cardiac Biomarker Evaluation Study

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Objectives This study sought to evaluate the incidence, correlates, and clinical implications of periprocedural myocardial injury (PMI) during percutaneous coronary intervention (PCI) of chronic total occlusions (CTO).

Background The risk of PMI during CTO PCI may be underestimated because systematic cardiac biomarker measurement was not performed in published studies.

Methods We retrospectively examined PMI among 325 consecutive CTO PCI performed at our institution between 2005 and 2012. Creatine kinase-myocardial band fraction and troponin were measured before PCI and 8 to 12 h and 18 to 24 h after PCI in all patients. PMI was defined as creatine kinase-myocardial band increase $\geq 3\times$ the upper limit of normal. Major adverse cardiac events during mid-term follow-up were evaluated.

Results Mean age was 64 $\pm$ 8 years. The retrograde approach was used in 26.8% of all procedures. The technical and procedural success was 77.8% and 76.6%, respectively. PMI occurred in 28 patients (8.6%, 95% confidence intervals: 5.8% to 12.2%), with symptomatic ischemia in 7 of those patients. The incidence of PMI was higher in patients treated with the retrograde than the antegrade approach (13.8% vs. 6.7%, $p = 0.04$). During a median follow-up of 2.3 years, compared with patients without PMI, those with PMI had a higher incidence of major adverse cardiac events (hazard ratio [HR]: 2.25, $p = 0.006$). Patients with only asymptomatic PMI also had a higher incidence of major adverse cardiac events on follow-up (HR: 2.26, $p = 0.013$).

Conclusions Systematic measurement of cardiac biomarkers post–CTO PCI demonstrates that PMI occurs in 8.6% of patients, is more common with the retrograde approach, and is associated with worse subsequent clinical outcomes during mid-term follow-up. (J Am Coll Cardiol Intv 2014;7:47–54) © 2014 by the American College of Cardiology Foundation

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Periprocedural myocardial injury (PMI) is a known complication of percutaneous coronary intervention (PCI) and has been associated with higher mortality, even when patients do not develop symptoms or electrocardiographic changes (1,2). PCI of chronic total occlusions (CTO) can be technically challenging and may require the use of advanced crossing techniques that could result in high rates of PMI (3). In a weighted meta-analysis of 18,061 patients from 65 studies reporting complications after CTO PCI, the incidence of PMI was 2.5% (95% confidence interval [CI]: 1.9% to 3.0%) and the incidence of Q-wave myocardial infarction (MI) was 0.2% (95% CI: 0.1% to 0.3%) (4). However, systematic cardiac biomarker measurements were not performed in these studies; hence, the true incidence of PMI may be underestimated. Furthermore, whereas in non-CTO PCI PMI is associated with higher immediate and long-term morbidity, the prognostic implications of PMI in CTO PCI remain unclear (4). To overcome these limitations, we performed the present study with the following goals: 1) to evaluate the incidence of both symptomatic and asymptomatic PMI in CTO PCI using serial biomarker measurements; 2) to assess the association of PMI with various CTO PCI techniques; and 3) to determine the impact of PMI on subsequent clinical outcomes.

Abbreviations and Acronyms

CABG = coronary artery bypass graft
CI = confidence interval(s)
CK-MB = creatine kinase-myocardial band
CTO = chronic total occlusion(s)
HR = hazard ratio(s)
IQR = interquartile range
MACE = major adverse cardiac events
MI = myocardial infarction(s)
OR = odds ratio(s)
PCI = percutaneous coronary intervention(s)
PMI = periprocedural myocardial injury
ULN = upper limit of normal

Methods

Patients. Between May 18, 2005, and May 23, 2012, 325 consecutive patients who underwent CTO PCI at our institution had their serial post-PCI cardiac biomarker measurements determined (which is standard policy at our institution for all PCI), and were included in the present study. Their medical records, electrocardiograms, and coronary angiograms were reviewed. The study was approved by the institutional review board of our institution.

Definitions. Coronary CTOs were defined as coronary lesions with Thrombolysis In Myocardial Infarction flow grade 0 for a duration of at least 3 months. Estimation of the occlusion duration was based on the first onset of anginal symptoms, previous history of MI in the target vessel territory, or comparison with a previous angiogram.

Technical success of CTO PCI was defined as successful CTO revascularization with achievement of <30% residual diameter stenosis within the treated segment and restoration of Thrombolysis In Myocardial Infarction flow grade 3 antegrade flow. Procedural success was defined as achievement of technical success with no in-hospital major adverse cardiac events (MACE).

For in-hospital events, MACE was defined as the composite of death and clinical MI (symptoms or signs suggestive of ischemia in addition to increase and fall of cardiac biomarker levels). For events during follow-up, MACE was defined as the composite of all-cause death, MI (defined according to the universal definition of MI 2012 version), or any coronary revascularization (5).

All patients underwent creatine kinase-myocardial band (CK-MB) and troponin measurement before PCI and at 8 to 12 and 18 to 24 h after PCI. PMI was defined as CK-MB increase ≥3× the upper limit of normal (ULN), if the baseline CK-MB levels were below ULN. If the baseline CK-MB levels were higher than the ULN, PMI was defined as a CK-MB increase ≥3× ULN if the relative increase of the highest post-PCI CK-MB was >20% above the baseline level. Periprocedural MI was defined as the subset of PMI patients who had evidence of prolonged ischemia as demonstrated by persistent chest pain (>20 min), or new pathological Q waves seen on the electrocardiogram (5). Cardiac troponin level elevation was reported using various cutoffs (≥3×, ≥10×, and ≥20× ULN). The ULN for CK-MB and troponin at our institution was 6.3 ng/ml and 0.03 ng/ml, respectively.

Statistical analysis. Continuous variables were presented as mean ± SD or median with interquartile range (IQR) and compared using the Student *t* test or Wilcoxon rank-sum test, as appropriate. Categorical variables were reported as percentages and compared using the chi-square or Fisher exact test, as appropriate. A 2-sided p value of <0.05 was considered statistically significant. Logistic regression analysis was performed to identify predictors of PMI in CTO PCI using the SAS (SAS Institute, Cary, North Carolina) macro written by Bursac et al. (6). Any variable having a significant univariate association with PMI ($p \leq 0.25$) was selected as a candidate for the multivariable analysis. Age, sex, diabetes, hypertension, previous coronary artery bypass graft (CABG) surgery, use of the retrograde approach, and procedure time were candidates for the multivariable model. In the iterative process of variable selection, covariates were removed from the model if they were nonsignificant and not confounders. Significance was evaluated at the 0.1 alpha level and confounding as a change in any parameter estimate >15%. At the end of this iterative process, the model contained significant covariates and confounders. At this point, any variable not selected for the original multivariable model was added back 1 at a time, with significant covariates and confounders retained earlier. Any that were significant at the 0.1 level were put in the model, and the model was iteratively reduced as before, but only for the variables that were additionally added.

The incidence of MACE was calculated using the Kaplan-Meier method and compared using the log-rank test, with hazard ratios (HR) calculated using Cox

Table 1. Clinical and Angiographic Characteristics and Outcomes of the Study Patients, Classified According to Whether They Underwent CTO PCI Using the Antegrade or the Retrograde Approach

	All Patients (N = 325)	Antegrade (n = 238)	Retrograde (n = 87)	p Value
Age, yrs	64 ± 8.4	64 ± 8.8	64 ± 7.4	0.704
Men	98.7	98.7	98.8	0.935
Hypertension	90.0	89.5	91.9	0.501
Hyperlipidemia	89.0	87.8	91.9	0.278
Diabetes	47.0	48.2	43.7	0.447
Heart failure	38.4	39.5	35.6	0.527
History of MI	47.3	45.4	53.9	0.231
History of CABG	26.0	20.7	40.2	0.001
History of stroke	4.3	3.8	5.7	0.452
Prior PCI	36.4	40.5	25.3	0.011
Initial presentation with ACS	20.9	23.5	13.8	0.048
CTO target vessel				0.001
RCA	56.2	47.0	79.1	
LCX	20.9	25.6	9.3	
LAD	21.6	26.1	10.5	
LMCA/graft	1.3	1.4	1.3	
Number of stents implanted	2 (0, 3)	2 (1, 3)	3 (0, 4)	0.387
Procedure time, min	124 (88–177)	107.5 (84.3–141.7)	192 (151–238)	0.001
Fluoroscopy time, min	34.7 (21.6–52.7)	28.6 (18.5–40.3)	55.2 (44.6–71.7)	0.001
Air kerma radiation exposure, Gy	4.4 (3.0–5.9)	3.4 (2.4–5.0)	5.7 (4.5–7.3)	0.001
Contrast volume, ml	338 (250–430)	310 (230–400)	400 (300–500)	0.001
Post-PCI CK-MB increase ≥3× ULN	8.6	6.7	13.8	0.044
Post-PCI Troponin ≥3× ULN	60.6	51.7	85.1	<0.0001
Post-PCI Troponin ≥10× ULN	43.1	33.2	70.1	<0.0001
Post-PCI Troponin ≥20× ULN	31.4	24.8	49.4	<0.0001
Technical success	77.8	80.7	70.1	0.047
Procedural success	76.6	80.3	66.7	0.014

Values are mean ± SD, percentage, or median (interquartile range).

ACS = acute coronary syndrome; CABG = coronary artery bypass graft; CK-MB = creatine kinase-myocardial band; CTO = chronic total occlusion; LAD = left anterior descending; LCX = left circumflex; LM = left main coronary artery; MI = myocardial infarction; PCI = percutaneous coronary intervention; RCA = right coronary artery; ULN = upper limit of normal.

proportional hazard. Sensitivity and specificity of post-PCI troponin values for the prediction of MACE were evaluated with receiver-operating characteristic curves, and the Youden index was calculated for each troponin cutoff value. Statistical analyses were performed using JMP (version 9.0, SAS Institute), SAS (version 9.2 for Linux, SAS Institute), and Stata (release 11, StataCorp, College Station, Texas).

Table 2. Clinical Presentation of Patients Who Underwent CTO PCI During the Study Period

Clinical Presentation	Number (N = 325)	Percentage of Total
Stable angina	257	79.1
Acute coronary syndrome	68	20.9
Unstable angina	31	9.5
NSTEMI	36	11.1
STEMI	1	0.31

NSTEMI = non–ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction; other abbreviations as in Table 1.

Results

Patient characteristics. The clinical and procedural characteristics of the study patients are presented in Table 1. As is common in CTO PCI series, most patients were men with a high prevalence of atherosclerosis risk factors. Approximately 1 in 4 patients had previous CABG, and 1 in 3 patients had previous PCI. The most common CTO target vessel was the right coronary artery. The retrograde approach was used in 26.8% of procedures and the technical and procedural success was 77.8% and 76.6%, respectively. Procedure time, fluoroscopy time, air kerma radiation exposure, and total contrast utilization were higher in patients treated with the retrograde approach (p = 0.001).

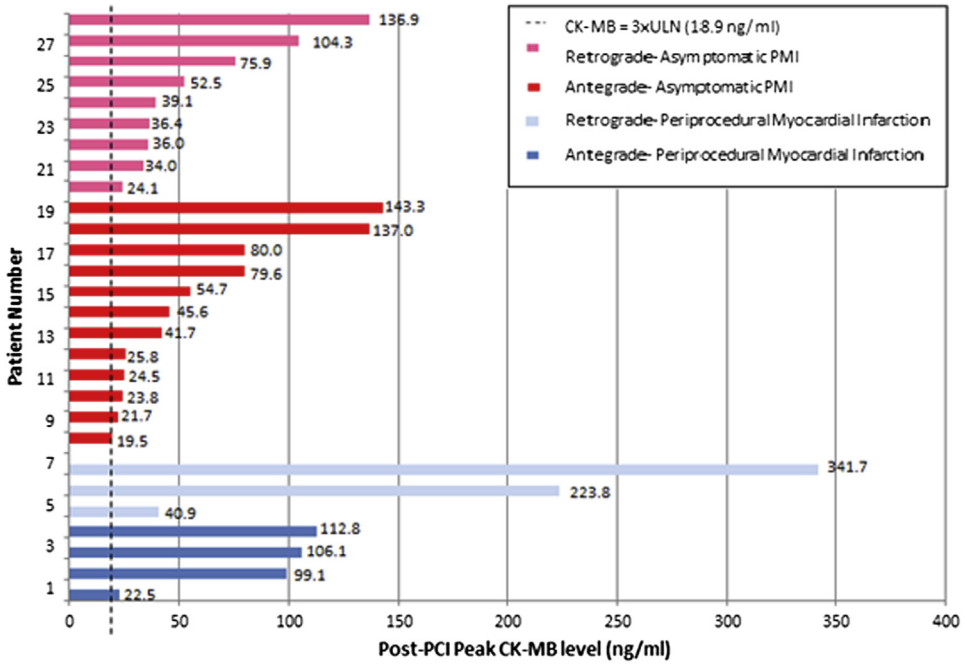

Figure 1. Post-PCI Peak CK-MB Levels of the 28 Patients Who Developed PMI During CTO PCI

Periprocedural myocardial infarction (MI) occurred in 7 of the 28 patients with periprocedural myocardial injury (PMI): 6 patients had prolonged ischemic symptoms >20 min, and 1 patient (Patient #7) had both prolonged chest pain and new Q-wave MI. CK-MB = creatine kinase-myocardial band; CTO = chronic total occlusion; PCI = percutaneous coronary intervention; ULN = upper limit of normal.

The clinical presentation of patients who underwent CTO PCI is shown in Table 2. Approximately 80% of patients presented with stable angina and 20% with recent acute coronary syndrome, mainly non–ST-segment elevation acute myocardial infarction or unstable angina. More patients presenting with acute coronary syndrome were treated using the antegrade than the retrograde approach (23.5% vs. 13.5%, p = 0.048) (Table 1).

Frequency of periprocedural myocardial injury. PMI occurred in 28 patients (8.6%; 95% CI: 5.8% to 12.2%). The mean and median CK-MB levels were 69 ± 73 and 39 (IQR: 22 to 103) ng/ml, respectively (Fig. 1). The baseline and maximum CK-MB for these 28 patients are presented in Table 3. Of the 325 CTO PCI patients studied, 30 had elevated baseline CK-MB ≥6.3 ng/ml (ULN): 9 of these 30 patients had peak post-PCI CK-MB ≥3× ULN, but 3 patients had peak post-PCI CK-MB that were less than baseline CK-MB and thus were not categorized as PMI. Therefore, 6 patients, or 21.4% of patients with PMI, had baseline CK-MB ≥ULN and still met the criteria for PMI (Table 3).

Periprocedural MI occurred in 7 of the 28 patients with PMI (25% of PMI patients or 2.1% of CTO PCI patients) as 6 patients had prolonged ischemic symptoms >20 min, and 1 patient (Patient #7) had both prolonged chest pain and new Q-wave MI (Q-wave MI developed in 3.6% of PMI patients or 0.3% of total CTO PCI patients) (Fig. 1). The frequency of periprocedural cardiac troponin elevation ≥3×, ≥10×, and ≥20× ULN was 61%, 43%, and 31%, respectively. Irrespective of the troponin cutoff used to define PMI, the frequency of periprocedural troponin elevation was greater when the retrograde approach was used (p < 0.0001) (Table 1).

Correlates of periprocedural myocardial injury. The frequency of PMI among 21 patients who had a procedural complication (e.g., emergency CABG, tamponade) was 19% versus 8% among patients who did not have a complication (p = 0.12). PMI was numerically higher among patients in whom CTO PCI failed compared with those in whom CTO PCI was successful (11.8% vs. 7.6%, p = 0.268).

The clinical characteristics and outcomes of patients with PMI versus those without PMI are shown in Table 4. Patients with PMI were more likely to have hypertension and previous CABG (p = 0.014). They were also more likely to have had CTO PCI using the retrograde approach: PMI occurred in 13.8% of patients in whom the retrograde approach was used compared with 6.7% of patients in whom only antegrade crossing was performed (p = 0.044). Antegrade dissection/re-entry was used in 29% of cases and antegrade wire escalation was used in 90.3% of cases. The incidence of PMI when antegrade dissection/re-entry

Table 3. Baseline and Peak Post-PCI CK-MB Levels for All Patients With PMI

Patient #	Baseline CK-MB (ng/ml)	Peak Post-PCI CK-MB (ng/ml)
1	6.9	22.5
2	1.9	99.1
3	1.1	106.1
4	1.9	112.8
5	6.6	40.9
6	2.4	223.8
7	12.3	341.7
8	4.1	19.5
9	1.7	21.7
10	5.0	23.8
11	3.0	24.5
12	3.3	25.8
13	2.6	41.7
14	6.2	45.6
15	7.2	54.7
16	2.1	79.6
17	1.2	80.0
18	2.5	137.0
19	24.9	143.3
20	1.1	24.1
21	6.8	34.0
22	4.3	36.0
23	2.9	36.4
24	1.3	39.1
25	1.8	52.5
26	3.0	75.9
27	5.6	104.3
28	1.0	136.9

PMI = periprocedural myocardial injury; other abbreviations as in Table 1.

Table 4. Clinical and Angiographic Characteristics and Outcomes of the Study Patients, Classified According to Whether They Had PMI

	All Patients (N = 325)	PMI (n = 28)	No PMI (n = 297)	p Value
Age, yrs	64 ± 8.4	63 ± 5.6	64 ± 8.7	0.281
Men	98.7	100.0	98.6	0.394
Hypertension	90.0	100.0	89.2	0.014
Hyperlipidemia	89.0	92.9	88.6	0.464
Diabetes	47.0	32.1	48.5	0.094
Heart failure	38.4	35.7	38.7	0.754
History of MI	47.3	50.0	47.1	0.772
History of CABG	26.0	46.4	24.0	0.014
History of stroke	4.3	3.6	4.4	0.837
Prior PCI	36.4	46.4	35.5	0.256
Retrograde approach	26.8	43.9	25.3	0.044
CTO target vessel				0.393
RCA	56.2	73.1	54.6	
LCX	20.9	15.4	21.5	
LAD	21.6	11.5	22.6	
LMCA/graft	1.3	0	1.5	
Technical success	77.8	67.9	78.8	0.201
Procedural success	76.6	67.9	77.4	0.268
Number of stents implanted	2 (0–3)	3 (0–4)	2 (0–3)	0.778
Procedure time, min	124 (88–177)	175 (147–241)	120 (88–174)	<0.0001
Fluoroscopy time, min	34.7 (21.6–52.7)	64.5 (43.5–72.7)	31.9 (21.1–50.0)	<0.0001
Air kerma radiation exposure, Gray	4.4 (3.0–5.9)	5.9 (5.3–7.4)	4.2 (2.8–5.6)	0.012
Contrast volume, ml	338 (250–430)	450 (375–545)	325 (245–415)	<0.0001

Values are mean ± SD, %, or median (interquartile range).
Abbreviations as in Tables 1 and 3.

crossing strategies were used was 11.2% versus 7.7% when such strategies were not used (antegrade wire escalation and/or retrograde approach, p = 0.311). If retrograde CTO PCI cases were excluded from the analysis, the PMI rate with antegrade dissection/re-entry was similar to that of antegrade wire escalation (8% of 50 cases vs. 7% of 213 cases, p = 0.821). On multivariable analysis, results of the purposeful selection model yielded 2 variables associated with PMI: diabetes (adjusted odds ratio [OR]: 0.45; 95% CI: 0.19 to 1.04; p = 0.061) and previous CABG (adjusted OR: 3.03; 95% CI: 1.36 to 6.75; p = 0.007). The incidence of PMI tended to increase over time in conjunction with an increase in the use of retrograde crossing strategies and was unrelated to the utilization of antegrade dissection/re-entry strategies (Fig. 2).

PMI and clinical outcomes after CTO PCI. During mid-term follow-up (median: 2.3 years; IQR: 0.8, 4.6 years), 40% of patients experienced MACE: 11% died; 9% had an acute coronary syndrome; 28.5% required PCI; and 3.4% underwent CABG. The incidence of MACE during mid-term follow-up was higher among patients who had PMI during the index PCI than in those who did not (HR: 2.25; 95% CI: 1.28 to 3.70; p = 0.006) (Fig. 3). When patients with asymptomatic PMI were analyzed separately from those with periprocedural MI, the incidence of MACE was still higher among patients who had asymptomatic PMI compared with those who had no PMI (HR: 2.26; 95% CI: 1.21 to 3.88; p = 0.013) (Fig. 4). Patients with periprocedural MI had a trend toward a higher incidence of MACE than did patients without PMI (HR: 2.23; 95% CI: 0.55 to 5.92; p = 0.226) (Fig. 4). As shown in Table 5, patients with asymptomatic PMI, periprocedural MI, and no PMI were discharged on similar medication regimens.

Receiver-operating characteristic curves were used to determine a threshold for post-PCI peak troponin association with MACE (Fig. 5). The area under the curve for the 1-year incidence of MACE was 0.577 (95% CI: 0.506 to 0.647, p = 0.034). The discriminatory capacity of troponin for the 1-year incidence of MACE was similarly low among patients undergoing antegrade (area under the curve: 0.579; 95% CI: 0.497 to 0.660, p = 0.0649) or retrograde (area under the curve: 0.588; 95% CI: 0.447 to 0.729, p = 0.200) CTO PCI. The optimal troponin value for 1-year incidence

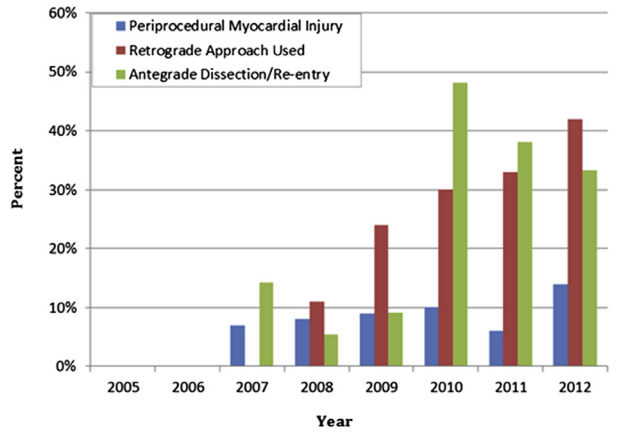

Figure 2. Temporal Trends

Temporal trends in the incidence of PMI, use of the retrograde approach, and use of the antegrade dissection/re-entry in CTO PCI. Abbreviations as in Figure 1.

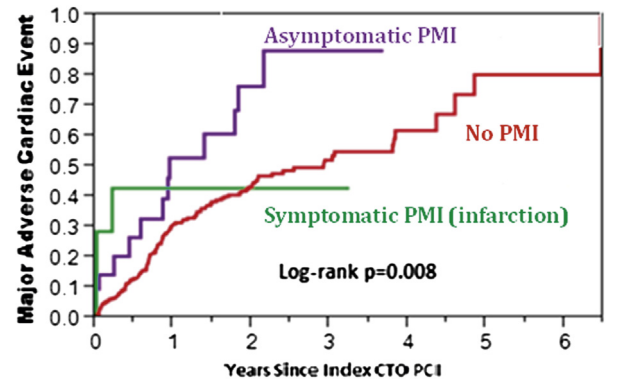

Figure 4. Incidence of MACE Among Study Patients, Classified According to the Occurrence of PMI

Kaplan-Meier curves describing the incidence of MACE among patients with asymptomatic PMI, symptomatic PMI, and no PMI. Abbreviations as in Figures 1 and 3.

of MACE as defined using the maximum Youden index was 1.64 ng/ml (approximately 50× ULN). This cutoff value provided 26% sensitivity and 88% specificity for the prediction of MACE and a positive likelihood ratio of 2.12 and negative likelihood ratio of 0.84, suggesting poor discriminatory capacity.

Discussion

The main findings of our study that used systematic evaluation of cardiac biomarkers after PCI are as follows: 1) PMI occurs more commonly than previously reported after CTO PCI; 2) it is more frequent when the retrograde approach is used; and 3) it is associated with worse subsequent clinical outcomes.

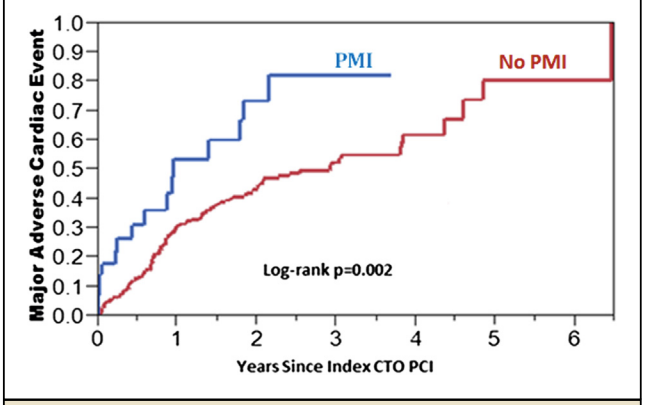

Figure 3. Kaplan-Meier Curves of the Incidence of MACE in Patients With and Without PMI After CTO PCI

The incidence of major adverse cardiac events (MACE) during a median of 2.3 years (interquartile range: 0.8 to 4.6 years) was higher among patients who had PMI during CTO PCI than in those who did not have PMI (hazard ratio: 2.25; 95% confidence interval: 1.28 to 3.70, p = 0.006). Abbreviations as in Figure 1.

Incidence and presentation of PMI after CTO PCI. A systematic review and meta-analysis of 65 studies that reported complications after CTO PCI found wide variability in the incidence of post-PCI MI (from 0% to 19.4%); however, the pooled estimate was low (2.8%; 95% CI: 1.5% to 4.1%). The incidence of Q-wave MI was very low (0.2%; 95% CI: 0% to 0.9%) (4). However, a major limitation of previous studies is that they did not perform systematic cardiac biomarker measurements, as is true for most contemporary PCI procedures in the United States (only 7% of patients had cardiac biomarker measurement post-PCI in the National Cardiovascular Data Registry) (7).

This limitation was addressed by our study, in which cardiac biomarkers were measured twice during the first 24 h after PCI and revealed that the actual incidence of PMI was approximately 3-fold higher (8.6%; 95% CI: 5.8% to 12.2%) than was suggested by previous reports. However, the incidence of Q-wave MI was 0.2%, suggesting that most PMI occurring during CTO PCI may affect limited areas of myocardium. Accordingly, 75% of all patients with PMI in our series did not have any ischemic symptoms.

Correlates of PMI after CTO PCI. The retrograde approach has revolutionized CTO PCI by enabling high success rates even in patients with very complex coronary anatomies (8,9). The retrograde approach entails insertion of a coronary guidewire via a collateral vessel in the coronary vessel distal to the distal cap followed either by retrograde true-to-true lumen crossing or by using a dissection/re-entry strategy, such as the controlled antegrade and retrograde tracking and dissection or reverse controlled antegrade and retrograde

Table 5. Discharge Medications of Patients Undergoing CTO PCI During the Study Period

	All Patients (N = 325)	Asymptomatic PMI (n = 21)	Periprocedural MI (n = 7)	No PMI or Periprocedural MI (n = 297)	p Value
Beta-blocker	93.5	95.2	100	93.2	0.579
ACEI or ARB	79.3	66.7	71.4	80.3	0.325
Statin	96.9	100	100	88.2	0.398
Aspirin	98.8	100	100	98.6	0.694
Thienopyridine	90.1*	81.0	85.7	90.9	0.383

Values are %. *Thienopyridine was administered in 98.8% of successful CTO PCI procedures versus 61.3% of failed CTO PCI procedures.
ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; other abbreviations as in Tables 1 and 3.

tracking technique (9). Previous studies had shown a trend for higher PMI with the retrograde approach. In an analysis of 1,983 lesions in 1,914 patients from the European registry of CTO, the retrograde approach was used in 11.8% of cases and a trend for higher frequency of post-PCI MI was observed in patients undergoing retrograde CTO PCI (2.1% vs. 1.0%, p = 0.08) (10). In the meta-analysis of 65 studies reporting on CTO PCI complications among 884 patients undergoing CTO PCI of 886 lesions using a retrograde approach, PMI occurred in 1.8% (95% CI: 1.5% to 4.1%) (4). Major complications such as death, emergent CABG, and stroke were rare, each occurring in 0.1% of patients.

In our study, the incidence of PMI was approximately 2-fold higher among patients treated using a retrograde versus an antegrade approach (13.8% vs. 6.7%, p = 0.044). The higher incidence of PMI with the retrograde approach may be because of injury of the myocardium along the collateral vessel used for retrograde crossing or could be related to the use of dissection strategies that could disrupt small coronary artery side branches. In a recent report, magnetic resonance imaging after retrograde CTO PCI via a septal collateral demonstrated a new area of delayed hyperenhancement in the septum, suggesting injury from guidewire or other equipment passage (11). The higher incidence of PMI with the retrograde approach may also be related to higher lesion complexity, as in most cases, the retrograde approach was used after antegrade crossing failure. Accordingly, the prevalence of previous CABG was twice as high among patients in whom the retrograde approach was used (Table 1), and previous CABG is known to be associated with higher rates of procedural failure (12). Similarly, right coronary artery CTO, which are more challenging to cross, were more likely to be approached using the retrograde approach (Table 1).

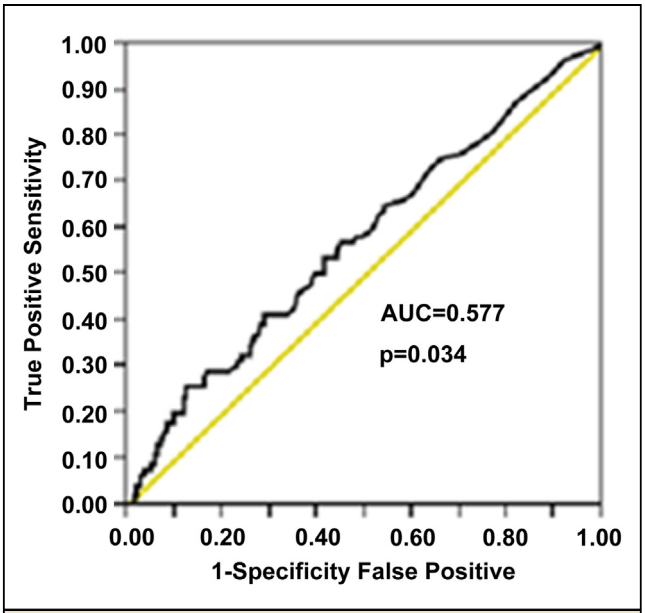

Figure 5. Peak Post-PCI Troponin Levels ROC Curve

Receiver-operating characteristic (ROC) curve of peak post-PCI troponin levels for determining the 1-year incidence of MACE. Abbreviations as in Figures 1 and 3.

Implications of periprocedural myocardial injury and infarction after CTO PCI. Although cardiac biomarker elevation after routine PCI has been associated with higher immediate and long-term mortality, the clinical and therapeutic implications of CTO PCI PMI remain controversial (5). Our study demonstrates a higher incidence of MACE during a median follow-up of 2.3 years among CTO PCI patients who developed PMI. Possible explanations include compromise of distal collateral vessels from microembolization, heightened inflammatory state post-PCI PMI, predisposition to arrhythmias after infarction, and higher rates of index CTO PCI failure (Table 4) (11,13,14). Moreover, PMI patients may be at higher risk for subsequent adverse events because of comorbidities or higher coronary lesion complexity.

Troponin release in CTO PCI. Our study shows that troponin release is common after both antegrade and retrograde CTO PCI. The threshold value of troponin above the ULN whereby an adverse prognosis is evident is not well defined (5,15). Currently, guidelines suggest that troponin elevation >5× ULN should be considered evidence of cardiac injury or infarction, but this threshold was arbitrarily chosen (5). In our population, post-CTO PCI troponin levels had limited association with MACE. A high troponin threshold (50× ULN) provided the best association with 1-year MACE,

suggesting that further studies are needed for determining a clinically useful troponin threshold.

Study limitations. Our study is limited by the retrospective single-center design and relatively small number of patients; however, it is the first study of its kind to be reported. Our sample size may not have accommodated a larger set of predictors, thereby potentially limiting replication. However, our final model revealed only 2 significant predictors and therefore had adequate statistical power. As is typical in veteran populations, most of the included patients were men, although men constitute the majority of patients in most CTO PCI series. Moreover, the study patients often had previous CABG, previous MI, and previous PCI, suggesting that this may be a higher-risk group than the general population. In the United States, the use of CK-MB is currently declining and hence CK-MB may not be available for clinical use at all institutions.

Conclusions

We found that PMI occurs in 8.6% of patients undergoing CTO PCI, is more common with the retrograde approach, and is associated with worse clinical outcomes during mid-term follow-up. Studies to better assess the pathophysiology of PMI in the CTO PCI setting, its implications, and preventive and treatment measures are needed.

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Key Words: acute myocardial infarction ■ chronic total occlusion ■ complications ■ percutaneous coronary intervention ■ periprocedural myocardial injury.