Percutaneous Coronary Intervention for Chronic Total Occlusion in Single Coronary Arteries

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We retrospectively compared the results of percutaneous coronary intervention (PCI) and optimal medical therapy (OMT) for chronic total occlusion (CTO) in single coronary arteries to determine whether outcomes depend on the artery involved.

From January 2004 through November 2015, a total of 731 patients were treated at our center for CTO in the left anterior descending coronary artery (LAD) (234 patients, 32%), left circumflex coronary artery (LCx) (184, 25.2%), or right coronary artery (RCA) (313, 42.8%). We further classified patients by treatment (PCI or OMT) and compared the cumulative incidence of major adverse cardiac events (MACE) and the composite of total death or myocardial infarction, as well as change in left ventricular ejection fraction from baseline.

The 5-year cumulative incidence of MACE was similar between the treatment groups regardless of target vessel. The 5-year cumulative incidence of the composite of total death or myocardial infarction was significantly lower after PCI than after OMT or failed PCI in the LCx (2.6% vs 11.5%; P=0.020; log-rank) and RCA (5.8% vs 17.2%; P=0.002) groups, but not in the LAD group. Cox proportional hazards regression analysis indicated that PCI independently predicted a lower incidence of the composite of total death or myocardial infarction in the LCx group (hazard ratio [HR]=0.184; 95% CI, 0.0035–0.972; P=0.046) and the RCA group (HR=0.316; 95% CI, 0.119–0.839; P=0.021).

The artery involved does not appear to affect clinical outcomes of successful PCI for single-vessel CTO. Further investigation in a randomized clinical trial is warranted. (Tex Heart Inst J 2021;48(2):e197023)

Advances in technique, drug-eluting stents, and device technology have led to increased use of percutaneous coronary intervention (PCI) to treat left main coronary artery (LMCA) bifurcation and multivessel disease. However, PCI for chronic total occlusion (CTO) of coronary arteries remains challenging and relatively underused. Despite an estimated incidence of 20% to 30% on diagnostic angiograms,1-3 CTO lesions are treated with PCI significantly less often than non-CTO lesions are.1,3-5 The reason may be related to concerns about lower procedural success rates, higher target lesion failure rates, and uncertainty about clinical benefits in patients with CTOs.6,7 Observational studies have shown that successful PCI of CTOs in general can improve symptoms,8,9 left ventricular (LV) systolic function,9,10 and survival.11,12 However, data on its benefits in different single target vessels are limited. Therefore, we retrospectively compared the clinical outcomes of PCI and optimal medical therapy (OMT) in patients treated for single CTO lesions in 3 different major coronary arteries.
### TABLE I. Demographic and Clinical Characteristics of the 731 Patients

| Variable               | Total (n=388) | OMT (n=343) | P Value | Target Vessel | Total (n=152) | OMT (n=82) | P Value | Total (n=144) | OMT (n=169) | P Value |
|------------------------|---------------|-------------|---------|---------------|---------------|-------------|---------|---------------|-------------|---------|
| **Demographic**        |               |             |         |               |               |             |         |               |             |         |
| Age (yr)               | 62.4 ± 10.7   | 66.3 ± 10.6 | <0.001  | 61.6 ± 10.9   | 65.4 ± 10.1   | 0.010       | 63.9 ± 9.9 | 65.8 ± 10.5 | 0.213       | 62.4 ± 11.0 | 67.1 ± 11.0 | <0.001 |
| Male                   | 291 (75.0)    | 238 (69.4)  | 0.09    | 108 (71.1)    | 56 (68.3)     | 0.66        | 71 (77.2) | 65 (70.7)    | 0.314       | 112 (77.8) | 117 (69.2) | 0.089  |
| **Clinical**           |               |             |         |               |               |             |         |               |             |         |
| LVEF (%)               | 52.4 ± 10.8   | 48.3 ± 13.1 | <0.001  | 51.4 ± 12.5   | 46.8 ± 14.3   | 0.017       | 52.8 ± 10.3 | 49.4 ± 12.4 | 0.050       | 53.1 ± 9.2 | 48.4 ± 12.8 | <0.001 |
| MI                     | 77 (19.8)     | 73 (21.3)   | 0.631   | 30 (19.7)     | 18 (22.0)     | 0.689       | 21 (22.8) | 24 (26.1)    | 0.607       | 26 (18.1) | 31 (18.3) | 0.948  |
| STEMI                  | 31 (8.0)      | 36 (10.5)   | 0.241   | 14 (9.2)      | 9 (11.0)      | 0.665       | 7 (17.6) | 13 (14.1)    | 0.155       | 10 (6.9) | 14 (8.3) | 0.657  |
| NSTEMI                 | 46 (11.9)     | 36 (10.5)   | 0.561   | 16 (10.5)     | 8 (9.8)       | 0.853       | 14 (15.2) | 11 (12.0)    | 0.519       | 16 (11.1) | 17 (10.1) | 0.763  |
| **Risk factors**       |               |             |         |               |               |             |         |               |             |         |
| Hypertension           | 244 (62.9)    | 241 (70.3)  | 0.035   | 97 (63.8)     | 56 (68.3)     | 0.492       | 57 (62.0) | 62 (67.4)    | 0.441       | 90 (62.5) | 123 (72.8) | 0.052  |
| Diabetes               | 150 (38.7)    | 136 (39.7)  | 0.784   | 55 (36.2)     | 31 (37.8)     | 0.806       | 33 (35.9) | 34 (37.0)    | 0.878       | 62 (43.1) | 71 (42.0) | 0.852  |
| Dyslipidemia           | 106 (27.3)    | 109 (31.8)  | 0.187   | 40 (26.3)     | 24 (29.3)     | 0.629       | 25 (27.2) | 35 (38.0)    | 0.116       | 41 (28.5) | 50 (29.6) | 0.829  |
| CKD                    | 26 (6.7)      | 30 (8.7)    | 0.299   | 8 (5.3)       | 6 (7.3)       | 0.527       | 5 (5.4)  | 8 (8.7)      | 0.388       | 31 (9.0)  | 16 (9.5) | 0.894  |
| Smoking                | 208 (53.6)    | 186 (54.2)  | 0.867   | 77 (50.7)     | 45 (54.9)     | 0.538       | 53 (57.6) | 49 (53.3)    | 0.553       | 78 (54.2) | 92 (54.4) | 0.962  |
| Current smoker         | 145 (37.4)    | 125 (36.4)  | 0.795   | 57 (37.5)     | 30 (36.6)     | 0.89        | 33 (35.9) | 32 (34.8)    | 0.877       | 55 (38.2) | 63 (37.3) | 0.868  |
| CVA                    | 34 (8.8)      | 42 (12.2)   | 0.124   | 11 (7.2)      | 8 (9.8)       | 0.501       | 10 (10.9) | 10 (10.9)    | >0.99       | 13 (9.0)  | 24 (14.2) | 0.158  |
| PAOD                   | 32 (8.2)      | 42 (12.2)   | 0.074   | 7 (4.6)       | 3 (3.7)       | 0.733       | 12 (13.0) | 15 (16.3)    | 0.532       | 13 (9.0)  | 24 (14.2) | 0.158  |
| **CCS classification**|               |             |         |               |               |             |         |               |             |         |
| I                      | 103 (26.5)    | 200 (58.3)  | <0.001  | 32 (21.1)     | 48 (58.5)     | <0.001      | 32 (34.8) | 59 (64.1)    | <0.001      | 39 (27.1) | 93 (55.0) | <0.001 |
| II                     | 84 (21.6)     | 64 (18.7)   | 0.315   | 32 (21.1)     | 13 (15.9)     | 0.336       | 17 (18.5) | 13 (14.1)    | 0.425       | 35 (24.3) | 38 (22.9) | 0.704  |
| III                    | 102 (26.3)    | 35 (10.2)   | <0.001  | 52 (34.2)     | 10 (12.2)     | <0.001      | 17 (18.5) | 8 (8.7)      | 0.053       | 33 (22.9) | 17 (10.1) | 0.002  |
| IV                     | 99 (25.5)     | 44 (12.8)   | <0.001  | 36 (23.7)     | 11 (13.4)     | 0.061       | 26 (28.3) | 12 (13.0)    | 0.011       | 37 (25.7) | 21 (12.4) | 0.003  |

CCS = Canadian Cardiovascular Society; CKD = chronic kidney disease; CTO = chronic total occlusion; CVA = cerebrovascular accident; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MVD = multivessel disease; NA = not applicable; NSTEMI = non-ST-segment-elevation myocardial infarction; OMT = optimal medical therapy; PAOD = peripheral arterial occlusive disease; PCI = percutaneous coronary intervention; RCA = right coronary artery; STEMI = ST-segment-elevation myocardial infarction

Data are presented as mean ± SD or as number and percentage. P <0.05 was considered statistically significant.
### TABLE I. Demographic and Clinical Characteristics of the 731 Patients (continued)

| Variable                        | Total (n=731) | Target Vessel |
|---------------------------------|---------------|---------------|
|                                 | PCI (n=388)   | OMT (n=343)   | P Value | PCI (n=152) | OMT (n=82) | P Value | PCI (n=92) | OMT (n=92) | P Value | PCI (n=144) | OMT (n=169) | P Value |
| Angiographic                    |               | LAD           | LCx      | RCA       |
| MVD                             | 206 (53.1)    | 268 (78.1)    | <0.001   | 59 (38.8) | 63 (76.8)   | <0.001   | 61 (66.3) | 75 (81.5)   | 0.019   | 86 (59.7) | 130 (76.9) | 0.001   |
| LMCA (>50%)                     | 19 (4.9)      | 49 (14.3)     | <0.001   | 3 (2.0)   | 13 (15.9)   | <0.001   | 6 (6.5)   | 13 (14.1)   | 0.090   | 10 (6.9) | 23 (13.6) | 0.056   |
| LAD (>70%)                      | 263 (67.8)    | 244 (71.1)    | 0.326    | 152 (100) | 82 (100)    | —        | 45 (48.9) | 56 (60.9)   | 0.103   | 66 (45.8) | 106 (62.7) | 0.003   |
| LCx (>70%)                      | 184 (47.4)    | 227 (66.2)    | <0.001   | 46 (30.3) | 41 (50.0)   | 0.003    | 92 (100.0) | 92 (100.0) | —       | 46 (31.9) | 94 (55.6) | <0.001   |
| RCA (>70%)                      | 209 (53.9)    | 256 (74.6)    | <0.001   | 26 (17.1) | 40 (48.8)   | <0.001   | 39 (42.4) | 47 (51.1)   | 0.237   | 144 (100) | 169 (100) | —       |
| No. vessels involved            | 1.73 ± 0.77   | 2.19 ± 0.77   | <0.001   | 1.47 ± 0.65 | 2.09 ± 0.74 | <0.001   | 1.97 ± 0.81 | 2.15 ± 0.71 | 0.100   | 1.85 ± 0.80 | 2.25 ± 0.81 | <0.001   |
| CTO, proximal location          | 167 (43.0)    | 170 (49.6)    | 0.078    | 64 (42.1) | 49 (59.8)   | 0.010    | 35 (38.0) | 30 (26.3)   | 0.441   | 68 (47.2) | 91 (53.8) | 0.243   |
| Collateral flow                 | 284 (73.2)    | 278 (81.0)    | 0.012    | 108 (71.1) | 64 (78.0)   | 0.247    | 71 (77.2) | 64 (69.6)   | 0.504   | 106 (73.6) | 151 (89.3) | <0.001   |
| Procedural                      |               |               |          |           |          |          |           |          |          |          |           |          |
| Failed CTO-PCI                  | NA            | 56 (16.3)     | <0.001   | NA        | 24 (29.3)  | <0.001   | NA        | 12 (13.0)  | <0.001   | NA        | 20 (11.8) | <0.001   |

CCS = Canadian Cardiovascular Society; CKD = chronic kidney disease; CTO = chronic total occlusion; CVA = cerebrovascular accident; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MVD = multivessel disease; NA = not applicable; NSTEMI = non-ST-segment-elevation myocardial infarction; OMT = optimal medical therapy; PAOD = peripheral arterial occlusive disease; PCI = percutaneous coronary intervention; RCA = right coronary artery; STEMI = ST-segment-elevation myocardial infarction

Data are presented as mean ± SD or as number and percentage. P <0.05 was considered statistically significant.

Clinical Outcomes of PCI for Chronic Total Occlusion

3 / 11
A total of 731 patients met our inclusion criteria and were divided into 3 groups according to the coronary artery in which the target lesion was located: left anterior descending (LAD), left circumflex (LCx), or right (RCA). Each group was further classified according to the treatment (PCI or OMT). Of note, the OMT group included patients in whom PCI was attempted but failed. The long-term incidence of individual and composite major adverse clinical outcomes and the change from baseline in LV systolic function were compared between treatments overall and in each target-vessel group.

The protocol for this retrospective, observational study was approved by our institutional review board, and all patients or their legal guardians gave written informed consent.

Study Design
The primary study endpoint was the 5-year cumulative incidence of major adverse cardiac events (MACE), which included total death, myocardial infarction (MI), target-vessel revascularization (TVR), target-lesion revascularization (TLR), and non-target-vessel revascularization (NTVR). We defined TVR as repeat PCI in the target vessel; TLR as repeat revascularization of CTO lesions within a previously treated target vessel or within 5 mm proximal or distal to that lesion; and NTVR as revascularization of a vessel other than the one containing the treated CTO. The secondary study endpoint was the change from baseline in LV ejection fraction (LVEF) at 2 years in patients who had at least 6 months of follow-up monitoring. Follow-up clinical data were collected through face-to-face interviews at outpatient clinic visits, medical chart reviews, and telephone interviews.

Statistical Analysis
Continuous data were expressed as mean ± SD, and differences between treatment groups were analyzed using the Student t test. Discrete data were expressed as number and percentage, and differences between treatment groups were analyzed using the χ² test. Cumulative incidences of MACE and of the composite of total death or MI were estimated using the Kaplan-Meier method, and differences between treatment groups were compared using the log-rank test. Clinical outcome risks were estimated using a multivariate Cox proportional hazards model. Univariate analysis included age, sex, and factors that differed significantly (P<0.05) between the OMT and PCI groups at baseline or were considered to be clinically important. Factors with a P value of <0.05 after univariate analysis were included in a multivariate analysis. Changes in LVEF from baseline were analyzed using the paired t test. For all analyses, P values of <0.05 were considered statistically significant. All statistical analyses were performed with SPSS version 22.0 (SPSS, an IBM company).

Results
Of the 713 patients included in the study, 313 (42.8%) had CTO in the RCA; 234 (32%), in the LAD; and 184 (25.2%), in the LCx (Table I). Percutaneous coronary intervention of the target-vessel CTO was attempted in 444 patients. The attempted PCI procedure was successful in 388 patients (87.4%); it failed in 56 patients (12.6%), including 20 in the RCA group, 24 in the LAD group, and 12 in the LCx group. The 56 patients were subsequently placed in the OMT group for the purposes of analysis. Overall, the OMT group had a higher incidence of multivessel disease (P<0.001) and a lower mean LVEF (P<0.001) at baseline than did those in the PCI group. In the LAD (P=0.01) and RCA (P<0.001) groups, patients who either had a failed PCI or received OMT were significantly younger than those who had successful PCI. Table I summarizes the baseline demographic and clinical characteristics of the study population overall and by target vessel.

Clinical Outcomes
Overall, the 5-year cumulative incidence of MACE did not differ significantly between treatment groups (Table I and Fig. 1A). However, the 5-year cumulative incidence of the composite of total death or MI was significantly lower in the PCI group (5.3%) than in the OMT group (13.6%) (P<0.001, log-rank) (Fig. 1B), consistent with findings in a previous study of ours.13 In the analysis of groups classified by the target artery, the 5-year cumulative incidences of both MACE and the composite of total death or MI in the LAD group were similar, regardless of treatment (Table I and Fig. 2). In the LCx (Fig. 3A) and RCA (Fig. 4A) groups, the 5-year cumulative incidence of MACE was also similar between treatment groups; however, differences were seen in the cumulative incidence of the composite of total death or MI. In the LCx group, the incidence was significantly lower after successful PCI (2.6%) than after OMT or failed PCI (11.5%) (P=0.020, log-rank) (Fig. 3B); likewise, in the RCA group, the incidence was significantly lower after successful PCI (5.8%) than after OMT or failed PCI (17.2%) (P=0.002, log-rank) (Fig. 4B).

In each target-vessel group, the incidence of TLR and TVR was significantly higher after successful PCI than after OMT or failed PCI (Table I). In the LCx group, the incidences of cardiac death and MI were significantly lower in the PCI group. In the RCA group, the individual incidences of total death and MI were significantly lower in the PCI group.
## TABLE II. Five-Year Cumulative Incidence of Major Adverse Clinical Outcomes

| Outcome          | Total                  | LAD                  | LCx                  | RCA                  |
|------------------|------------------------|----------------------|----------------------|----------------------|
|                  | PCI (n=388)            | OMT (n=343)          | PCI (n=152)          | OMT (n=82)           | Log-rank $P$ Value | PCI (n=92)          | OMT (n=92)          | Log-rank $P$ Value | PCI (n=144)          | OMT (n=169)          | Log-rank $P$ Value |
| Total death      | 17 (4.8)               | 34 (10.4)            | 8 (5.5)              | 3 (4.1)              | 0.548               | 2 (2.6)              | 8 (9.2)              | 0.059               | 7 (5.8)              | 23 (14.1)            | 0.016               |
| Cardiac death    | 12 (3.4)               | 23 (7.1)             | 6 (4.1)              | 3 (4.1)              | 0.867               | 0                   | 6 (6.9)              | 0.015               | 6 (5.0)              | 14 (8.6)             | 0.166               |
| MI               | 8 (2.2)                | 18 (6.0)             | 6 (4.0)              | 3 (4.3)              | 0.858               | 0                   | 4 (5.0)              | 0.046               | 2 (1.7)              | 11 (7.4)             | 0.030               |
| STEMI            | 7 (1.9)                | 6 (2.0)              | 6 (4.0)              | 0                   | 0.071               | 0                   | 2 (2.6)              | 0.156               | 1 (0.8)              | 4 (2.7)              | 0.248               |
| Revascularization| 64 (19.1)              | 41 (13.6)            | 27 (20.2)            | 10 (13.8)            | 0.198               | 18 (21.7)            | 7 (9.0)              | 0.017               | 19 (16.0)            | 34 (16.1)            | 0.874               |
| TLR              | 37 (11.0)              | 9 (2.9)              | <0.001               | 15 (11.2)            | 2 (2.7)              | 0.032               | 7 (8.5)              | 1 (1.2)              | 0.033               | 15 (12.2)            | 6 (4.0)              | 0.014               |
| TVR              | 43 (12.7)              | 10 (3.3)             | <0.001               | 18 (13.3)            | 2 (2.7)              | 0.012               | 9 (11.2)             | 2 (2.5)              | 0.03                | 16 (12.9)            | 6 (4.0)              | 0.008               |
| NTVR             | 36 (10.8)              | 39 (13.1)            | 0.424                | 12 (9.1)             | 11 (15.3)            | 0.230               | 12 (14.2)            | 6 (7.8)              | 0.137               | 12 (10.3)            | 22 (14.8)            | 0.216               |
| Stroke           | 1 (0.3)                | 0                   | 0.323                | 0                   | 0                   | 1 (1.4)              | 0                   | 0.311               | 0                   | 0                   | —                   |
| MACE             | 79 (22.8)              | 72 (22.2)            | 0.878                | 34 (24.1)            | 13 (17.7)            | 0.178               | 19 (22.6)            | 14 (16.3)            | 0.295               | 26 (21.4)            | 45 (27.6)            | 0.143               |
| Total death or MI| 19 (5.3)               | 44 (13.6)            | <0.001               | 10 (6.8)             | 6 (8.4)              | 0.920               | 2 (2.6)              | 10 (11.5)            | 0.020               | 7 (5.8)              | 28 (17.2)            | 0.002               |

CTO = chronic total occlusion; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LV = left ventricle; MACE = major adverse cardiac events; MI = myocardial infarction; NTVR = non-target-vessel revascularization; OMT = optimal medical therapy; PCI = percutaneous coronary intervention; RCA = right coronary artery; STEMI = ST-segment-elevation myocardial infarction; TLR = target-lesion revascularization; TVR = target-vessel revascularization

Data are reported as cumulative number of events and Kaplan-Meier estimated cumulative percentage, along with the log-rank test values for differences between groups. $P < 0.05$ was considered statistically significant.
**Fig. 1** Graphs show Kaplan-Meier estimates of the overall cumulative incidence of **A** major adverse cardiac events and **B** composite of total death or myocardial infarction in patients with chronic total occlusion in a single coronary artery who underwent successful percutaneous coronary intervention (PCI) or who either had a failed PCI or received optimal medical therapy (OMT).

*P* <0.05 was considered statistically significant.

**Fig. 2** Graphs show Kaplan-Meier estimates of the cumulative incidence of **A** major adverse cardiac events and **B** composite of total death or myocardial infarction in patients with chronic total occlusion in the left anterior descending coronary artery who underwent successful percutaneous coronary intervention (PCI) or who either had a failed PCI or received optimal medical therapy (OMT).

*P* <0.05 was considered statistically significant.
**Fig. 3** Graphs show Kaplan-Meier estimates of the cumulative incidence of **A** major adverse cardiac events and **B** composite of total death or myocardial infarction in patients with chronic total occlusion in the left circumflex coronary artery who underwent successful percutaneous coronary intervention (PCI) or who either had a failed PCI or received optimal medical therapy (OMT).

*P* <0.05 was considered statistically significant.

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**Fig. 4** Graphs show Kaplan-Meier estimates of the cumulative incidence of **A** major adverse cardiac events and **B** composite of total death or myocardial infarction in patients with chronic total occlusion of the right coronary artery who underwent successful percutaneous coronary intervention (PCI) or who either had a failed PCI or received optimal medical therapy (OMT).

*P* <0.05 was considered statistically significant.
Predictors of Composite of Total Death or Myocardial Infarction

In the LCx group, successful PCI (hazard ratio [HR]=0.184; 95% CI, 0.035–0.972; P=0.046) and age (HR=1.145; 95% CI, 1.041–1.260; P=0.005) were independent predictors of the composite of total death or MI (Table III). In the RCA group, successful PCI (HR=0.316; 95% CI, 0.119–0.839; P=0.0216), age (HR=1.043; 95% CI, 1.003–1.085; P=0.036), and chronic kidney disease (HR=2.813; 95% CI, 1.207–6.554; P=0.017) were independent predictors of the composite.

Changes in Left Ventricular Systolic Function

Overall, at 2-year follow-up, the mean LVEF improved significantly in both treatment groups: from 49.1% before to 52.5% after treatment in the PCI group (P<0.001) and from 46.9% before to 49.6% after treatment in the OMT group (P=0.002) (Table IV).

In analysis of the target-vessel groups, the mean LVEF improved significantly after successful PCI in those with CTO in the LAD (from 47.3% to 51.5%; P<0.001; mean follow-up time, 1.7 yr) and LCx (from 49.8% to 54.9%; P<0.001; mean follow-up, 1.7 yr), but not in those with CTO in the RCA (from 50.5% to 52.1%; P=0.194; mean follow-up, 1.6 yr). After failed PCI or OMT, the mean LVEF improved significantly in those with CTO in the LCx (from 48.6% to 52.8%; P=0.015; mean follow-up, 2.0 yr), but not in those with CTO in the LAD (from 45.6% to 48.0%, P=0.214; mean follow-up, 2.2 yr) or RCA (from 46.8% to 48.9%, P=0.065; mean follow-up, 1.6 yr).

Discussion

We found that the 5-year cumulative incidence of MACE was similar in the PCI and OMT groups, regardless of which coronary artery contained the CTO. However, among patients with CTO in the LCx or RCA, we found that the composite of total death or MI was significantly less frequent in those who underwent successful PCI. Furthermore, successful PCI in the LCx or RCA independently predicted lower total death or MI.

The clinical benefits of CTO revascularization remain debatable. Several observational studies and meta-analyses have revealed the beneficial effects of successful CTO-PCI, such as improvement in angina

| TABLE III. Cox Proportional Hazards Model Analysis of Composite of Total Death or Myocardial Infarction |
|----------------------------------------|---------------|----------------|----------------|---------------|----------------|---------------|----------------|---------------|----------------|
| Variable                              | Univariate HR (95% CI) | P Value | Multivariate HR (95% CI) | P Value | Univariate HR (95% CI) | P Value | Multivariate HR (95% CI) | P Value |
| Age                                   | 1.111 (1.040–1.187) | 0.002 | 1.145 (1.041–1.260) | 0.005 | 1.044 (1.011–1.078) | 0.009 | 1.043 (1.003–1.085) | 0.036 |
| Male                                  | 0.512 (0.163–1.615) | 0.254 | — | — | 1.307 (0.594–2.878) | 0.506 | — | — |
| Diabetes                              | 1.832 (0.591–5.682) | 0.294 | — | — | 1.315 (0.677–2.551) | 0.419 | — | — |
| CKD                                   | 2.807 (0.615–12.815) | 0.183 | — | — | 3.226 (1.464–7.107) | 0.004 | 2.813 (1.207–6.564) | 0.017 |
| Current smoker                        | 0.337 (0.074–1.538) | 0.160 | — | — | 1.221 (0.625–2.384) | 0.559 | — | — |
| Multivessel disease                   | 1.163 (0.315–4.301) | 0.821 | — | — | 1.948 (0.851–4.461) | 0.115 | — | — |
| CTO, proximal location                | 1.364 (0.433–4.301) | 0.596 | — | — | 1.712 (0.862–3.398) | 0.124 | — | — |
| Collateral flow                       | 2.044 (0.448–9.336) | 0.356 | — | — | 0.647 (0.303–1.381) | 0.261 | — | — |
| LVEF                                  | 0.962 (0.919–1.007) | 0.099 | — | — | 0.959 (0.937–0.981) | <0.001 | 0.978 (0.953–1.003) | 0.089 |
| Successful CTO-PCI                    | 0.199 (0.043–0.906) | 0.037 | 0.184 (0.035–0.972) | 0.046 | 0.298 (0.130–0.682) | 0.004 | 0.316 (0.119–0.839) | 0.021 |

CKD = chronic kidney disease; CTO = chronic total occlusion; HR = hazard ratio; LCx = left circumflex coronary artery; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; RCA = right coronary artery

* 12 events (2 in PCI group; 10 in OMT group)
** 35 events (7 in PCI group; 28 in OMT group)
P<0.05 was considered statistically significant.
In cases of acute MI\textsuperscript{19,20} or stable coronary disease\textsuperscript{21} physicians tend to consider CTO in the LAD more clinically important.\textsuperscript{22} One study found a survival benefit of successful PCI for CTO in the LAD as opposed to the LCx and RCA, although the investigators reported no information on collateral flow.\textsuperscript{23} In our study, multivessel disease was significantly more frequent and LVEF significantly lower in the OMT group than in the PCI group in each of the 3 different target-vessel groups, suggesting a higher risk for adverse clinical outcomes in medically treated patients. Even after adjusting for baseline covariables, we found significantly better clinical outcomes (namely, a lower incidence of the composite of total death or MI) among patients with CTO in the LCx or RCA who underwent successful PCI as opposed to OMT or a failed PCI. We cautiously suggest that CTO revascularization by PCI can enhance myocardial reserves, which may in turn decrease the risk of ischemic insults in case of future coronary events in non-CTO lesions and thus prevent poorer clinical outcomes. Although CTO-PCI was associated with a lower 5-year cumulative incidence of total death or MI, it increased the risk of TLR and TVR, which may explain why our findings regarding MACE and the composite of total death or MI are inconsistent across the 3 target-vessel groups. In brief, the 5-year cumulative incidence of TLR after successful PCI ranged from 8.5\% to 12.2\% and that of TVR, from 11.2\% to 13.3\%, similar to findings in previous studies.\textsuperscript{13,24} Reocclusion of stented CTOs remains a problem.

Our findings regarding LV systolic function suggest that PCI for CTO in both the LAD and the LCx, but not the RCA, improves LVEF. Various groups\textsuperscript{8,16} have reported improved LVEF after CTO recanalization; however, none have reported data on the change in LVEF specific to the different target vessels treated. The effect of single-vessel CTO revascularization on clinical outcomes and LV systolic function is difficult to determine when other potentially confounding factors, such as myocardial viability and lesion severity and complexity in non-CTO vessels, are present. Nevertheless, the results of our study offer some support for CTO as an indication for PCI in clinical practice. In the randomized EXPLORE (Evaluating Xience V and Left Ventricular Function in Percutaneous Coronary Intervention on Occlusions After ST-Elevation Myocardial Infarction) trial, patients who underwent PCI for CTO in the LAD had significantly higher LVEF at 4 months than did those who underwent PCI for non-CTO lesions,\textsuperscript{25} consistent with the findings in our study.

TABLE IV. Change from Baseline in Left Ventricular Ejection Fraction by Treatment

| Target Vessel | PCI | OMT |
|---------------|-----|-----|
|               | Baseline | Follow-Up* | P Value | Baseline | Follow-Up** | P Value |
| Overall       | 49.1 ± 11.4 | 52.5 ± 12.1 | <0.001 | 46.9 ± 12.8 | 49.6 ± 12.8 | 0.002 |
| LAD           | 47.3 ± 12.6 | 51.5 ± 11.9 | <0.001 | 45.6 ± 13.8 | 48.0 ± 13.1 | 0.214 |
| LCx           | 49.8 ± 11.2 | 54.9 ± 10.4 | <0.001 | 48.6 ± 11.7 | 52.8 ± 9.6  | 0.015 |
| RCA           | 50.5 ± 10.0 | 52.1 ± 13.3 | 0.194  | 46.8 ± 12.9 | 48.9 ± 13.7 | 0.065 |

CTO = chronic total occlusion; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; OMT = optimal medical therapy; PCI = percutaneous coronary intervention; RCA = right coronary artery

* Mean ± SD follow-up (yr): overall, 1.6 ± 1.0; LAD, 1.7 ± 1.0; LCx, 1.7 ± 1.2; RCA, 1.6 ± 1.0

** Mean ± SD follow-up (yr): overall, 1.9 ± 1.1; LAD, 2.2 ± 1.2; LCx, 2.0 ± 0.9; RCA, 1.6 ± 1.0

Data are presented as mean ± SD. P<0.05 was considered statistically significant.
Limitations
Our study has limitations. First, it was a nonrandomized, retrospective, single-center, observational study. On average, patients who received OMT or a failed PCI were older, more often had multivessel disease, and had worse LVEF at baseline than did patients who had successful PCI, and these factors could have affected the decision whether to perform PCI. Although we used multivariate Cox regression analysis to adjust for confounding factors, a prospective, randomized trial is warranted to clarify the effect of successful PCI in a single CTO on major clinical outcomes and LV systolic function. Second, the study was statistically underpowered because of the relatively small sample size (especially the number of patients whose CTO-PCI failed) and small number of events. Third, our study population did not routinely undergo functional studies, such as dobutamine stress testing, single-photon emission computed tomography, or cardiac magnetic resonance imaging, which would have helped to better understand myocardial viability before and after PCI. Fourth, although our registry database contained adequate data on symptoms at baseline, it lacked sufficient data on symptoms or quality of life at follow-up.

Conclusion
Successful PCI for CTO in single coronary arteries does not appear to offer any benefit over OMT in preventing long-term MACE. However, PCI for CTO in the LCx or RCA may reduce the frequency of total death or MI. Prospective randomized trials in larger study populations are warranted to clarify our findings.

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