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Successful Recanalization of Native Coronary Chronic Total Occlusion Is Not Associated With Improved Long-Term Survival

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ABSTRACT

OBJECTIVES The purpose of this study was to evaluate long-term clinical outcomes after drug-eluting stent-supported percutaneous coronary intervention (PCI) for native coronary total occlusion (CTO).

BACKGROUND The benefit of successful recanalization of CTO on prognosis remains uncertain.

METHODS Between March 2003 and May 2014, 1,173 consecutive patients with CTO of native coronary vessels requiring PCI were enrolled. Drug-eluting stent implantation was performed in all successful procedures (1,004 patients, 85.6%).

RESULTS During a median follow-up of 4.6 years, the adjusted risks of all-cause mortality (hazard ratio [HR]: 1.04; 95% confidence interval [CI]: 0.53 to 2.04; $p = 0.92$) and the composite of death or myocardial infarction (HR: 1.05; 95% CI: 0.56 to 1.94; $p = 0.89$) were found to be comparable between patients with successful and failed CTO-PCI, whereas the adjusted risk of target vessel revascularization (HR: 0.15; 95% CI: 0.10 to 0.25; $p < 0.001$) and coronary artery bypass grafting (HR: 0.02; 95% CI: 0.006 to 0.06, $p < 0.001$) was significantly higher in patients with failed CTO-PCI. Among patients ($n = 879$) in whom complete revascularization for non-CTO vessels was performed, the risk of death or the composite of death or myocardial infarction were not found to differ between patients who underwent successful recanalization of the remaining CTO and patients who did not. This finding was consistent regardless of whether the patient had a multivessel disease including CTO or only had a single CTO disease.

CONCLUSIONS Successful CTO-PCI compared with failed PCI was not associated with a lesser risk for mortality. However, successful CTO-PCI was associated with significantly less subsequent coronary artery bypass grafting. (J Am Coll Cardiol Intv 2016;9:530–8) © 2016 by the American College of Cardiology Foundation.

Recanalization of chronic total occlusion (CTO) continues to be 1 of the most challenging procedures in coronary intervention. Despite safety concerns associated with high doses of radiation exposure or contrast use and the possibility of disastrous complications associated with the procedure, percutaneous coronary intervention (PCI) of coronary CTO accounts for more than 10% of all PCI procedures on the basis of national registry data (1,2). The procedural success rates of CTO-PCI have dramatically improved in recent years due to improved operator experience and the development of dedicated devices and techniques (3,4). Moreover, the introduction of drug-eluting stents (DES) has resulted in a marked

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reduction in restenosis or repeated revascularization procedures compared with bare-metal stents and has consequently provided interventional cardiologists with the advantage of performing PCI for more complex coronary CTOs (5).

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Successful reopening of CTO has been reported to alleviate symptoms, improve left ventricular function, and reduce the need for coronary artery bypass graft surgery (CABG) (6–9). Results from previous cohort studies have been inconsistent with regard to the potential survival benefit of successful versus failed CTO-PCI, although many of these studies were conducted before the widespread use of dedicated devices or techniques, DES, and current standards of medical management (10–13). Following the continuous improvement in procedural techniques, coronary stent systems, and optimal medical therapy in coronary artery disease, reassessment of the effect of the success or failure of CTO-PCI in a population with a relatively high success rate of contemporary stent treatment is essential. The aim of our study was to evaluate the effect of successful recanalization of native coronary CTOs using DES on long-term clinical outcomes compared with failed CTO-PCI.

METHODS

PATIENT POPULATION AND PROCEDURE. The CTO registry database, involving the prospective recruitment of consecutive patients undergoing PCI for CTO at the Asan Medical Center, Seoul, South Korea, was used for the current study. The CTO was defined as a coronary artery obstruction with a Thrombolysis In Myocardial Infarction flow grade of 0 within the occluded segment. The duration of the occlusion was estimated to be ≥3 months based on previous coronary angiogram or clinical features. In patients in whom there was no clinical evidence of the duration of the occlusion, a CTO was diagnosed based on angiographic anatomy suggestive of long-standing occlusion (degree of calcification, collateral developments, and nontapered stump) (14). From March 2003 to May 2014, 1,287 patients in whom PCI for CTO lesions was attempted were included in the study. The patients had either symptomatic angina or a positive functional stress test, such as a treadmill test or a myocardial perfusion imaging study. The decision to perform PCI of a CTO was based on multiple factors including the probability of achieving technical success, the extent of other coronary artery diseases, and the amount of viable myocardium supplied by the CTO vessel (15).

PCI and stent implantation were performed in a standard manner. The use of specialized devices or techniques and the choice of type of DES were left to the operator's discretion. Periprocedural anticoagulation was administered according to the standard regimens. All patients were prescribed aspirin (loading dose, 200 mg) and clopidogrel (loading dose, 300 or 600 mg) before the coronary intervention. Following the procedure, aspirin was continued indefinitely, and patients treated with a DES were prescribed clopidogrel for at least 12 months. Further cilostazol use or the duration of antiplatelet therapy in patients who underwent failed PCI was left to the discretion of each attending physician. Procedural success was defined as successful recanalization of the intended CTO lesion with DES implantation, restoration of Thrombolysis In Myocardial Infarction flow grade 3, and residual diameter stenosis <30% on visual assessment.

ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass graft surgery
CI = confidence interval
CTO = chronic total occlusion
DES = drug-eluting stent(s)
HR = hazard ratio
MI = myocardial infarction
PCI = percutaneous coronary intervention
TVR = target vessel revascularization

ENDPOINTS AND DEFINITIONS. The primary safety endpoints between patients with successful and failed PCI were all-cause mortality and a composite of all-cause death or Q-wave myocardial infarction (MI). The primary efficacy endpoint was target vessel revascularization (TVR) and CABG. Cardiac death, Q-wave MI, stroke, stent thrombosis, any repeat revascularization, and changes in angina severity were also assessed as secondary endpoints. All events were based on clinical diagnoses by each patient's physician and were adjudicated by an independent group of clinicians. Causes of death were considered as cardiac unless an unequivocal noncardiac cause could be established. Q-wave MI was defined as documentation of a new, pathological Q-wave in 2 contiguous leads and an increase in creatine kinase-MB concentration to greater than the upper limit of the normal range with ischemic symptoms or signs after index treatment. Stroke, which was detected by the occurrence of a new neurological deficit, was confirmed by a neurologist on the basis of imaging modalities. TVR was defined as any percutaneous or surgical revascularization procedure of an index vessel. Stent thrombosis was defined according to the Academic Research Consortium definitions (16), and definite or probable stent thrombosis was used as the endpoint for stent thrombosis in the present study. Severity of angina was assessed according to the Canadian Cardiovascular Society functional classification.

DATA COLLECTION AND FOLLOW-UP. Clinical, procedural or operative, and outcome data were recorded in the dedicated database by independent research personnel. Clinical follow-up was performed

TABLE 1 Patient Clinical Characteristics According to the Procedural Success or Failure

	Successful PCI (n = 1,004)	Failed PCI (n = 169)	p Value
Age, yrs	59.4 ± 10.6	60.5 ± 9.3	0.16
Male	829 (82.6)	141 (83.4)	0.87
Body mass index, kg/m^2	25.5 ± 3.1	25.2 ± 2.7	0.28
Hypertension	600 (59.8)	109 (64.5)	0.28
Diabetes mellitus	311 (31.0)	54 (32.0)	0.87
Hypercholesterolemia	644 (64.1)	100 (59.2)	0.25
Current smoker	271 (27.0)	39 (23.1)	0.33
Previous PCI	205 (20.4)	35 (20.7)	1.00
Previous myocardial infarction	82 (8.2)	23 (13.6)	0.03
Previous CABG	26 (2.6)	7 (4.1)	0.38
Previous heart failure	100 (10.0)	18 (10.7)	0.89
Previous stroke	63 (6.3)	11 (6.5)	1.00
Peripheral vascular disease	18 (1.8)	1 (0.6)	0.42
Chronic lung disease	28 (2.8)	4 (2.4)	0.96
Renal dysfunction*	19 (1.9)	8 (4.7)	0.05
Clinical diagnosis at presentation			0.20
Stable angina	730 (72.7)	134 (79.3)	
Unstable angina	184 (18.3)	24 (14.2)	
Acute myocardial infarction	90 (9.0)	11 (6.5)	
Atrial fibrillation	18 (1.8)	2 (1.2)	0.81
Left ventricular ejection fraction, %	57.6 ± 8.6	57.5 ± 8.5	0.88
Left ventricular ejection fraction <40%	41 (4.1)	3 (1.8)	0.21
Reversible perfusion defect on MPI†	382/425 (89.9)	58/65 (89.2)	0.83
Positive treadmill test	153/281 (54.4)	27/47 (57.4)	0.75
Medications at discharge			
Aspirin	1,003 (99.9)	169 (100)	1.00
Clopidogrel	993 (98.9)	132 (81.7)	<0.001
Cilostazol	388 (38.6)	43 (25.4)	0.001
ACE inhibitor or ARB	601 (59.9)	107 (63.3)	0.45
Beta-blocker	866 (86.3)	157 (92.9)	0.023
Calcium-channel blocker	830 (82.7)	144 (85.2)	0.48
Nitrate	544 (54.2)	130 (76.9)	<0.001
Statin	967 (96.3)	161 (95.3)	0.66

Values are mean ± SD or n (%). *Renal dysfunction was defined as creatinine ≥2.0 mg/dl or requiring dialysis. †Results apply to the CTO artery-related territory.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CABG = coronary artery bypass grafting; CTO = chronic total occlusion; MPI = myocardial perfusion imaging; PCI = percutaneous coronary intervention.

at 1 month, 6 months, 1 year, and annually thereafter from visits or telephone contact with living patients or family members. Digital angiograms were submitted to the angiographic core analysis center, and the CTO length, total lesion length of the target vessel, and the total stent length were analyzed using an automated edge-detection system (CASS II, Pie Medical Imaging, Maastricht, the Netherlands). Data were carefully verified and adjudicated by an independent events committee blinded to the results of the PCI. For validation of complete follow-up data regarding mortality, information on vital status was obtained from the National Population Registry of the Korea National Statistical Office through the use of a unique personal identification number.

STATISTICAL ANALYSIS. Differences between the groups were evaluated by the Student *t* test for continuous variables and Fisher exact test for categorical variables. Unadjusted cumulative event rates and survival curves were generated using the Kaplan-Meier method and compared using the log-rank test. Follow-up was censored at the date of the last follow-up or at 4.6 years, whichever came first. A landmark analysis was also performed with a pre-specified landmark time point at 6 months. Cox proportional-hazard models were used to estimate the risk of the successful CTO-PCI group compared with the failed CTO-PCI group. Clinically relevant baseline and angiographic factors from **Tables 1 and 2** were selected as potential risk-adjusting variables. Variables with a p value ≤0.1 in univariate analyses were included in the multivariable Cox regression model. The final models for each endpoint were determined using backward stepwise elimination procedures where the least significant variable was removed 1 at a time from the full model (Online Table 1). The proportional hazards assumption was confirmed by examination of log (−log[survival]) curves and partial (Schoenfeld) residuals. Statistical analyses were performed using R software version 2.13 (R Foundation for Statistical Computing, Vienna, Austria). All reported p values are 2-sided, and a p value <0.05 was considered to be statistically significant.

RESULTS

PATIENT CHARACTERISTICS. Between March 2003 and May 2014, recanalization was attempted for 1,346 CTO lesions in 1,287 patients. All CTO procedures were performed in stable elective patients. Patients who underwent PCI for in-stent restenosis, underwent vein graft CTO-PCI, or received bare-metal stent implantation were excluded. The final study population comprised 1,004 patients who successfully underwent DES implantation for 1,021 CTO lesions (including 15 patients with 2 CTO lesions and 1 patient with 3CTO lesions) and 169 patients with failed CTO-PCI (**Figure 1**). Of 1,004 patients treated with DES, 463 (46.1%) received first-generation DES, and the remaining 541 (53.9%) received newer-generation DES.

The cohort comprised 970 (82.7%) men who had a mean age of 60 years. Demographic and clinical characteristics were observed to be similar between both groups, with the exception of the frequency of previous MI and renal dysfunction, which was more common in patients who had a failed procedure (**Table 1**). In the majority of patients, clinical

presentation of stable angina was observed. In 309 (26.3%) patients with an initial clinical presentation of acute coronary syndrome, CTO was discovered incidentally. Patients were most frequently in Canadian Cardiovascular Society class II (41.9%) before the admission (Figure 2). Clopidogrel and cilostazol were more frequently prescribed to patients who received successful PCI. Regarding the lesion and procedural characteristics, the right coronary artery was more frequently targeted in patients in the failed PCI group than in patients in the successful PCI group (Table 2). Furthermore, patients with a failed PCI had longer occlusion lengths and more frequent multivessel coronary artery disease. In 87.6% of the CTO lesions in patients with successful PCI, stent implantation was guided by intravascular ultrasound.

CLINICAL OUTCOMES. Coronary perforation occurred in 2 patients (0.2%) in the successful PCI group and in 5 patients (3.0%) in the failed PCI group ($p = 0.001$). Although there were no cases of in-hospital death, emergency CABG was performed on the same day of the index procedure in 4 patients who had failed PCI. Surgery was performed due to cardiogenic shock resulting from coronary perforation in 2 patients, coronary intramural hematoma in 1 patient, and dissection in 1 patient. After the index procedure, most patients with successful CTO-PCI reported improved symptom at their follow-up visit, in that 95.2% were free from any chest pain (Figure 2). However, among patients in the failed PCI group, which included 22 patients who underwent subsequent CABG at the time of their visit, more than one-half of them complained of certain degree of angina difficulties.

The median follow-up time was 4.6 years (interquartile range: 2.1 to 7.3 years). During follow-up, 101 patients died, of whom 68 died of a cardiovascular cause. A total of 17 patients experienced a Q-wave MI, and 11 had a stroke. TVR was performed in 78 patients, and CABG was performed in 33 patients. Kaplan-Meier curves for clinical endpoints at 4.6 years are shown in Figure 3. The cumulative rate of all-cause mortality (8.0% vs. 7.1%; $p = 0.83$) and the composite of death or Q-wave MI (9.0% vs. 8.5%; $p = 0.94$) did not differ between patients with successful CTO-PCI and patients with failed CTO-PCI. The incidence of cardiac death, Q-wave MI, and stroke were also comparable between the 2 groups (Table 3). Patients with failed CTO-PCI had significantly higher rates of TVR (4.4% vs. 20.9%; $p < 0.001$) and CABG (0.4% vs. 16.7%; $p < 0.001$). Accordingly, the overall incidence of any coronary revascularization and the composite of death, Q-wave MI, or TVR were also significantly higher in the failed CTO-PCI group. The majority of bypass surgeries (67%) were performed within 30 days of the index procedure. Landmark analyses starting 6 months after the index procedure demonstrated that the cumulative rate of TVR did not differ between the 2 groups ($p = 0.59$), whereas the rate of CABG remained significantly higher in patients with failed CTO-PCI ($p = 0.03$). The total incidence of stent thrombosis in patients who underwent successful stent implantation was 0.9% according to the Kaplan-Meier estimate. A similar rate was observed in patients who received first- and newer-generation DES (1.0% vs. 0.8%; $p = 1.00$). Table 3 summarizes the outcomes after adjustment for possible clinical confounders using the multivariable Cox regression model. The proportional

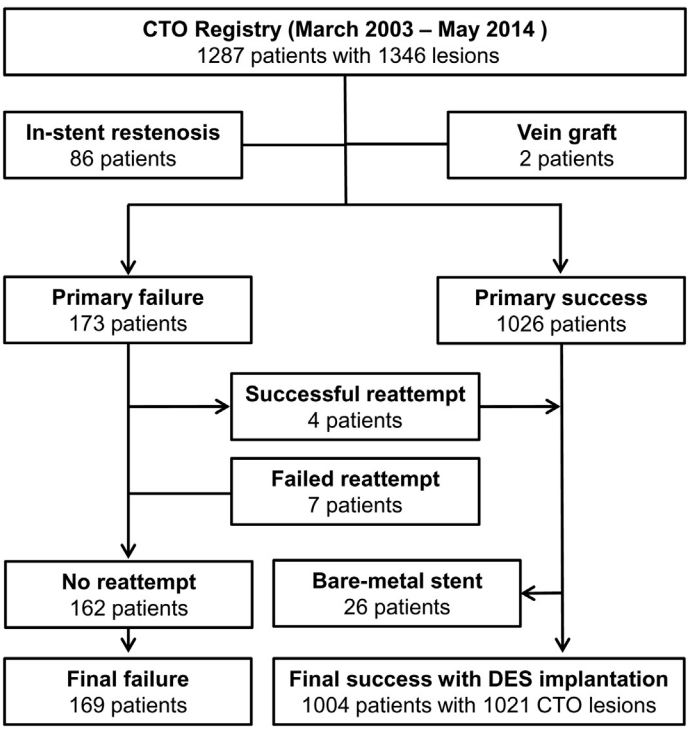
TABLE 2 Angiographic and Procedural Characteristics According to the Procedural Success or Failure

	Successful PCI (n = 1,004)	Failed PCI (n = 169)	p Value
CTO located in*			0.02
Left anterior descending artery	460 (45.1)	55 (32.5)	
Left circumflex artery	151 (14.8)	28 (16.6)	
Right coronary artery	407 (39.9)	86 (50.9)	
Left main coronary artery	3 (0.3)	0	
Multiple (≥2) CTO	76 (7.6)	17 (10.1)	0.34
Multivessel disease	558 (55.6)	117 (69.2)	0.001
Triple-vessel disease	190 (18.9)	47 (27.8)	0.01
Left main disease	42 (4.2)	9 (5.3)	0.64
CTO length, mm*	13.7 ± 9.1	18.8 ± 11.7	<0.001
Lesion length, mm*	39.0 ± 19.4	45.0 ± 21.5	<0.001
Collateral flow, Rentrop scale*			0.19
0/1	228 (22.3)	38 (22.5)	
2	374 (36.6)	73 (43.2)	
3	419 (41.0)	58 (34.3)	
Stent type			NA
1st generation DES	463 (46.1)	NA	
2nd generation DES	541 (53.9)	NA	
Number of stents per lesion*	1.77 ± 0.78	NA	NA
Length of stent per lesion, mm*	46.2 ± 21.0	NA	NA
Average stent diameter, mm*	3.15 ± 0.32	NA	NA
Double coronary injection*	331 (32.4)	45 (26.6)	0.16
Success by retrograde approach*	87 (8.5)	NA	NA
Intravascular ultrasound use*	894 (87.6)	NA	NA
Contrast media amount, ml	426 ± 200	514 ± 233	<0.001
Nontarget lesion intervention	349 (34.8)	70 (41.4)	0.11
Complete revascularization	759 (75.6)	0	<0.001
Complete revascularization (except CTO)	759 (75.6)	120 (71.0)	0.21
Complete revascularization at 6 months	757/998 (75.9)	19/167 (11.4)	<0.001
Complete revascularization at 6 months (except CTO)	756/998 (75.9)	129/167 (77.2)	0.77

Values are n (%) or mean ± SD. *Values apply to 1,190 CTO lesions (1,021 successful PCI vs. 169 failed PCI) in which percutaneous intervention was attempted.

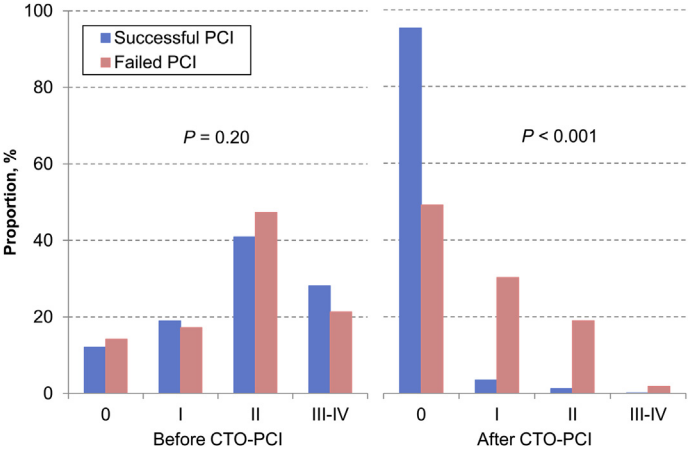
DES = drug-eluting stent; NA = not applicable; other abbreviations as in Table 1.

FIGURE 1 Study Flowchart



CTO = chronic total occlusion; DES = drug-eluting stent(s).

FIGURE 2 Distribution of Study Patients According to Canadian Cardiovascular Society Functional Class



Post-percutaneous coronary intervention (PCI) angina severity was assessed at the first clinical visit beyond 1 month after the index procedure. CTO = chronic total occlusion.

hazards assumption was met in all models. The adjusted risk for all-cause mortality and the composite of death or Q-wave MI remained comparable between the 2 groups, whereas the adjusted risk of TVR and CABG was significantly higher in patients with failed CTO-PCI.

After the index procedure, 879 subjects had complete revascularization for the non-CTO vessels. Primary safety endpoints were not found to differ between patients who underwent successful recanalization of the remaining CTO and patients who did not (Table 4). This finding was consistent regardless of whether the patient had a multivessel disease including CTO or whether the patient had a single CTO disease.

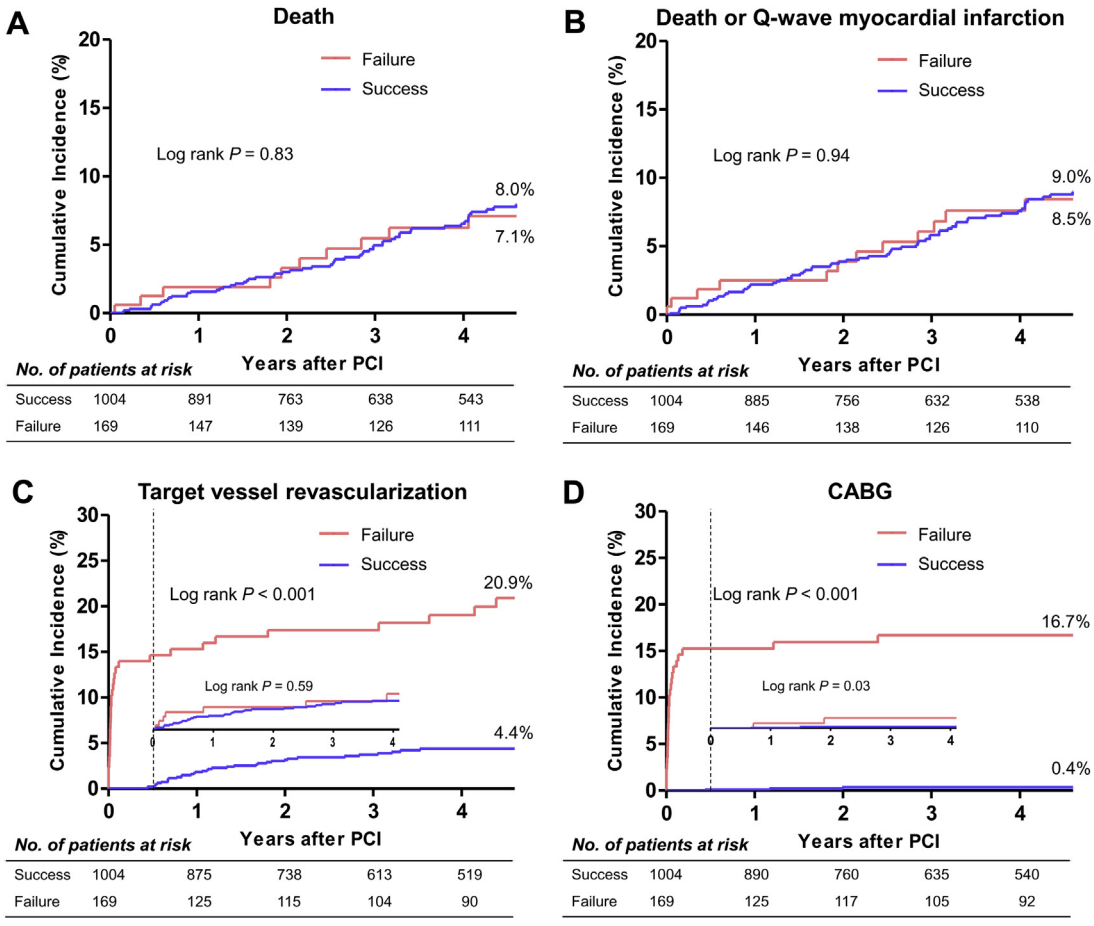
Multivariable analysis revealed that age (per 10 year increment; hazard ratio [HR]: 1.96; 95% confidence interval [CI]: 1.47 to 2.60; $p < 0.001$), body mass index (per 2.5 kg/m^2 increment; HR: 0.67; 95% CI: 0.54 to 0.83; $p < 0.001$), presence of diabetes (HR: 1.82; 95% CI: 1.12 to 2.94; $p = 0.015$), and presence of renal failure (HR: 4.47; 95% CI: 2.07 to 9.65; $p < 0.001$) were independently associated with increased mortality at 4.6 years of follow-up. A trend toward a high risk of death was observed to be associated with an increase in the number of CTO vessels per patient (HR: 1.85; 95% CI: 0.97 to 3.53, $p = 0.06$). Failed CTO-PCI was not an independent predictor of mortality but remained as an independent determinant for TVR (HR: 6.11; 95% CI: 3.79 to 9.84; $p < 0.001$) and CABG (HR: 55.78; 95% CI: 16.84 to 184.84; $p < 0.001$).

DISCUSSION

The present study demonstrated that the survival and Q-wave MI rates during the 4.6-year follow-up period did not significantly differ between patients who underwent a successful CTO-PCI and patients with a failed CTO-PCI. Furthermore, patients with a failed CTO-PCI were much more likely to be referred for surgical revascularization.

During the last few decades, there has been much debate on the benefit of reopening a coronary CTO primarily because of the lack of high-level evidence from studies. Previous observational studies demonstrated that successful CTO recanalization increases survival and reduces cardiac events (12,13,17–20). This benefit in patient prognosis has been an important rationale behind performing PCI for CTOs (21,22). However, in the present study, the effect of successful CTO recanalization on survival was in contrast to previous studies. We observed that the risk of death and Q-wave MI were comparable during long-term

FIGURE 3 Kaplan-Meier Curves for Clinical Endpoints



Kaplan-Meier curves of cumulative incidence of **(A)** all-cause mortality, **(B)** composite of death and myocardial infarction, **(C)** target vessel revascularization, and **(D)** coronary artery bypass grafting (CABG). PCI = percutaneous coronary intervention.

follow-up regardless of the procedure success. One plausible explanation of this finding is that the revascularization strategy for non-CTO vessels may have affected the clinical outcome. The non-CTO vessels usually serve as a donor for collateral circulation that conveys blood to the ischemic myocardium perfused by an occluded artery. Although the functional role of the collateral circulation has been long disputed, and the presence of a well-developed collateral circulation does not imply lack of inducible ischemia, a prognostic benefit of well-functioning collateral blood supply was demonstrated in various clinical settings (23,24). Considering that the function of collateral circulation is proportional to donor epicardial artery patency, maintaining patency of non-CTO vessels may have a prognostic effect via maintenance of myocardial perfusion at both non-CTO and CTO artery-related territories. In our study, the complete revascularization rates for non-CTO arteries were similar between the 2 groups after the index procedure, and for those patients, the long-term outcomes did not show statistical difference whether or not CTO-PCI succeeded in our subgroup analysis Thus, if feasible, strategies to achieve patency of non-CTO vessels may be necessary, even in patients with failed CTO-PCI. Accordingly, the high rate of subsequent CABG in patients with failed PCI may have affected the outcome. Patients referred to an elective CABG following failed PCI can be considered as a "treated" group, and analyses conducted with these patients in the failed PCI group may attenuate the possible long-term mortality benefit of patients in the successful PCI group. Moreover, in our study, all patients referred for CABG had multivessel coronary

TABLE 3 Crude and Adjusted Hazard Ratios of Clinical Outcomes in Patients with Successful and Failed PCI of a CTO

	Outcomes Rates (%) at 4.6 Years					
	Successful PCI (n = 1004)	Failed PCI (n = 169)	Hazard Ratio (95% CI)	p Value	Multivariable-Adjusted Hazard Ratio (95% CI)	p Value
All-cause mortality	59 (8.0)	10 (7.1)	1.08 (0.55–2.10)	0.83	1.04 (0.53–2.04)	0.92
Cardiac death	38 (5.3)	7 (5.1)	1.00 (0.45–2.24)	1.00	1.00 (0.45–2.26)	0.99
Death or Q-wave MI	68 (9.0)	12 (8.5)	1.02 (0.55–1.89)	0.94	1.05 (0.56–1.94)	0.89
Q-wave MI	11 (1.3)	3 (2.1)	0.63 (0.18–2.28)	0.49	0.57 (0.16–2.06)	0.39
TVR	36 (4.4)	32 (20.9)	0.17 (0.11–0.27)	<0.001	0.15 (0.10–0.25)	<0.001
Death, Q-wave MI, or TVR	100 (12.8)	41 (27.1)	0.38 (0.26–0.54)	<0.001	0.42 (0.29–0.60)	<0.001
CABG	3 (0.4)	27 (16.7)	0.02 (0.01–0.06)	<0.001	0.02 (0.01–0.06)	<0.001
Any coronary revascularization	65 (8.6)	41 (28.1)	0.24 (0.16–0.35)	<0.001	0.23 (0.16–0.34)	<0.001
Stroke	3 (0.5)	2 (1.5)	0.28 (0.05–1.68)	0.16	0.29 (0.05–1.72)	0.17

Event rates are shown as Kaplan-Meier estimates, n (%). Hazard ratios are for patients who received successful PCI compared with patients with failed PCI.
CI = confidence interval; MI = myocardial infarction; TVR = target vessel revascularization; other abbreviations as in Table 1.

artery disease, which has been reported to have a long-term survival advantage with CABG compared with PCI (25,26). Analysis excluding patients who underwent subsequent CABG demonstrated the risk of death for patients with successful PCI compared with patients with failed PCI to be decreased by 18% (HR: 0.90; 95% CI: 0.46 to 1.76) compared with the original result (Table 3). Finally, low life-threatening complication rates in our study may have influenced the survival outcome. Periprocedural complications during CTO-PCI are more frequent in patients undergoing a failed procedure (11,13,27). Previous studies showed relatively high rates of serious complications and adverse events, particularly in studies that reported a low success rate (60% to 70%) (13,28,29). Interestingly, similar long-term rates of death and MI between successful PCI and failed PCI were reported in patients with a failed but uncomplicated procedure (10,30). Although 4 serious complications requiring emergency CABG (0.3%) were observed in this study, this frequency is far lower than those previously reported.

Given the specific clinical and angiographic characteristics of CTOs, the optimal medical therapy alone for these complex lesions has been advocated, particularly in view of results of a previous large randomized trial demonstrating no clear death or MI benefit from an initial strategy of revascularization in patients with stable coronary artery disease, even though complex lesions like CTOs were not included in that trial (31). Furthermore, considering that the true beneficial effect of successful CTO-PCI cannot be made by comparing outcomes after successful PCI with outcomes after failed PCI, a randomized comparison between CTO-PCI and optimal medical therapy is required to define the prognostic effect of CTO-PCI. The DECISION-CTO (Drug-Eluting Stent Implantation Versus Optimal Medical Treatment in Patients with Chronic Total Occlusion trial) is currently underway and aims to resolve this long-standing open question.

TABLE 4 Subgroup Analysis of Clinical Outcomes According to the Complete Revascularization Including and Excluding CTOs

	CR Including CTO	CR Excluding CTO	Hazard Ratio (95% CI)	p Value
Single-vessel disease, n	446	52		
All-cause mortality	27 (8.2)	2 (4.7)	1.57 (0.37–6.60)	0.54
Death or Q-wave MI	31 (9.3)	3 (7.5)	1.20 (0.37–3.93)	0.76
TVR	18 (5.0)	8 (17.9)	0.22 (0.10–0.51)	<0.001
Multivessel disease, n	313	68		
All-cause mortality	22 (9.2)	6 (10.8)	0.82 (0.33–2.01)	0.66
Death or Q-wave MI	24 (9.9)	6 (10.8)	0.89 (0.37–2.18)	0.80
TVR	6 (2.3)	7 (11.9)	0.18 (0.06–0.53)	0.002
Total, n	759	120		
All-cause mortality	49 (8.7)	8 (8.3)	1.00 (0.47–2.11)	1.00
Death or Q-wave MI	55 (9.6)	9 (9.5)	1.00 (0.49–2.02)	0.99
TVR	24 (3.9)	15 (14.3)	0.23 (0.12–0.44)	<0.001

Values are n (%). Hazard ratios are for patients who received complete revascularization including CTO compared with patients who received revascularization excluding CTO.
CR = complete revascularization; other abbreviations as in Tables 1 and 3.

STUDY LIMITATIONS. The main limitation of our study lies in its nonrandomized, observational nature. The influence of unmeasured confounding factors and selection bias cannot be eliminated even after adjusting for a wide range of patient characteristics and may have contributed to the observed differences. Second, the high success rate in our cohort conversely resulted in a relatively small sample size of patients in the failed CTO-PCI group, and leads to the possibility of lack of statistical power. Third, a progressive improvement in procedural techniques and devices and evolving medical treatments throughout the long study period should be taken

into consideration and may have been a potential cause of differences between groups. Last, our data do not include serial information on individual medical treatments of patients following the CTO procedure.

CONCLUSIONS

In patients with native coronary CTOs, successful PCI using a DES was not associated with a lower risk for long-term mortality compared with failed CTO-PCI, but was associated with significantly less subsequent CABG. Further well-designed studies are required to define optimal treatment strategies for these patients.

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PERSPECTIVES

WHAT IS KNOWN? Survival benefit of successful coronary CTO recanalization has been a rationale behind performing PCI for CTOs. However, this knowledge is based on many observational studies that predate the widespread use of dedicated devices or techniques, DES, and current standards of medical management, making them low-quality evidence from the current perspective.

WHAT IS NEW? Our study showed that successful PCI using DES was not associated with a lower risk for mortality compared with failed CTO-PCI. The revascularization strategy for non-CTO vessels, high frequency of subsequent CABG in patients with failed PCI, and high procedural success with low life-threatening complication rate may all have contributed to our study finding.

WHAT IS NEXT? The true prognostic effect of CTO-PCI should be defined by a randomized comparison between successful CTO-PCI and optimal medical therapy.

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KEY WORDS chronic total occlusion, drug-eluting stent, percutaneous coronary intervention, prognosis

APPENDIX For a supplemental table, please see the online version of this article.