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A Novel Algorithm for Treating Chronic Total Coronary Artery Occlusion

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ABSTRACT

BACKGROUND Guidewire manipulation time is rarely used in chronic total occlusion (CTO) percutaneous coronary intervention (PCI) strategies.

OBJECTIVES This study sought to develop an algorithm based on angiographic characteristics and guidewire manipulation time.

METHODS This study assessed 5,843 patients undergoing CTO PCI between January 2014 and December 2017 and enrolled in the Japanese CTO-PCI expert registry and analyzed their CTO-PCI strategies, procedural outcomes, and guidewire manipulation time.

RESULTS Primary retrograde approach was performed on 1,562 patients. The average Japanese CTO score of primary antegrade approach and primary retrograde approach were 1.7 ± 1.1 and 2.3 ± 1.1, respectively ($p < 0.001$). The overall guidewire and technical success rates were 92.8% and 90.6%, respectively. Median guidewire manipulation time of guidewire success and failure were 56 min (interquartile range [IQR]: 22 to 111 min) and 176 min (IQR: 130 to 229 min), respectively. Median successful guidewire crossing time of single wiring and parallel wiring in the antegrade alone were 23 min (IQR: 11 to 44 min) and 60 min (IQR: 36 to 97 min), and rescue retrograde approach and primary retrograde approach were 126 min (IQR: 87 to 174 min) and 107 min (IQR: 70 to 161 min), respectively ($p < 0.001$). Significant predictors for antegrade guidewire failure in primary antegrade approach, which were reattempt, CTO length of ≥20 mm, and no stump, did not predict guidewire failure after collateral channel crossing in primary retrograde approach.

CONCLUSIONS Results from a large registry with information on guidewire manipulation time as well as CTO characteristics suggest a redefinition of the current strategy algorithms. (J Am Coll Cardiol 2019;74:2392–404)
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Advances in technologies and techniques have improved the procedural success rates of percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) lesions in recent years (1-5). Additionally, antegrade or retrograde crossing strategy by well-skilled CTO-PCI operators have been reported, and some multicenter registries have shown effectiveness of the retrograde procedure to improve procedural success (6-15). Moreover, angiographic scoring systems and CTO-PCI algorithms help decision-making of an optimal CTO-PCI strategy in preprocedural planning (16-23). However, few studies evaluated guidewire manipulation time, although the lesion complexity of a CTO and skill

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level of the operator significantly influence guidewire crossing time, timing to switch crossing strategies, and timing of termination of CTO PCI. Our aim was to develop an algorithm to perform a more efficient procedure by exploring the clinical impact of contemporary CTO-PCI strategies based on guidewire manipulation time in real-world settings by Japanese CTO-PCI expert operators (**Central Illustration**).

SEE PAGE 2405

METHODS

STUDY POPULATION. The Japanese CTO-PCI expert registry is a prospective, nonrandomized study, enrolling 9,424 consecutive patients undergoing CTO PCI performed by Japanese CTO operators (Online Appendix). The design and enrollment status of this registry have previously been reported in detail (4). This registry data is managed by the secretariat of the registry (Clinical Research Center, Kurashiki Central Hospital, Ohara Healthcare Foundation, Okayama, Japan) (Online Appendix). Diagnostic coronary angiograms, computed tomography images of coronary arteries before interventions, coronary angiograms, and intravascular ultrasound (IVUS) images obtained during interventions are sent to an independent core laboratory (Cardiovascular Imaging Center, Aichi, Japan) for further analysis. The Japanese Board of CTO Interventional Specialists was established in July 2013 and certified a total of 46 highly experienced Japanese specialists by the end of 2017. The planned patient enrollment period is from January 2014 to December 2022, and clinical follow-up will continue until December 2027. Written informed consent was obtained from all patients.

DEFINITIONS AND STUDY ENDPOINTS. The definition of CTO and the angiographic analysis of the target procedures have already been described (4). Lesion difficulty of a target CTO lesion was assessed using the J-CTO (Japanese Multicenter CTO Registry) score (16). Interventional collateral vessels were defined as collateral vessels considered amenable to crossing by a guidewire and a microcatheter by the operator. The retrograde approach was defined as CTO PCI with an attempt to cross a collateral channel with a guidewire to reach the distal end of CTO vessel. Each CTO-PCI procedure was initially planned to cross a CTO lesion and was divided into 2 groups: primary antegrade approach and primary retrograde approach. Moreover, cases were divided into 3 groups according to the approach taken during the intervention: antegrade alone, primary retrograde approach, and rescue retrograde approach. The rescue retrograde approach was to switch to a retrograde approach from an initial antegrade attempt to cross the CTO lesion. The selection of a CTO-PCI strategy was dependent on the operator's discretion. In-hospital major adverse cardiac and cerebrovascular events (MACCEs) were defined as death, myocardial infarction, stroke, and revascularization during the same admission. Technical success was defined as successful guidewire CTO with achievement of <50% residual diameter stenosis without major side branch occlusion and Thrombolysis In Myocardial Infarction flow grade 3. Procedural success was defined as the achievement of technical success without in-hospital MACCE. Guidewire manipulation time was evaluated using coronary angiograms at the core laboratory. In-hospital MACCEs, procedural time (defined as the time from initial insertion of guidewire into the coronary lumen to the final angiography of the CTO lesion), guidewire manipulation time (defined as the time required to cross the CTO or abort the procedure), total fluoroscopy time, total air kerma radiation exposure, and total contrast volume were evaluated in this registry. The algorithm described in this study was derived from the analysis of the current data and was not known to the operators during the data collection period. We retrospectively divided the current data into 2 groups: those that followed the algorithm and those that did not.

ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting

CTO = chronic total occlusion

IQR = interquartile range

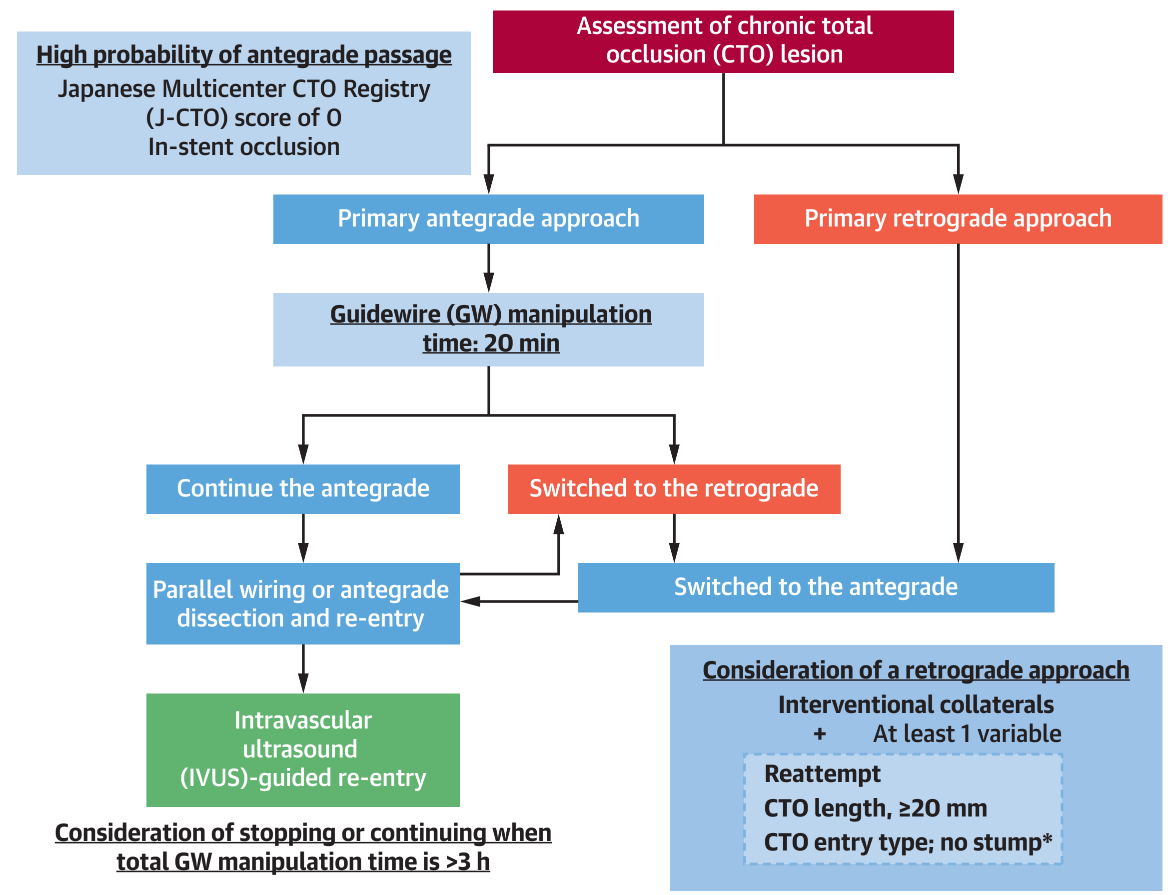
IVUS = intravascular ultrasound

MACCE = major adverse cardiac and cerebrovascular event

PCI = percutaneous coronary intervention

STATISTICAL ANALYSES. Categorical variables are expressed as number (%) and were compared using the chi-square test. Continuous variables are presented as mean ± SD or median (interquartile range [IQR]). Continuous variables were compared using Student's *t*-test or nonparametric methods. We evaluated the possible predictors of technical success, which were expressed as odds ratio and 95% confidence interval. A multivariate analysis of technical success was performed using the variables with p values <0.05 in the univariate analysis. We also evaluated possible predictors of the successful antegrade guidewire in the primary antegrade approach and those of the successful guidewire after collateral channel crossing in the primary retrograde approach, which were expressed as odds ratio and 95% confidence interval. A multivariate analysis of successful guidewire crossing was performed using all angiographic variables. All statistical analyses were performed using IBM SPSS Statistics version 25 (IBM Corporation, Armonk, New York). All reported p values were 2-sided, and p values of <0.05 were considered statistically significant.

CENTRAL ILLUSTRATION A Novel Algorithm for Treating Coronary Chronic Total Occlusion



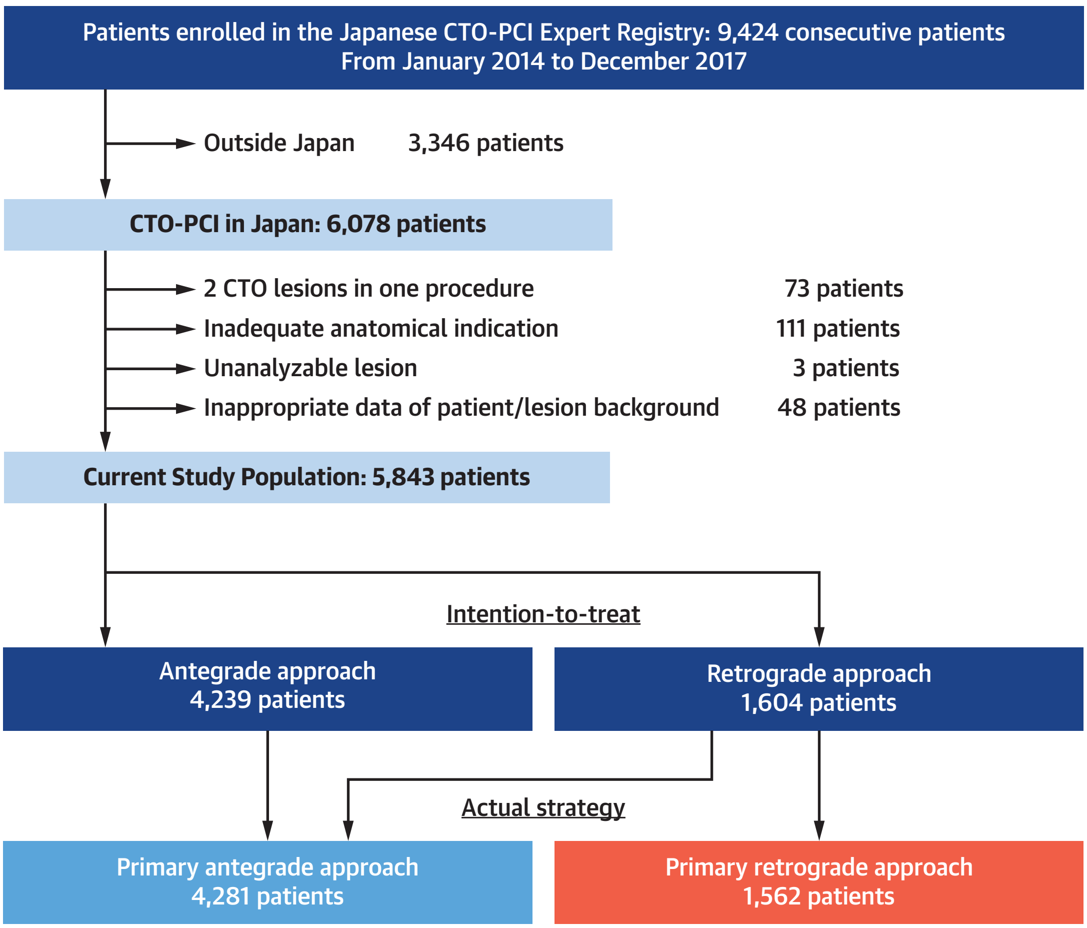
Tanaka, H. et al. J Am Coll Cardiol. 2019;74(19):2392–404.

*No stump: the absence of a visible entry, even when using intravascular ultrasound. CTO = chronic total occlusion; GW = guidewire.

RESULTS

PATIENTS, LESIONS, AND PROCEDURAL CHARACTERISTICS. A total of 9,424 patients with CTO lesions underwent PCI between January 2014 and December 2017. We excluded those who lived outside Japan from this study owing to difficulties in continuing clinical follow-up and data collection. In total, we investigated 5,843 patients in this study. Figure 1 shows the patient flowchart and Figure 2 shows the selected CTO-PCI strategy. A primary retrograde approach was performed on 1,562 patients and a primary antegrade approach was performed on 4,281 patients. In 1,077 patients in whom an antegrade guidewire failed to pass, 981 patients were switched to a retrograde approach, but 96 patients were not due to the absence of interventional collaterals. In the primary antegrade approach, the rate of the parallel wiring was 15.7%, IVUS guide crossing was 3.2%, and antegrade dissection and re-entry was 0.5%. Baseline patient and lesion characteristics are summarized in Table 1. The primary retrograde approach group had more patients who were men, had dyslipidemia, had a history of coronary artery bypass grafting (CABG), and had a history of PCI compared with the primary antegrade approach group. The number of in-stent occlusion in the primary antegrade approach group was greater than that in the primary retrograde approach group. Compared with patients in the primary antegrade approach group, those in the primary retrograde approach group had a higher J-CTO score, more right coronary artery lesions, more with a CTO

FIGURE 1 Patient Flowchart

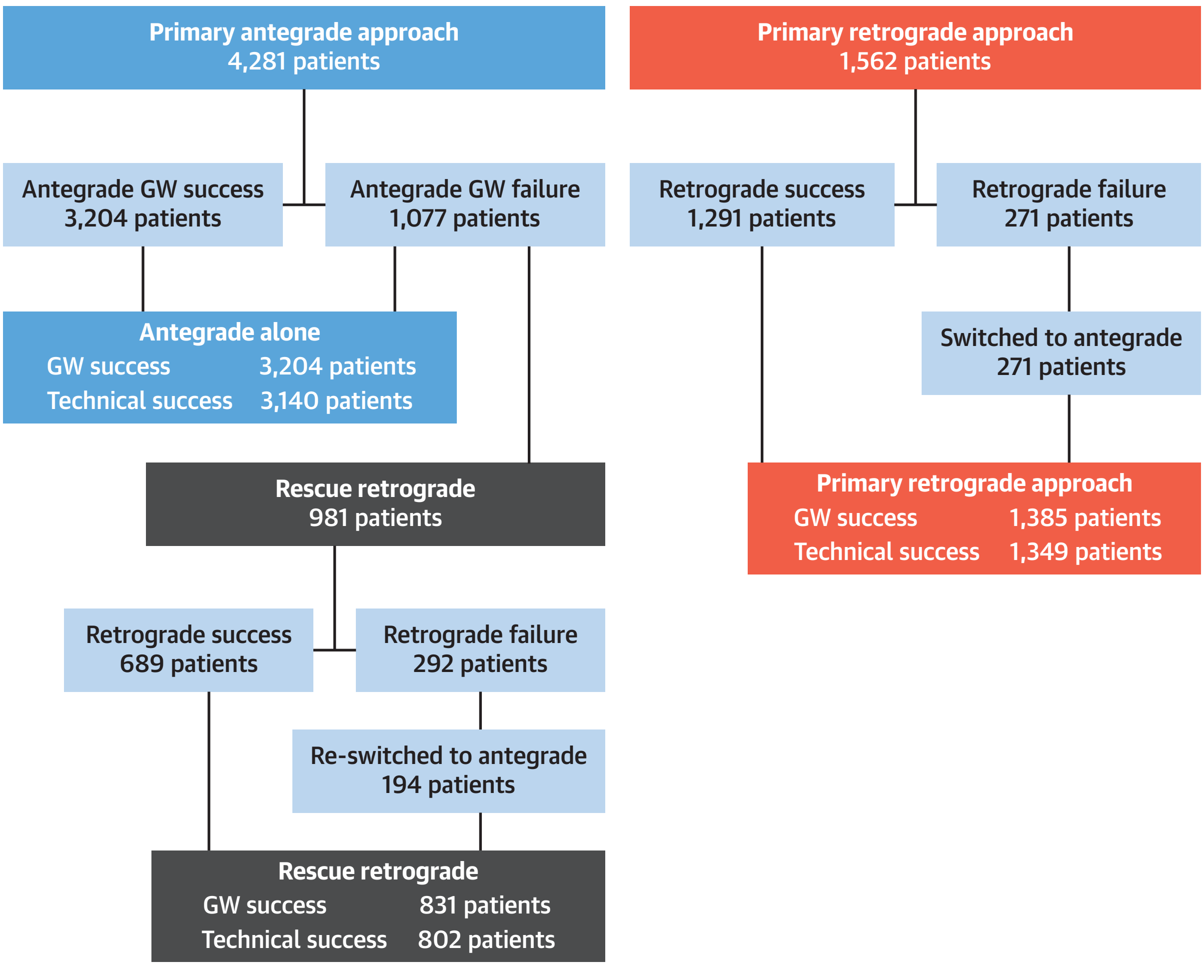


CTO = chronic total occlusion; PCI = percutaneous coronary intervention.

length ≥20 mm, more ostial lesions, more calcification lesions, and more tortuous CTO lesions (Table 1). The average J-CTO score of the antegrade approach alone was 1.6 ± 1.1, the rescue retrograde approach was 2.1 ± 1.1, and the primary retrograde approach was 2.3 ± 1.1 ($p < 0.001$). The average J-CTO score of the primary retrograde approach was higher than that of the rescue retrograde approach.

IN-HOSPITAL CLINICAL OUTCOMES. In-hospital outcomes are summarized in Table 2. Overall guidewire, technical, and procedural success rates were 91.2%, 90.5%, and 89.5%, respectively. Both procedural and technical success rates were significantly higher in the primary antegrade approach group than in the primary retrograde approach group. Compared with patients in the primary antegrade approach group, those in the primary retrograde group had longer stent length, greater number of stents, longer procedural time, and larger contrast volume. In-hospital MACCE occurred in 88 (1.5%) patients, and death occurred in 18 (0.3%) patients. One patient had a procedural-related death due to cardiac tamponade. There was no significant difference between groups in terms of death, stroke, acute stent thrombosis, and emergent CABG or PCI. The primary retrograde approach group had significantly higher rates of MI, coronary embolism, coronary perforation, cardiac tamponade, and contrast-induced nephropathy compared with the primary antegrade approach group. Table 3 and Online Table 1 present the results of univariate and multivariate analyses investigating possible predictors of technical success. In a multivariate analysis, chronic hemodialysis, prior CABG, reattempt, CTO length ≥20 mm, side branch at proximal cap, severe lesion calcification, tortuosity of CTO lesion, and no stump were independent

FIGURE 2 Selected CTO-PCI Strategies



GW = guidewire; other abbreviations as in Figure 1.

predictors of technical failure. Severe lesion calcification was a strong predictor of technical failure.

PROCEDURAL OUTCOMES. Median procedural time was 140 min (IQR: 91 to 205 min), median fluoroscopic time was 64 min (IQR: 39 to 99 min), median air kerma radiation dose was 3.4 Gy (IQR: 2.0 to 5.6 Gy), and median contrast volume was 200 ml (IQR: 147 to 280 ml). Distribution of guidewire manipulation time is shown in Figure 3. Median guidewire manipulation time of the primary antegrade approach was 39 min (IQR: 17 to 90 min) and that of the primary retrograde approach was and 113 min (IQR: 72 to 170 min) ($p < 0.001$). Median guidewire manipulation time of the antegrade alone and the rescue retrograde approach in the primary antegrade approach were 28 min (IQR: 13 to 56 min) and 128 min (IQR: 89 to 183 min), respectively ($p < 0.001$) (Figure 3A). Median guidewire manipulation time of guidewire success and failure were 56 min (IQR: 22 to 111 min) and 176 min (IQR: 130 to 229 min), respectively ($p < 0.001$) (Figure 3B). Median successful guidewire crossing time of single wiring and parallel wiring in the antegrade alone were 23 min (IQR: 11 to 44 min) and 60 min (IQR: 36 to 97 min), and rescue retrograde approach and primary retrograde approach were 126 min (IQR: 87 to 174 min) and 107 min (IQR: 70 to 161 min), respectively ($p < 0.001$) (Figure 4). Median successful guidewire crossing time of the primary retrograde approach was shorter than that of the rescue retrograde approach.

GUIDEWIRE CROSSING STRATEGY AND ANGIOGRAPHIC CHARACTERISTICS. The guidewire success rate of the

TABLE 1 Baseline Patient and Lesion Characteristics

	Overall (N = 5,843)	Primary Antegrade (n = 4,281)	Primary Retrograde (n = 1,562)	p Value
Age, yrs	67.2 ± 11.0	67.3 ± 11.1	66.8 ± 10.8	0.15
BMI, kg/m^2	24.7 ± 4.0	24.7 ± 3.9	24.7 ± 4.3	0.91
LVEF, %	54.5 ± 12.9	54.8 ± 12.9	53.6 ± 13.0	<0.01
eGFR, ml/min/1.73 m^2	63.0 ± 25.9	63.4 ± 26.6	62.0 ± 24.2	0.08
Male	4,969 (85.0)	3,599 (84.1)	1,370 (87.7)	<0.01
Symptom of angina	3,184 (54.5)	2,391 (55.9)	793 (50.8)	<0.01
Heart failure	1,338 (22.9)	998 (23.3)	340 (21.8)	0.04
Hypertension	4,540 (77.7)	3,306 (77.2)	1,234 (79.0)	0.29
Dyslipidemia	4,550 (77.9)	3,301 (77.1)	1,249 (80.0)	0.04
Diabetes	2,630 (45.0)	1,943 (45.4)	687 (44.0)	0.44
Current smoking	1,002 (17.1)	720 (16.8)	282 (18.1)	0.24
Chronic hemodialysis	391 (6.7)	286 (6.7)	105 (6.7)	0.96
History of MI	2,882 (49.3)	2,102 (49.1)	780 (49.9)	0.84
Prior CABG	424 (7.3)	268 (6.3)	156 (10.0)	<0.01
Prior PCI	3,902 (66.8)	2,768 (64.7)	1,134 (72.6)	<0.01
History of stroke	426 (7.3)	320 (7.5)	106 (6.8)	0.37
Number of diseased vessels				<0.01
Single VD	2,615 (44.8)	1,889 (44.1)	726 (46.5)	
Double VD	1,769 (30.3)	1,305 (30.5)	464 (29.7)	
Triple VD	1,242 (21.3)	945 (22.1)	297 (19.0)	
LMCA + multiple VD	217 (3.7)	142 (3.3)	75 (4.8)	
Target vessel				<0.01
LAD	1,865 (31.9)	1,454 (34.0)	411 (26.3)	
LCX	1,020 (17.5)	880 (20.6)	140 (9.0)	
LMCA	22 (0.4)	14 (0.3)	8 (0.5)	
RCA	2,935 (50.2)	1,932 (45.1)	1,003 (64.2)	
Graft	1 (0.0)	1 (0.0)	0 (0.0)	
Reattempt	1,123 (19.2)	590 (13.8)	533 (34.1)	<0.01
SYNTAX score	17.2 ± 9.1	17.3 ± 9.1	16.7 ± 9.3	<0.01
J-CTO score	1.9 ± 1.2	1.7 ± 1.1	2.3 ± 1.1	<0.01
In-stent occlusion	750 (12.8)	651 (15.2)	99 (6.3)	<0.01
Mean distal reference diameter <3.0 mm	4,015 (68.7)	2,956 (69.0)	1,059 (67.8)	0.56
CTO length ≥20 mm	3,192 (54.6)	2,115 (49.4)	1,077 (69.0)	<0.01
Side branch at proximal cap	1,505 (25.8)	1,113 (26.0)	392 (25.1)	0.49
Bifurcation at exit point	1,042 (17.8)	751 (17.5)	291 (18.6)	0.34
Ostial location	287 (4.9)	164 (3.8)	123 (7.9)	<0.01
Collateral filling				<0.01
Contralateral	2,927 (50.1)	1,961 (45.8)	966 (61.8)	
Ipsilateral	756 (12.9)	651 (15.2)	105 (6.7)	
Both	2,081 (35.6)	1,594 (37.2)	487 (31.2)	
None	48 (0.8)	46 (1.1)	2 (0.1)	
CC grade				<0.01
2	3,066 (52.5)	2,130 (49.8)	936 (59.9)	
1	2,414 (41.3)	1,813 (42.3)	601 (38.5)	
0	335 (5.7)	311 (7.3)	24 (1.5)	
Calcification	2,974 (50.9)	2,128 (49.7)	846 (54.2)	<0.01
Severe lesion calcification	410 (7.0)	263 (6.1)	147 (9.4)	<0.01
Proximal tortuosity	2,938 (50.3)	2,139 (50.0)	799 (51.2)	<0.01
Tortuosity of CTO lesion	1,288 (22.0)	835 (19.5)	453 (29.0)	<0.01
Morphology of proximal cap				<0.01
Blunt	1,161 (19.9)	822 (19.2)	339 (21.7)	
No stump	1,026 (17.6)	677 (15.8)	349 (22.3)	
Tapered/tunnel	3,597 (61.6)	2,749 (64.2)	848 (54.3)	

Values are mean ± SD or n (%).

BMI = body mass index; CABG = coronary aorta bypass grafting; CC = collateral connection; CTO = chronic total occlusion; eGFR = estimated glomerular filtration rate; J-CTO = Japanese Multicenter CTO Registry; LAD = left anterior descending artery; LCX = left circumflex artery; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; RCA = right coronary artery; SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery; VD = vessel disease.

TABLE 2 Procedural Characteristics and In-Hospital Clinical Outcomes

	Overall (N = 5,843)	Primary Antegrade (n = 4,281)	Primary Retrograde (n = 1,562)	p Value
GW success	5,420 (92.8)	4,035 (94.3)	1,385 (88.7)	<0.01
Technical success	5,291 (90.6)	3,942 (92.1)	1,349 (86.4)	<0.01
Procedural success	5,218 (89.3)	3,900 (91.1)	1,318 (84.4)	<0.01
Stent size				<0.01
<2.5 mm	382 (6.5)	328 (7.7)	54 (3.5)	
2.5–2.9 mm	1,088 (18.6)	880 (20.6)	208 (13.3)	
3.0–3.4 mm	1,670 (28.6)	1,218 (28.5)	452 (28.9)	
≥3.5 mm	1,977 (33.8)	1,329 (31.0)	648 (41.5)	
Total stent length, mm	62.6 ± 30.0	58.3 ± 28.6	74.4 ± 30.5	<0.01
Number of stents	2.1 ± 0.9	2.0 ± 0.9	2.4 ± 0.9	<0.01
GW manipulation time, min	60 (23–120)	40 (17–90)	113 (72–170)	<0.01
Procedural time, min	140 (91–205)	120 (81–180)	190 (145–255)	<0.01
Contrast volume, ml	215.3 ± 100.9	209.8 ± 99.4	230.1 ± 103.5	<0.01
Reasons for technical failure	552 (9.4)	339 (7.9)	213 (13.6)	<0.01
GW did not pass	425 (7.3)	248 (5.8)	177 (11.3)	<0.01
Device did not pass	29 (0.5)	22 (0.5)	7 (0.4)	0.75
Poor runoff of distal artery	68 (1.2)	48 (1.1)	20 (1.3)	0.62
Major side branch occlusion	22 (0.4)	16 (0.4)	6 (0.4)	1.0
Others	26 (0.4)	18 (0.4)	8 (0.5)	0.64
In-hospital adverse outcomes				
MACCE	88 (1.5)	52 (1.2)	36 (2.3)	<0.01
Death	18 (0.3)	11 (0.3)	7 (0.4)	0.24
Procedure-related death	1 (0.0)	1 (0.0)	0 (0.0)	0.55
Non-procedure-related death	15 (0.3)	8 (0.2)	7 (0.4)	0.08
Unknown	2 (0.0)	2 (0.0)	0 (0.0)	0.39
Stroke	11 (0.2)	8 (0.2)	3 (0.2)	0.97
Myocardial infarction	58 (1.0)	31 (0.7)	27 (1.7)	<0.01
Acute stent thrombosis	11 (0.2)	7 (0.2)	4 (0.3)	0.47
Emergent CABG	2 (0.0)	1 (0.0)	1 (0.1)	0.46
Emergent PCI	7 (0.1)	6 (0.1)	1 (0.1)	0.46
Other complications				
Coronary embolism	10 (0.2)	4 (0.1)	6 (0.4)	0.02
Coronary perforation	232 (4.0)	119 (2.8)	113 (7.2)	<0.01
Cardiac tamponade	22 (0.4)	11 (0.3)	11 (0.7)	0.01
Complication of puncture site	88 (1.5)	60 (1.4)	28 (1.8)	0.28
Contrast-induced nephropathy	324 (5.5)	216 (5.0)	108 (6.9)	<0.01

Values are n (%), mean ± SD, or median (interquartile range).
GW = guidewire; MACCE = major adverse cardiac and cerebrovascular events; other abbreviations as in Table 1.

antegrade alone in the primary antegrade approach was 74.8% (Figure 2). The antegrade guidewire success in the primary antegrade approach was associated with in-stent occlusion (88.6% vs. 72.4%; $p < 0.001$), J-CTO score of 0 (88.5% vs. 72.3%; $p < 0.001$), and collateral connection grade ≤1 (77.8% vs. 71.6%; $p < 0.001$). The results of multivariate analysis investigating possible predictors of antegrade guidewire success in the primary antegrade approach are shown in Table 4. The results of multivariate analysis investigating possible predictors of guidewire success after channel crossing in the primary retrograde approach group are shown in Table 5. On multivariate analysis, in-stent occlusion and collateral connection grade ≤1 were independent predictors of antegrade guidewire success in the primary antegrade approach. Reattempt, CTO length of ≥20 mm, and no stump were independent predictors of antegrade guidewire failure in the primary antegrade approach, but those of guidewire failure after collateral channel crossing in the primary retrograde approach were not. Severe lesion calcification and lesion tortuosity were independent predictors of antegrade guidewire failure in the primary antegrade approach and those of guidewire failure after collateral channel crossing in the primary retrograde approach. The algorithm was developed using angiographic characteristics and guidewire manipulation time (Central Illustration). The baseline characteristics according to the algorithm are shown

TABLE 3 Univariate and Multivariate Analyses of Technical Success

	Univariate			Multivariate		
	OR	95% CI	p Value	OR	95% CI	p Value
Diabetes	0.80	0.67–0.96	0.015	0.93	0.77–1.12	0.437
Chronic hemodialysis	0.40	0.31–0.53	<0.001	0.59	0.44–0.80	0.001
Prior CABG	0.53	0.40–0.69	<0.001	0.66	0.49–0.89	0.007
Prior PCI	0.72	0.59–0.88	<0.001	0.85	0.69–1.06	0.153
Reattempt	0.63	0.51–0.77	<0.001	0.74	0.59–0.93	0.008
CTO length ≥20 mm	0.48	0.40–0.58	<0.001	0.56	0.45–0.68	<0.001
Side branch at proximal cap	0.78	0.64–0.95	0.011	0.79	0.64–0.98	0.032
Ostial location	0.56	0.40–0.78	0.001	0.85	0.59–1.23	0.394
Severe lesion calcification	0.31	0.24–0.39	<0.001	0.38	0.29–0.50	<0.001
Tortuosity of CTO lesion	0.45	0.37–0.54	<0.001	0.56	0.46–0.69	<0.001
Morphology of proximal cap, no stump	0.60	0.49–0.74	<0.001	0.66	0.52–0.83	<0.001

CI = confidence interval; OR = odds ratio; other abbreviations as in Table 1.

in Online Table 2. Median successful guidewire crossing time of the group following the algorithm and that of the group not following the algorithm were 45 min (IQR: 19 to 88 min) and 199 min (IQR: 134 to 249 min), respectively ($p < 0.001$).

DISCUSSION

We assessed 5,843 patients enrolled in the Japanese CTO-PCI expert registry and subsequently developed the algorithm by exploring the clinical impact of the CTO-PCI strategy based on guidewire manipulation time in real-world settings of Japanese CTO-PCI expert operators (**Central Illustration**).

Several studies have reported an algorithm of CTO PCI based on the experiences of expert operators according to angiographic characteristics (21–23). However, the CTO-PCI strategy based on guidewire manipulation time has rarely been reported. A higher lesion complexity requires longer guidewire manipulation time for successful guidewire crossing, and guidewire success rate decreases nearly time-dependently, as a longer time of guidewire manipulation leads to relatively long fluoroscopic time and large contrast volume (2,16). Therefore, it is necessary to determine an appropriate CTO-PCI strategy based on angiographic characteristics and guidewire manipulation time to perform a more efficient procedure and reduce the risk of complications.

We found that the primary antegrade approach had significantly lower J-CTO score and significantly shorter guidewire manipulation time compared with the primary retrograde approach. Additionally, the primary retrograde approach had shorter guidewire crossing time despite higher J-CTO scores compared with the rescue retrograde approach. Therefore, although the primary antegrade approach leads to a shortening of the procedural time, the primary retrograde approach is useful for dealing with lesions which are difficult to pass by antegrade alone. Our data showed that in-stent occluded lesions and lesions with a J-CTO score of 0 led to a high probability of passage with antegrade alone; this suggests that such lesions should be attempted with the primary antegrade approach. On the other hand, reattempt, CTO length of ≥20 mm, and no stump were independent predictors of antegrade guidewire failure, but not those of guidewire failure after collateral channel crossing in the primary retrograde approach. Using a primary retrograde approach are considered because of the presence of these 3 variables and interventional collaterals. When using a primary retrograde approach, however, the probability of antegrade passage with IVUS guidance and parallel wiring and the advantage of the shorter guidewire crossing time when using an antegrade approach alone need to be taken into account. Also, a bifurcation with distal cap at distal landing is recommended for the primary retrograde approach in several CTO-PCI algorithms (21–23). A bifurcation with distal cap at the distal landing has the possibility of guidewire failure in the antegrade alone as well as a risk of side branch occlusion following the antegrade guidewire crossing. However, in this study, bifurcation at the distal landing was not associated with guidewire failure in the antegrade alone. Because we did not evaluate the morphology of the exit point in the core laboratory, the presence of a distal cap at the landing zone could not be precisely analyzed.

In the RECHARGE (REgistry of CrossBoss and Hybrid procedures in FrAnce, the NetheRlands, BelGium, and UnitEd Kingdom), Maeremans et al. (22) suggested that the threshold for switching strategies should be low (i.e., within 15 to 30 min) to

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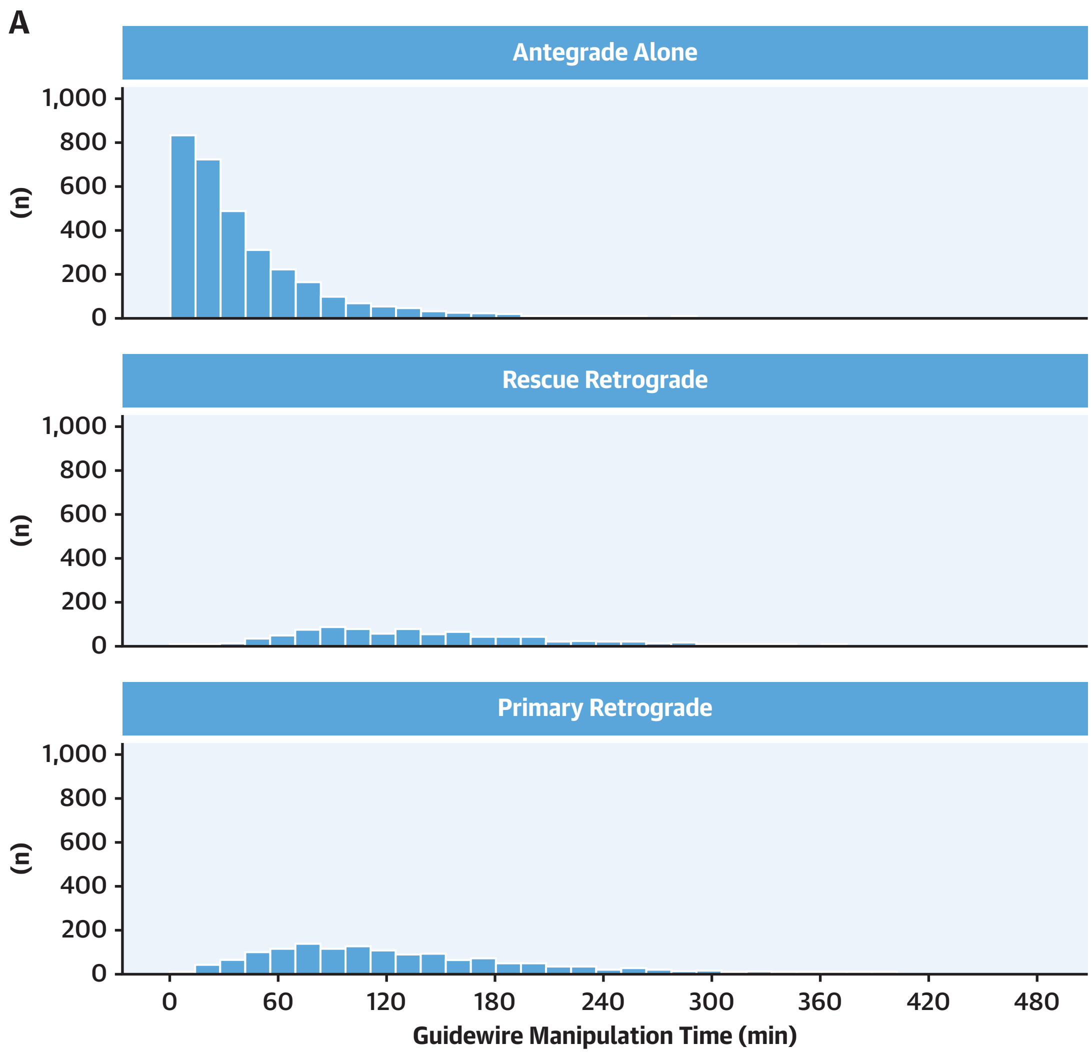
NOVEMBER 12, 2019:2392-404

FIGURE 3 **Frequency Distribution of GW Manipulation Time**

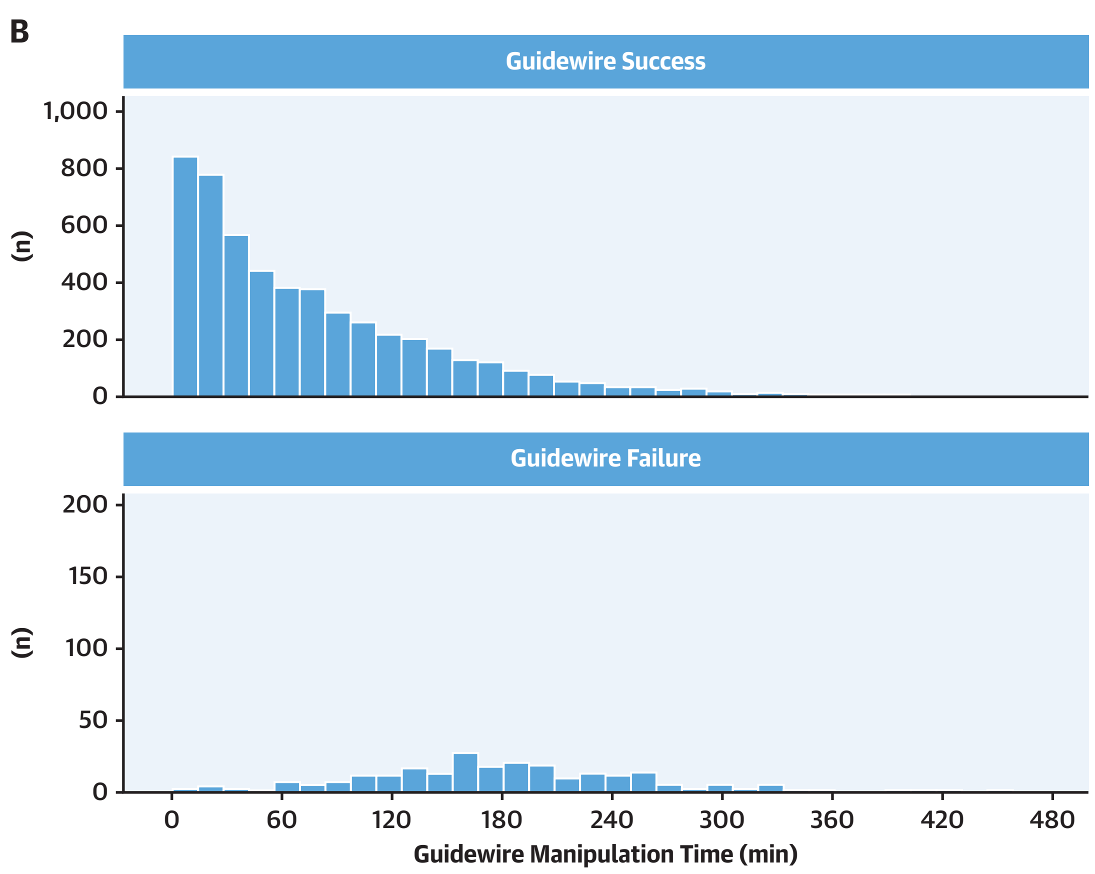


Frequency distribution of GW manipulation time for **(A)** each CTO-PCI strategy and **(B)** GW success and failure. **(A)** Median guidewire manipulation time of the antegrade alone and the rescue retrograde approach in the primary antegrade approach were 28 min (interquartile range [IQR]: 13 to 56 min) and 128 min (IQR: 89 to 183 min), respectively ($p < 0.001$). **(B)** Median guidewire manipulation time of guidewire success and failure were 56 min (IQR: 22 to 111 min) and 176 min (IQR: 130 to 229 min), respectively ($p < 0.001$). Abbreviations as in Figure 2.

Continued on the next page

reduce the procedural time. We set 20 min as the threshold of the initial timing at which to review CTO-PCI strategies in the primary antegrade approach for the following reasons: 1) median successful guidewire crossing time of the antegrade single wiring was 23 min; and 2) the difference in the guidewire crossing time between the primary retrograde approach and the rescue retrograde approach was 19 min. Furthermore, the guidewire crossing time may take an additional 40 min if parallel wiring is selected, and an additional 100 min if rescue retrograde is selected. Therefore, based on the expected guidewire manipulation time as well as the angiographic characteristics, whether to continue antegrade approach or switch to retrograde approach is determined. Recently, Karacsonyi et al. (24) reported that the crossing time of antegrade dissection and re-entry using the CrossBoss catheter and

FIGURE 3 Continued

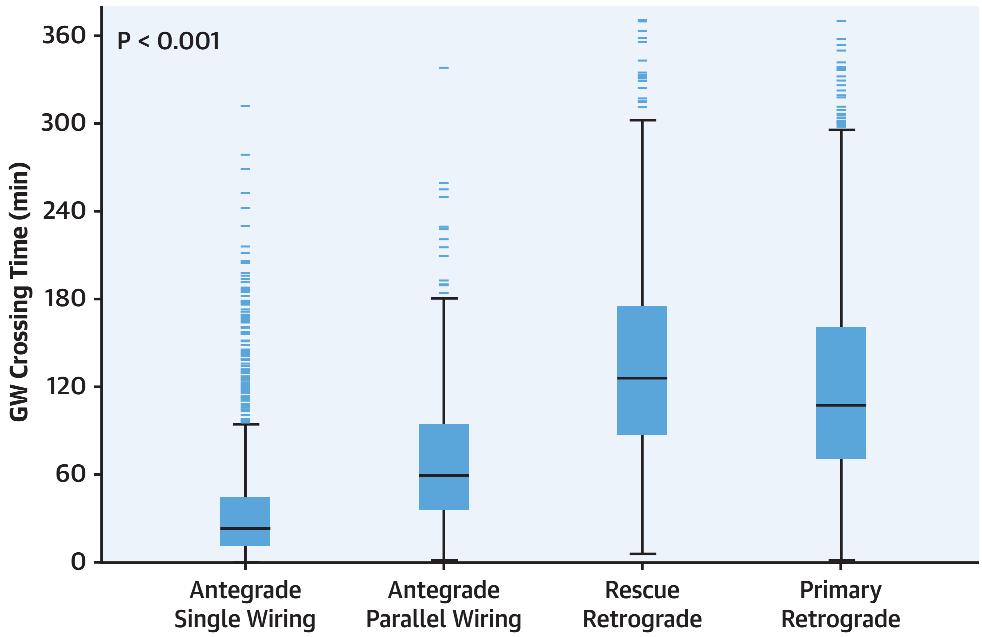


Stingray re-entry balloon and guidewire (Boston Scientific, Natick, Massachusetts) was similar to that of antegrade wire escalation. Also, several CTO-PCI algorithms recommend antegrade dissection and re-entry for CTO length ≥20 mm (21,22). The Stingray system, which is used before enlargement of the subintimal space, may shorten the crossing time with the use of the primary antegrade approach in cases with CTO length ≥20 mm.

Severe lesion calcification and tortuosity of CTO lesion were predictors of guidewire failure in the antegrade alone, guidewire failure after collateral channel crossing in the primary retrograde approach, and also technical failure. The presence of these lesions may lead to long guidewire manipulation time or failed CTO PCI. A long procedural time also leads to an increased risk of radiation skin injury and contrast-induced nephropathy due to high radiation dose and large contrast volume (25,26). The Asia Pacific CTO club suggests that operators should consider stopping a CTO procedure if guidewire manipulation time exceeds 3 h (23). Median guidewire manipulation time of guidewire failure in this study supports the termination of a procedure with 3 h of guidewire manipulation time as proposed by the Asia Pacific CTO club. Well-experienced operators make a sound judgment on whether to switch or continue the strategy. However, less experienced operators may find it more difficult to switch the strategy. We expect that using this algorithm may help perform any strategy more efficiently and complete the procedure, even in cases of difficult lesions.

STUDY LIMITATIONS. This was a nonrandomized multicenter study, and each procedure was dependent on the decisions of each operator. All CTO PCIs were performed by well-skilled specialists and the results may not be generalized to the daily clinical practice of less experienced specialists. However, the attempt of an appropriate CTO-PCI strategy based on angiographic characteristics in a limited guidewire manipulation time can lead to reduced radiation dose and contrast medium. The Stingray system was not available in Japan until December 2016. Finally, the

FIGURE 4 Frequency Distribution of Successful GW Crossing Time for Each CTO-PCI Strategy



Median successful guidewire crossing time of single wiring and parallel wiring in the antegrade alone approach were 23 min (IQR: 11 to 44 min) and 60 min (IQR: 36 to 97 min), and rescue retrograde approach and primary retrograde approach were 126 min (IQR: 87 to 174 min) and 107 min (IQR: 70 to 161 min), respectively ($p < 0.001$). Abbreviations as in Figures 2 and 3.

presence of interventional collaterals to predict collateral channel crossing may be ambiguous. The J-channel score may be useful as one of the assessments of interventional collateral, although it was not be used in this study (27).

CONCLUSIONS

We developed an algorithm to determine optimal CTO-PCI strategy based on angiographic characteristics and guidewire manipulation time using a cohort

TABLE 4 Univariate and Multivariate Analyses of Successful Antegrade Guidewire Crossing in Primary Antegrade Approach

	Univariate			Multivariate		
	OR	95% CI	p Value	OR	95% CI	p Value
In-stent occlusion	2.98	2.31–3.83	<0.001	4.08	3.10–5.36	<0.001
CC grade ≤1	2.95	2.29–3.80	<0.001	1.28	1.10–1.50	0.001
Reattempt	0.47	0.39–0.56	<0.001	0.49	0.40–0.59	<0.001
Severe lesion calcification	0.64	0.49–0.83	<0.001	0.72	0.54–0.96	0.027
Tortuosity of CTO lesion	0.51	0.43–0.60	<0.001	0.57	0.47–0.69	<0.001
CTO length ≥20 mm	0.42	0.37–0.49	<0.001	0.41	0.35–0.48	<0.001
Morphology of proximal cap, no stump	0.58	0.49–0.69	<0.001	0.60	0.49–0.73	<0.001
Bifurcation at exit point	0.77	0.65–0.92	0.004	0.88	0.73–1.06	0.173
Ostial location	0.65	0.47–0.91	0.012	0.84	0.58–1.22	0.356
Non-LAD CTO	0.84	0.72–0.97	0.018	0.85	0.71–1.02	0.072
Contralateral collateral	0.78	0.68–0.90	<0.001	0.95	0.82–1.11	0.536
Mean distal reference diameter <3.0 mm	1.13	0.97–1.31	0.119	1.06	0.90–1.25	0.497
Side branch at proximal cap	0.99	0.85–1.16	0.936	1.03	0.86–1.23	0.757
Proximal tortuosity	0.90	0.79–1.04	0.141	1.11	0.94–1.30	0.231

Abbreviations as in Tables 1 and 3.

TABLE 5 Univariate and Multivariate Analyses of Successful Guidewire Crossing After Collateral Channel Crossing in Primary Retrograde Approach

	Univariate			Multivariate		
	OR	95% CI	p Value	OR	95% CI	p Value
In-stent occlusion	0.41	0.21–0.81	0.010	0.48	0.22–1.03	0.060
CC grade ≤1	0.63	0.41–0.98	0.041	0.63	0.39–1.01	0.056
Reattempt	0.98	0.62–1.56	0.937	0.90	0.55–1.46	0.660
Severe lesion calcification	0.24	0.14–0.40	<0.001	0.23	0.13–0.41	<0.001
Tortuosity of CTO lesion	0.39	0.25–0.61	<0.001	0.46	0.27–0.80	0.006
CTO length ≥20 mm	0.55	0.32–0.94	0.030	0.55	0.31–1.01	0.053
Morphology of proximal cap, no stump	1.16	0.67–2.01	0.596	1.23	0.66–2.29	0.526
Bifurcation at exit point	0.75	0.45–1.26	0.279	0.75	0.43–1.32	0.314
Ostial location	0.68	0.34–1.35	0.268	0.90	0.40–2.05	0.801
Non-LAD CTO	0.86	0.51–1.45	0.566	1.49	0.76–2.94	0.249
Contralateral collateral	0.96	0.61–1.52	0.870	1.29	0.79–2.13	0.312
Mean distal reference diameter <3.0 mm	1.92	1.23–2.99	0.004	1.57	0.97–2.55	0.067
Side branch at proximal cap	0.75	0.47–1.22	0.253	0.60	0.34–1.06	0.076
Proximal tortuosity	1.11	0.72–1.72	0.642	0.85	0.52–1.41	0.539

Abbreviations as in Tables 1 and 3.

from a large prospective registry, the Japanese CTO-PCI expert registry. Results from a large registry with information on guidewire manipulation time, as well as CTO characteristics, suggest a redefinition of the current strategy algorithms.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: In patients undergoing percutaneous revascularization of CTOs, low lesion complexity and chronically occluded stents favor a primary antegrade approach. A retrograde approach can be most useful when guidewire manipulation time exceeds 20 min, when there is no arterial stump, and for second attempts. Special considerations apply to parallel wiring, antegrade dissection with re-entry, and IVUS-guided procedures, but cessation of attempts should be strongly considered when guidewire manipulation time extends for 3 h.

TRANSLATIONAL OUTLOOK: Further technological improvement may shorten guidewire crossing times and enhance the success rate for patients with complex coronary CTO.

REFERENCES

1. Rathore S, Matsuo H, Terashima M, et al. Procedural and in-hospital outcomes after percutaneous coronary intervention for chronic total occlusions of coronary arteries 2002 to 2008: Impact of novel guidewire techniques. J Am Coll Cardiol Intv 2009;2:489–97.

2. Morino Y, Kimura T, Hayashi Y, et al. In-hospital outcomes of contemporary percutaneous coronary intervention in patients with chronic total occlusion insights from the J-CTO Registry (Multicenter CTO Registry in Japan). J Am Coll Cardiol Intv 2010;3:143–51.

3. Wilson WM, Walsh SJ, Yan AT, et al. Hybrid approach improves success of chronic total occlusion angioplasty. Heart 2016;102:1486–93.

4. Suzuki Y, Tsuchikane E, Katoh O, et al. Outcomes of percutaneous coronary interventions for chronic total occlusion performed by highly experienced Japanese specialists: the First Report From the Japanese CTO-PCI Expert Registry. J Am Coll Cardiol Intv 2017;10:2144–54.

5. Tajti P, Karmpaliotis D, Alaswad K, et al. The Hybrid Approach to Chronic Total Occlusion Percutaneous Coronary Intervention: update from the PROGRESS CTO Registry. J Am Coll Cardiol Intv 2018;11:1325–35.

6. Colombo A, Mikhail GW, Michev I, et al. Treating chronic total occlusions using subintimal tracking and reentry: the STAR technique. Catheter Cardiovasc Interv 2005;64:407–11.

7. Surmely JF, Tsuchikane E, Katoh O, et al. New concept for CTO recanalization using controlled antegrade and retrograde subintimal tracking: The CART technique. J Invasive Cardiol 2006;18:334–8.

8. Kimura M, Katoh O, Tsuchikane E, et al. The efficacy of a bilateral approach for treating lesions with chronic total occlusions the CART (controlled antegrade and retrograde subintimal tracking) registry. J Am Coll Cardiol Intv 2009;2:1135–41.

9. Tsuchikane E, Katoh O, Kimura M, et al. The first clinical experience with a novel catheter for collateral channel tracking in retrograde approach for chronic coronary total occlusions. J Am Coll Cardiol Intv 2010;3:165–71.

10. Whitlow PL, Burke MN, Lombardi WL, et al. Use of a novel crossing and re-entry system in coronary chronic total occlusions that have failed standard crossing techniques: results of the FAST-CTOs (Facilitated Antegrade Steering Technique in Chronic Total Occlusions) trial. J Am Coll Cardiol Intv 2012;5:393–401.

11. Suzuki Y, Muto M, Yamane M, et al. Independent predictors of retrograde failure in CTO-PCI after successful collateral channel crossing. Catheter Cardiovasc Interv 2017;90:E11–8.

12. Galassi AR, Tomasello SD, Reifart N, et al. In-hospital outcomes of percutaneous coronary intervention in patients with chronic total occlusion: Insights from the ERCTO (European Registry of Chronic Total Occlusion) registry. EuroIntervention 2011;7:472–9.

13. Karmpaliotis D, Michael TT, Brilakis ES, et al. Retrograde coronary chronic total occlusion revascularization: Procedural and in-hospital outcomes from a multicenter registry in the United States. J Am Coll Cardiol Intv 2012;5:1273–9.

14. Tsuchikane E, Yamane M, Mutoh M, et al. Japanese multicenter registry evaluating the retrograde approach for chronic coronary total occlusion. Catheter Cardiovasc Interv 2013;82:E654–61.

15. Galassi AR, Sianos G, Werner GS, et al. Retrograde recanalization of chronic total occlusions in Europe: procedural, in-hospital, and long-term outcomes from the multicenter ERCTO registry. J Am Coll Cardiol 2015;65:2388–400.

16. Morino Y, Abe M, Morimoto T, et al. Predicting successful guidewire crossing through chronic total occlusion of native coronary lesions within 30 minutes: The J-CTO (multicenter CTO registry in japan) score as a difficulty grading and time assessment tool. J Am Coll Cardiol Intv 2011;4:213–21.

17. Alessandrino G, Chevalier B, Lefèvre T, et al. A clinical and angiographic scoring system to predict the probability of successful first-attempt percutaneous coronary intervention in patients with total chronic coronary occlusion. J Am Coll Cardiol Intv 2015;8:1540–8.

18. Christopoulos G, Kandzari DE, Yeh RW, et al. Development and validation of a novel scoring system for predicting technical success of chronic total occlusion percutaneous coronary interventions: The PROGRESS CTO (prospective global registry for the study of chronic total occlusion intervention) score. J Am Coll Cardiol Intv 2016;9:1–9.

19. Karatasakis A, Danek BA, Karmpaliotis D, et al. Comparison of various scores for predicting success of chronic total occlusion percutaneous coronary intervention. Int J Cardiol 2016;224:50–6.

20. Ellis SG, Burke MN, Murad MB, et al. Predictors of successful hybrid-approach chronic total coronary artery occlusion stenting: An improved model with novel correlates. J Am Coll Cardiol Intv 2017;10:1089–98.

21. Brilakis ES, Grantham JA, Rinfret S, et al. A percutaneous treatment algorithm for crossing coronary chronic total occlusions. J Am Coll Cardiol Intv 2012;5:367–79.

22. Maeremans J, Walsh S, Knaapen P, et al. The hybrid algorithm for treating chronic total occlusions in Europe: The RECHARGE registry. J Am Coll Cardiol 2016;68:1958–70.

23. Harding SA, Wu EB, Lo S, et al. A new algorithm for crossing chronic total occlusions from the Asia Pacific Chronic Total Occlusion Club. J Am Coll Cardiol Intv 2017;10:2135–43.

24. Karacsonyi J, Tajti P, Rangan BV, et al. Randomized comparison of a CrossBoss first versus standard wire escalation strategy for crossing coronary chronic total occlusions: the CrossBoss First trial. J Am Coll Cardiol Intv 2018;11:225–33.

25. Chambers CE, Fetterly KA, Holzer R, et al. Radiation safety program for the cardiac catheterization laboratory: Catheter. Cardiovasc Interv 2011;77:546–56.

26. Laskey WK, Jenkins C, Selzer F, et al. Volume-to-creatinine clearance ratio: a pharmacokinetically based risk factor for prediction of early creatinine increase after percutaneous coronary intervention: J Am Coll Cardiol 2007;50:584–90.

27. Nagamatsu W, Tsuchikane E, Oikawa Y, et al. Predicting successful guidewire crossing via collateral channel at retrograde percutaneous coronary intervention for chronic total occlusion: the J-shannel score as a difficulty estimating tool for collateral channel guidewire crossing success from the Japanese CTO-PCI Expert Registry. EuroIntervention 2019 Apr 23 [E-pub ahead of print].

KEY WORDS algorithm, chronic total occlusion, guidewire manipulation time, percutaneous coronary intervention

APPENDIX For a list of the participating centers and the certified CTO operators, study organization, and supplemental tables, please see the online version of this paper.