JACC: CARDIOVASCULAR INTERVENTIONS VOL. 10, NO. 21, 2017
© 2017 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER http://dx.doi.org/10.1016/j.jcin.2017.06.024

CORONARY: CHRONIC TOTAL OCCLUSIONS FOCUS

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

Yoriyasu Suzuki, MD,[a] Etsuo Tsuchikane, MD, PhD,[b] Osamu Katoh, MD,[c] Toshiya Muramatsu, MD,[d] Makoto Muto, MD,[e] Koichi Kishi, MD,[f] Yuji Hamazaki, MD,[g] Yuji Oikawa, MD,[h] Tomohiro Kawasaki, MD,[i] Atsunori Okamura, MD[j]

ABSTRACT

OBJECTIVES This report describes the registry and presents an initial analysis of outcomes for the different PCI approaches taken by the specialists.

BACKGROUND Strategies for percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) are complex. The Japanese Board of CTO Interventional Specialists has developed a prospective, nonrandomized registry of patients undergoing CTO-PCIs performed by 41 highly experienced Japanese specialists.

METHODS Over the study period of January 2014 to December 2015, the registry included 2,846 consecutive CTO-PCI cases undertaken in Japan. The authors compared clinical outcomes between the different PCI approaches, following the intention-to-treat principle.

RESULTS The overall technical success rate of the procedures was 89.9%. The specialists frequently chose a retrograde approach as the primary CTO-PCI strategy (in 27.8% of cases). The technical success rate of the primary antegrade approach was significantly better than that of the primary retrograde approach (91.0% vs. 87.3%; $p < 0.0001$). The technical success rate decreased to 78.0% with the rescue retrograde approach. Parallel guidewire crossing and intravascular ultrasound-guided wire crossing were performed after guidewire escalation during antegrade CTO-PCI with a high technical success rate (75.0% to 88.9%). Severe lesion calcification was a strong predictor of failed CTO-PCI.

CONCLUSIONS CTO-PCI performed by highly experienced specialists achieved a high technical success rate. (J Am Coll Cardiol Intv 2017;10:2144–54) © 2017 by the American College of Cardiology Foundation.

From the [a]Division of Cardiovascular Medicine, Nagoya Heart Center, Aichi, Japan; [b]Department of Cardiology, Toyohashi Heart Center, Aichi, Japan; [c]Japanese CTO-PCI Expert Foundation, Okayama, Japan; [d]Department of Cardiology, Tokyo General Hospital, Tokyo, Japan; [e]Division of Cardiology, Saitama Prefecture Cardiovascular and Respiratory Center, Saitama, Japan; [f]Department of Cardiology, Tokushima Red Cross Hospital, Tokushima, Japan; [g]Division of Cardiology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan; [h]Department of Cardiovascular Medicine, The Cardiovascular Institute, Tokyo, Japan; [i]Department of Cardiology, Shin-Koga Hospital, Fukuoka, Japan; and the [j]Division of Cardiology, Sakurabashi-Watanabe Hospital, Osaka, Japan. Dr. Tsuchikane is a consultant for Asahi Intecc, Boston Scientific, and NIPRO Corporation. Dr. Katoh is a consultant for Asahi Intecc and NIPRO Corp.; and is board chairman of and stock holder in RetroVascular. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received December 23, 2016; revised manuscript received June 11, 2017, accepted June 15, 2017.

Percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) is a well-accepted revascularization procedure that accounts for around 10% of PCI procedures. The initial success rate is increasing because of improvements in technology and techniques (1–7).

SEE PAGE 2155

The current procedure for CTO-PCIs involves placing 2 guide catheters to facilitate a seamless transition between the antegrade wire-based, antegrade dissection re-entry-based, and retrograde (wire or dissection re-entry) techniques, the so-called "hybrid" interventional strategy (8–11). Thus, CTO-PCI strategies are highly complex and pre-procedural planning is important, as was described in the 2012 consensus document from the EuroCTO Club (12). Recently, some studies limited to the retrograde approach such as the Retrograde Summit registry have been reported from Japan (13,14). However, there are still few studies to evaluate CTO strategies. Because the skill level of the operators strongly influences the success of CTO-PCIs, results of CTO-PCI strategies by highly skilled operators should be important to assess CTO-PCIs.

To evaluate CTO-PCI strategies, the Japanese Board of CTO Interventional Specialists has developed a registry of Japanese CTO-PCI cases undertaken by highly experienced specialists. In this report, we describe the registry and present an initial investigation of clinical outcomes using "intention-to-treat" (ITT) analysis (15,16).

METHODS

THE CTO-PCI EXPERT REGISTRY. The Japanese Board of CTO Interventional Specialists was established in July 2013. Initially, 30 highly experienced physicians were certified in 2013. This board certified a total of 41 physicians by the end of 2015. The board arranged for the development of a prospective, nonrandomized registry of patients undergoing CTO-PCIs performed by these 41 highly experienced Japanese specialists who had been certified by the board for this registry. The requirements for certification were that the specialist performed more than 50 CTO-PCIs per year and that they had performed more than 300 CTO-PCIs in total (12). The certified specialists are required to enroll all consecutive CTO-PCI cases into the registry, including cases undertaken abroad. The planned patient enrollment period is from January 2014 to December 2022, and clinical follow-up will continue until December 2027. Written informed consent is obtained from all patients in accordance with the protocol for this registry.

Short-term and long-term primary and secondary endpoints have been defined for the registry. The primary short-term endpoint is the technical success of all the CTO-PCI cases, and the secondary short-term endpoints are as follows: the number of in-hospital major adverse cardiac and cerebrovascular events (MACCEs) after CTO-PCIs (death, myocardial infarction, stroke, and revascularization during the same admission); an evaluation of the procedure time, irradiation time, contrast volumes, and the incidences of contrast-induced nephropathy; and the incidence of irradiation skin injury after CTO-PCIs for the interventions performed in Japan. The long-term primary and secondary endpoints (MACCEs and target vessel revascularizations, respectively) are evaluated after CTO-PCIs every year until 5 years.

ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting

CTO = chronic total occlusion

ITT = intention-to-treat

IVUS = intravascular ultrasound

MACCE = major adverse cardiac and cerebrovascular event(s)

PAA = primary antegrade approach

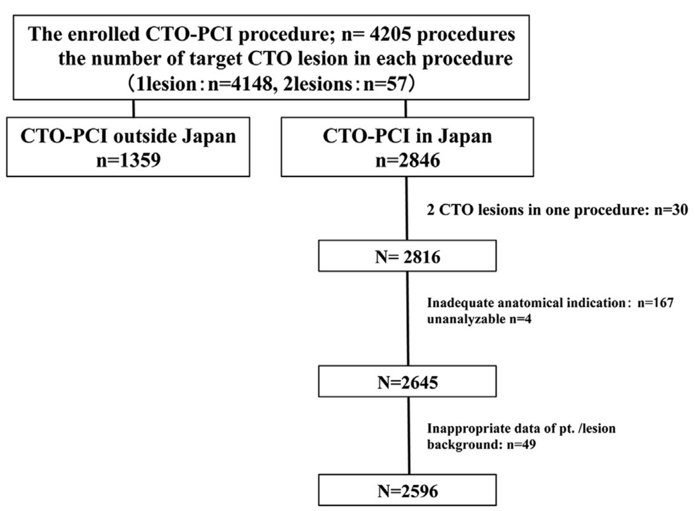
PCI = percutaneous coronary intervention

PRA = primary retrograde approach

RRA = rescue retrograde approach

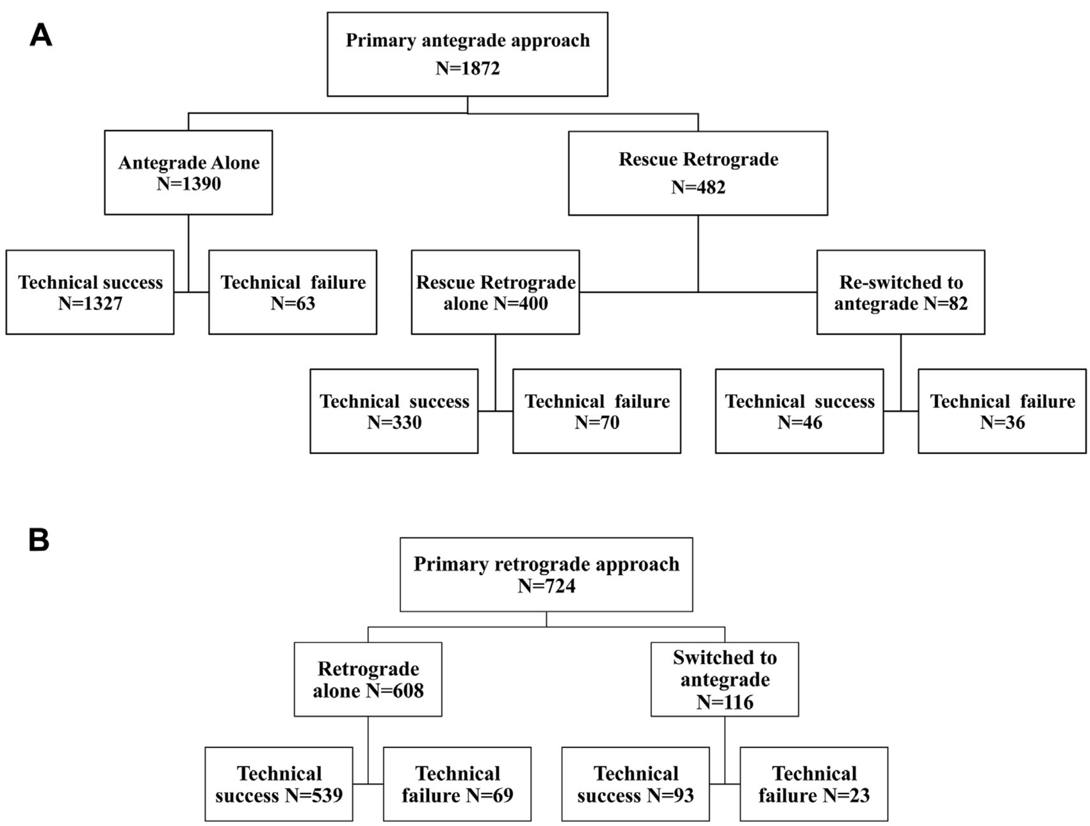
REGISTRY DATA. All clinical data, including patient background data and details of the procedures, are input via an electronic capture system provided by the Japanese Board of CTO Interventional Specialists. The data are managed by the secretariat of the registry (Clinical Research Center, Kurashiki Central Hospital, Ohara Healthcare Foundation, Okayama,

FIGURE 1 Flowchart for the Study



From January 2014 to December 2015, 41 certified specialists performed 4,205 CTO-PCIs in Japan and other countries. Initially, 2,846 CTO-PCIs performed in Japan were included in this study. The registry secretariat and independent core laboratory excluded 250 procedures due to missing data or inappropriate angiographic assessment of target lesions. Therefore, 2,596 CTO-PCIs were finally investigated in this study. CTO = chronic total occlusion; PCI = percutaneous coronary intervention.

FIGURE 2 The Steps Taken for Each Procedure in This Study



(A) In the primary antegrade approach (PAA) group, 1,390 CTO-PCIs (74.2%) were performed using only the antegrade approach. **(B)** After antegrade approach failed, 482 CTO-PCIs (25.7%) were switched to the retrograde approach (PRA). In the PRA group, 16.0% of cases (n = 116) were switched to the antegrade approach after the retrograde approach failed. Abbreviations as in Figure 1.

Japan), who would also perform the analyses of clinical data. Diagnostic coronary angiograms, computed tomography images of coronary arteries before the interventions, and coronary angiograms and intravascular ultrasound (IVUS) images obtained during interventions are sent as DICOM data to an independent core laboratory (Cardiovascular Imaging Center, Aichi, Japan) for further analysis. This laboratory assesses all coronary angiograms to centralize the appropriate assessment of the target CTO lesions, the morphologies of the target CTO lesions, and the CTO-PCI procedure outcomes.

EVALUATION OF OUTCOMES. The present analysis evaluated the initial outcomes of CTO-PCI cases performed in 2014 and 2015, comparing the CTO-PCI strategies adopted by the specialists. The CTO-PCI procedure was defined here as the retrograde approach where an attempt was made to cross the collateral channel supplying the vessel distal to the target CTO lesion for retrograde revascularization techniques (17). The cases were divided into 3 groups according to the approach taken during the intervention: primary antegrade approach (PAA), primary retrograde approach (PRA), and rescue retrograde approach (RRA). The PAA group included procedures where the initial plan was to cross the CTO lesion antegradely, including cases where the antegrade approach failed and the procedure was switched to a retrograde approach. The PRA group included procedures initially planned to cross the CTO lesion using a retrograde approach. This group included cases where the retrograde approach failed and the procedure was switched to the antegrade approach. The RRA group included the PAA cases where the procedure was switched to a retrograde approach after the initially planned antegrade approach failed.

STUDY DEFINITIONS. CTO was defined as the presence of Thrombolysis In Myocardial Infarction flow grade 0 within an occluded arterial segment for more than 3 months. Collateral connection grade was classified as previously reported (18). The J-CTO (Multicenter CTO Registry in Japan) score was used to classify lesion difficulty as previously reported (19). The angiographic classifications were defined as previously reported (20). In-hospital MACCEs were defined as death, myocardial infarction, stroke, and revascularization during the same admission. Contrast-induced nephropathy is defined as either a 25% increase in serum creatinine from baseline or a 0.5 mg/dl increase in absolute serum creatinine value within 72 h after CTO-PCIs (21,22).

Guidewire success, technical success, and procedural success were defined as previously described (20).

STATISTICAL ANALYSIS. Comparisons between the PAA and PRA groups followed the ITT principle. Continuous data are presented as mean ± SD, and differences were compared using the Student *t* test and nonparametric methods. Discrete variables are expressed as counts and percentages. These were assessed using the Fisher exact test and the chi-square test, depending on the table size. A regression model was applied to identify the prognostic factors. A univariate regression analysis was performed to obtain the odds ratio for the possible predictors of failed CTO-PCIs in the overall, PAA, and PRA groups. Thereafter, a multivariate analysis was performed using the variables with p values <0.05 in the univariate analysis in order to examine the independent associations of failed CTO-PCIs in the overall, PAA, and PRA groups. In all analyses, p < 0.05 was considered to indicate statistical significance. Statistical analysis was performed using SPSS version 23 (IBM, Armonk, New York).

TABLE 1 Baseline Patient Characteristics and Baseline Angiographic Characteristics

	Overall (N = 2,596)	PAA (n = 1,872)	PRA (n = 724)	PAA vs. PRA p Value
Age, yrs	66.9 ± 10.9	66.8 ± 10.9	66.9 ± 10.7	0.863
BMI, kg/m^2	24.7 ± 3.8	24.7 ± 3.8	24.6 ± 3.8	0.413
LVEF	54.8 ± 12.9	54.9 ± 12.9	54.6 ± 12.8	0.458
eGFR	64.9 ± 29.0	65.1 ± 30.2	64.3 ± 25.7	0.458
Male	86.1	85.1	88.4	0.018
Hypertension	78.5	78.0	80.8	0.12
Dyslipidemia	77.5	76.1	82.1	0.001
Diabetes	44.9	44.9	45.8	0.35
Current smoking	54.4	58.0	62.3	0.057
OMI	51.0	51.7	51.3	0.895
Prior CABG	7.9	7.4	9.4	0.105
Prior PCI	63.2	61.8	67.5	0.007
Reattempt	20.6	15.1	34.8	<0.0001
Syntax score	15.9 ± 8.6	16.0 ± 8.4	15.6 ± 8.9	0.062
J-CTO score	2.0 ± 1.1	1.9 ± 1.1	2.4 ± 1.1	<0.0001
Number of diseased vessels				0.015
Single VD	49.1	50.6	45.1	
Double VD	30.1	28.8	33.5	
Triple VD	17.1	17.3	16.6	
LMT + multiple VD	3.8	3.3	4.9	
Target vessel				<0.0001
LAD	30.9	32.9	25.7	
LCX	17.1	20.4	8.6	
LMT	0.6	0.6	0.6	
RCA	51.5	46.2	65.2	
In-stent occlusion	13.6	16.9	5.1	<0.0001
Distal runoff <3.0 mm	65.0	64.9	67.2	0.274
CTO length ≥20 mm	60.5	57.0	69.6	<0.0001
Side branch at proximal cap	34.1	34.8	32.0	0.181
Collateral filling				<0.0001
Contralateral	50.7	47.6	58.8	
Ipsilateral	13.3	15.9	6.6	
Both	35.2	35.5	34.4	
None	0.7	1.0	0.1	
Lesion calcification	52.3	50.5	56.9	0.003
Proximal tortuosity	50.7	49.1	49.3	0.108
Tortuosity of CTO lesion	24.6	21.6	32.5	<0.0001
Morphology of proximal cap				0.002
Blunt	23.7	23.6	23.9	
No stump	19.1	17.7	22.7	
Tapered/tunnel	56.7	58.3	52.3	

Values are mean ± SD or %.

BMI = body mass index; CABG = coronary artery bypass grafting; CTO = chronic total occlusion; eGFR = estimated glomerular ejection fraction; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; LMT = left main trunk artery; LVEF = left ventricular ejection fraction,; OMI = old myocardial infarction; PAA = primary antegrade approach; PCI = percutaneous coronary intervention; PRA = primary retrograde approach; RCA = right coronary artery; VD = vessel disease.

RESULTS

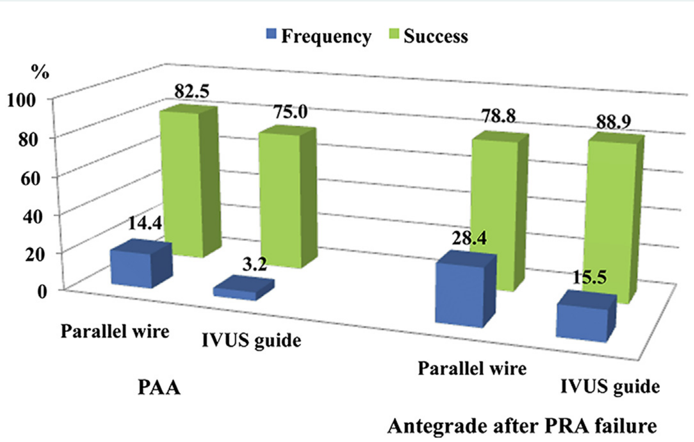
A flowchart of this study is shown in **Figure 1**. From January 2014 to December 2015, the 41 certified specialists performed 4,205 CTO-PCIs in Japan and other countries. Also, 1,359 cases with CTO-PCIs outside Japan were excluded from this study because it may be difficult to continue the clinical follow-up and missing data would increase. Therefore, of these 4,205 CTO-PCIs, 2,846 CTO-PCIs performed in Japan were initially included in this study. However, the registry secretariat and independent core laboratory excluded 250 procedures due to missing data or inappropriate angiographic assessment of target lesions. Thus, 2,596 CTO-PCIs were investigated for this study. **Figure 2** shows the steps taken for each procedure. For 724 cases (27.8%), PRA was chosen as the primary CTO-PCI strategy. In addition, approximately one-quarter of the cases in the PAA group were switched to a retrograde approach after the antegrade approach failed.

TABLE 2 The Clinical Results of This Study

	Overall (N = 2,596)	PAA (n = 1,872)	PRA (n = 724)	PAA vs. PRA p Value
GW success	92.0	92.9	90.1	0.016
Technical success	89.9	91.0	87.3	0.006
Procedural success	88.8	90.3	85.0	<0.0001
Stent size				<0.0001
<2.5 mm	7.1	8.7	3.0	
2.5–2.9 mm	20.5	23.2	13.7	
3.0–3.4 mm	33.0	32.1	35.5	
≥3.5 mm	39.4	36.1	47.9	
Total stent length, mm	63.2 ± 29.6	59.0 ± 28.5	74.1 ± 29.6	<0.0001
Procedure time	160.4 ± 89.6	143.8 ± 81.9	201.5 ± 94.4	<0.0001
Contrast volume	230.8 ± 105.9	224.7 ± 104.5	245.8 ± 108.0	<0.0001
Reasons for technical failure				0.502
GW did not pass	85.5	84.2	88.0	
Device did not pass	4.7	5.9	2.4	
Poor runoff of distal artery	9.8	9.9	9.6	
Others	2.6	4.2	5.1	
In-hospital death	0.2	0.2	0.4	0.362
Myocardial infarction	1.2	0.8	2.0	0.018
Acute stent thrombosis	0.2	0.2	0.1	1.000
Stroke	0.2	0.2	0.3	0.628
Emergent CABG	0	0	0	
Emergent PCI	0.2	0.2	0.1	1.000
Coronary embolism	0.2	0.1	0.6	0.06
Coronary perforation (tamponade)	0.4	0.2	0.9	<0.0001
Complication of puncture site	1.3	1.2	1.4	0.844
CIN	1.7	1.2	3.1	0.031

Values are % or mean ± SD.
CIN = contrast-induced nephropathy; GW = guidewire; other abbreviations as in Table 1.

FIGURE 3 The Frequency and Technical Success Rate of Parallel Wire Crossing and IVUS-Guided Wire Crossing in the PAA and in the Antegrade Approach After a Failed PRA



In the PAA group, parallel wire crossing was attempted in 14.4% of cases (technical success 82.5%) and IVUS-guided wire crossing was attempted in 3.2% of cases after antegrade guidewire escalation failed (technical success 75.0%). In the PRA group, parallel wire crossing was attempted in 28.4% of 116 cases after retrograde approach failed (technical success 78.8%), and IVUS-guided wire crossing was attempted in 15.5% of these cases (technical success 88.9%). IVUS = intravascular ultrasound; other abbreviations as in Figure 2.

The baseline patient characteristics, baseline angiographic characteristics, and clinical results of this study are presented in Tables 1 and 2. There was a high prevalence of coronary risk factors such as hypertension (78.5%), dyslipidemia (77.5%), and diabetes mellitus (44.9%). The prevalence of male sex, dyslipidemia, multivessel disease, reattempted cases, and complex CTO lesion morphology (lesion length ≥20 mm, lesion tortuosity, lesion calcification, and morphology of the proximal cap) was significantly higher in the PRA group than in the PAA group. The J-CTO scores of the PRA group were significantly higher than those of the PAA group (PAA vs. PRA 1.9 ± 1.1 vs. 2.4 ± 1.1; $p < 0.001$).

The overall success rate of the procedures in this analysis was about 90% (guidewire success 92.0%; technical success 89.9%; and procedural success 88.8%). The clinical outcomes for PAA were significantly better than those for PRA (PAA vs. PRA for technical success 91.0% vs. 87.3%; $p = 0.006$). The total stent length and implanted stent size were significantly longer and bigger in PRA than those in PAA. Procedure times and contrast volume were significantly higher for PRA than for PAA. The reason of technical failure was mostly failed guidewire crossing in both groups. The incidence of in-hospital MACCEs and complications, such as coronary perforation and contrast-induced nephropathy, were <2%. The incidence of irradiation skin injury was 0.2%.

In the PAA group, 1,390 CTO-PCIs (74.2%) were performed using only the antegrade approach, with guidewire success 97.1% and technical success 95.5%. Parallel wire crossing was attempted in 14.4% of these 1,390 cases (technical success 82.5%), and IVUS-guided wire crossing was attempted in 3.2% of cases after antegrade guidewire escalation failed (technical success 75.0%), as shown in Figure 3. In the PRA group, 16.0% of cases (n = 116) were switched to the antegrade approach after the retrograde approach failed, and the technical success rate of those cases was 80.2%. Parallel wire crossing was attempted in 28.4% of these 116 cases (technical success 78.8%), and IVUS-guided wire crossing was attempted in 15.5% of these cases (technical success 88.9%).

Table 3 shows the difference in the baseline characteristics between the cases involving only the antegrade approach and the RRA cases. The prevalence of reattempted cases and the complex CTO lesion morphology was significantly higher in the RRA group, and the J-CTO scores of the RRA were also significantly higher (RRA vs. only the antegrade technique 2.2 ± 1.1 vs. 1.7 ± 1.1; $p < 0.001$).

The J-CTO scores, the prevalence of reattempted cases, the distribution of target vessels, and the collateral filling differed significantly between PRA and RRA (shown in Online Table 1). The distribution of ultimately used collateral channels in both PRA and RRA is shown in **Figure 4**. The septal channel was mostly used for the collateral channel crossing in both groups. There was no significant difference. The prevalence of cases that failed the collateral channel crossing in the RRA group showed a tendency to be higher than that for the PRA group. The technical success rate for PRA was significantly better than those for RRA (RRA vs. PRA technical success 78.0% vs. 87.3%; $p < 0.0001$, shown in Online Table 1).

Table 4 shows the differences between successful and failed cases in the overall, PAA, and PRA groups. In the failed cases, the J-CTO scores, severe lesion calcification, complex morphology of proximal cap (without a stump), prevalence of the side branch at the proximal cap, and long CTO lesions were significantly higher.

The distribution of the crossing strategies in the cases with guidewire success is shown in **Figure 5**. In cases using only antegrade approach, single wire crossing was mostly performed. Conversely, the prevalence of parallel wire crossing and IVUS-guided wire crossing was significantly increased in cases using antegrade approach after the retrograde approach failed. Reverse controlled antegrade and retrograde subintimal tracking was mostly performed in cases using the retrograde approach. In 76.8% of 405 cases with jeopardized collateral arteries, PCI for donor arteries was performed before CTO-PCI (PRA 80.6%; RRA 70.1%; $p = 0.016$).

Table 5 and Online Table 2 present the results of uni- and multivariate analyses investigating possible predictors of failed CTO-PCIs in the overall, PAA, and PRA groups. In all groups, severe lesion calcification was a strong predictor of procedure failure.

DISCUSSION

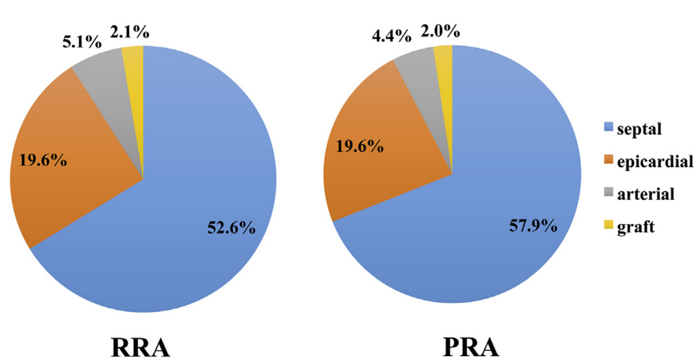
This is the first report to evaluate the clinical outcomes of primary CTO-PCI strategies adopted by highly experienced Japanese specialists following the ITT principle. The main findings of the present study were as follows: 1) Highly experienced Japanese specialists frequently chose the retrograde approach as the primary CTO-PCI strategy (in 27.8% of cases), especially for more complex CTO lesions, with a success rate of about 90%; 2) For intermediate CTO lesions (J-CTO score <2), these specialists mainly performed CTO-PCIs using the antegrade approach

TABLE 3 The Baseline Characteristics Between the Cases Involving Only the Antegrade Approach and the RRA Cases

	Antegrade Alone (n = 1,390)	RRA (n = 482)	Antegrade vs. RRA p Value
Age, yrs	67.1 ± 11.0	66.2 ± 10.8	0.171
Male	84.1	88.2	0.031
BMI, kg/m^2	49.7	55.0	0.120
Prior CABG	6.6	9.6	0.096
Prior PCI	59.9	65.5	0.025
Syntax score	16.1 ± 8.5	15.8 ± 8.1	0.797
J-CTO score	1.7 ± 1.1	2.2 ± 1.1	<0.0001
Target vessel			<0.0001
LAD	33.9	29.9	
LCX	22.9	13.3	
LMT	0.6	0.4	
RCA	42.6	56.4	
Reattempt	12.7	22.2	<0.0001
In-stent occlusion	20.2	7.3	<0.0001
Distal runoff <3.0 mm	64.2	65.1	0.762
CTO length ≥20 mm	53.5	67.2	<0.0001
Side branch at proximal cap	35.5	33.0	0.325
Collateral filling			<0.0001
Contralateral	46.6	50.4	
Ipsilateral	18.4	8.9	
Both	33.8	40.5	
None	1.2	0.2	
Lesion calcification	48.8	55.4	0.013
Proximal tortuosity	49.2	49.0	0.836
Tortuosity of CTO lesion	18.7	29.9	<0.0001
Morphology of proximal cap			0.008
Blunt	24.6	20.7	
No stump	16.0	22.6	
Tapered/tunnel	59.1	56.2	

Values are mean ± SD or %.
Abbreviations as in Table 1.

FIGURE 4 The Distribution of Ultimately Used Collateral Channels in PRA and RRA



The septal channel was mostly used for the collateral channel crossing in both groups. No significant difference was observed. PRA = primary retrograde approach; RRA = rescue retrograde approach.

TABLE 4 The Differences Between Successful and Failed Cases

	Overall			PAA			PRA		
	Success (n = 2,209)	Failure (n = 278)	p Value	Success (n = 1,601)	Failure (n = 171)	p Value	Success (n = 632)	Failure (n = 92)	p Value
Dyslipidemia	77.6	76.5	0.531	75.5	78.2	0.567	83.0	73.8	0.048
Prior CABG	7.2	14.7	<0.0001	6.7	14.6	0.001	8.6	15.0	0.084
Prior PCI	62.0	70.9	0.014	60.5	68.4	0.11	66.1	74.8	0.119
Syntax score	15.7 ± 8.5	17.0 ± 9.2	0.054	15.9 ± 8.5	16.6 ± 8.2	0.276	15.2 ± 8.5	17.6 ± 10.5	0.056
J-CTO score	1.95 ± 1.13	2.48 ± 1.10	<0.001	1.80 ± 1.10	2.29 ± 1.10	<0.0001	2.4 ± 1.1	2.8 ± 1.0	<0.0001
Target vessel			0.135			0.442			0.178
LAD	31.7	24.8		33.6	27.5		26.8	20.6	
LCX	16.9	18.3		20.4	21.6		7.7	13.1	
LMT	0.6	0.7		0.6	0.6		0.5	0.9	
RCA	50.7	56.1		45.3	50.3		65.0	65.4	
Reattempt	19.5	28.4	0.001	14.1	20.5	0.026	33.6	41.1	0.152
In-stent occlusion	13.9	11.9	0.361	17.3	15.2	0.497	4.9	6.5	0.310
Distal run off <3.0 mm	66.0	60.4	0.036	65.4	60.2	0.006	67.6	60.7	0.341
CTO length ≥20 mm	58.8	71.6	<0.0001	55.1	68.4	<0.0001	68.6	76.6	0.179
Side branch at proximal cap	33.4	36.7	0.269	34.8	30.4	0.252	29.6	46.7	<0.0001
Collateral filling			0.008			0.327			0.685
Contralateral	50.9	52.5		47.0	50.3		59.2	56.1	
Ipsilateral	13.7	9.4		16.4	11.7		6.7	5.6	
Both	35.3	36.0		35.9	34.5		33.9	38.3	
None	0.6	2.2		0.8	3.5		0.2	0	
Severe lesion calcification	5.4	18.3	<0.0001	4.6	18.1	<0.0001	7.4	18.7	0.001
Proximal tortuosity			<0.0001			0.017			0.018
Straight	51.4	44.2		51.7	41.5		50.5	48.6	
Mild	35.1	32.0		34.9	36.3		35.7	25.2	
Moderate	11.3	19.8		11.6	19.3		10.5	20.6	
Severe	2.0	3.6		1.7	2.9		3.0	4.7	
Tortuosity of CTO lesion	22.8	39.9	<0.0001	19.9	37.4	<0.0001	30.5	43.9	0.026
Morphology of proximal cap			0.01			0.387			0.044
Blunt	23.7	23.7		23.5	24.0		24.0	23.4	
No stump	18.7	23.0		17.4	22.2		22.2	24.3	
Tapered/tunnel	57.2	51.4		58.7	53.2		53.1	48.6	

Values are % or mean ± SD.
Abbreviations as in Table 1.

alone, with a very high success rate (more than 95%); 3) However, for RRA, the success rate decreased to <80%; 4) The specialists performed the parallel guidewire crossing and IVUS-guided wire crossing after the guidewire escalation failed during antegrade CTO-PCIs, with high technical success (75.0% to 88.9%); and 5) Severe lesion calcification was a strong predictor of failed CTO-PCIs.

Recently, reports from American and European CTO-PCI registries have been published (7,23). The overall technical success of CTO-PCI in the American registry was 90.0%, and the technical success rate for retrograde CTO-PCI in the European registry was 75.3%. The technical success rate in the present study was higher than those in the previous reports. In particular, the success rate for the antegrade approach was more than 90% using guidewire escalation, parallel wire crossing, and IVUS-guided wire crossing, without antegrade dissection/re-entry devices.

The retrograde approach was frequently used as the primary CTO-PCI strategy (our registry 27.8%; U.S. registry 19.0%; European registry 12.5%). Pre-procedural planning for CTO-PCI is very important, and identifying clinical and angiographic characteristics associated with procedural failure could lead to improved patient selection and overall success of CTO-PCIs. A prediction rule based on J-CTO scores has recently been applied to grading the difficulty of CTO-PCIs (19). A hybrid algorithm for CTO-PCIs has demonstrated that the primary retrograde approach is favored in cases with complex CTO morphology based on angiographic factors similar to those used in the J-CTO score (11,24). In the present study, the prevalence of reattempted cases and complex CTO lesion morphology was significantly higher in the PRA group than in the PAA group. This finding suggests that the assessment of target CTO morphology and pre-operative planning by Japanese specialists was similar to the assessment of the J-CTO score and the hybrid algorithm, and Japanese specialists frequently chose the retrograde approach as the primary CTO-PCI strategy for more complex CTO lesions. The retrograde approach could be a feasible procedure when the antegrade approach seems to be particularly difficult. However, this technique requires high skill and extensive experience with CTO-PCIs. The retrograde approach should be familiar to the highly experienced specialists selected for this registry, which may partly explain the high prevalence of the retrograde approach as the primary CTO-PCI strategy in this study.

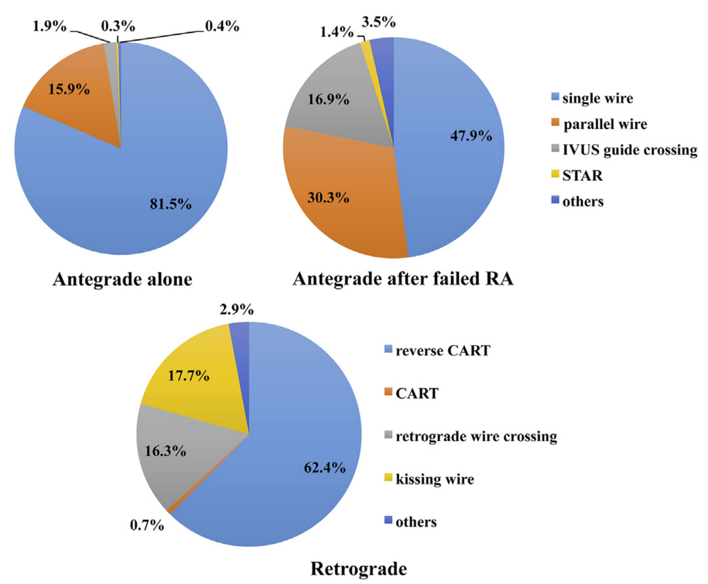
In the present study, the technical success rate for PRA was 87.3%. In the PRA group, 16.0% of cases were switched to the antegrade approach after the retrograde approach failed, and the technical success rate of those cases was 80.2%. Parallel wire crossing was performed in 28.4% of cases and IVUS-guided wire crossing in 15.5% of cases. The technical success of each technique was high (parallel wire crossing 78.8%; IVUS-guided wire crossing 88.9%). A recent analysis showed that the success rate of antegrade guidewire crossing after retrograde failure was 74.8% to 54.6% and that IVUS-guided wire crossing contributed to the success of using the antegrade approach after the retrograde approach failed (25). In the present study, the technical success rate for parallel wire crossing and IVUS-guided wire crossing in the antegrade approach after failed retrograde approach was higher than in that previous study, which may partly explain the high success rate of PRA in this study.

The success rate for RRA was significantly lower than that for PRA even though the baseline characteristics of the RRA cases exhibited less complex CTO morphology than the PRA cases. There may have been no suitable collateral for the collateral channel crossing. In addition, the first antegrade failure may have led to deteriorated visualization of the CTO distal vessel because of antegrade dissection, higher surgeon/patient fatigue, and increased contrast consumption or radiation exposure, and these factors may have compromised the success of RRA.

In our study, the prevalence of patients with prior coronary artery bypass grafting (CABG) history (7.9%) was lower than those in U.S. (33.9%) and European (17.6%) registries (7,23). The technical success rate of CTO-PCI of a native coronary artery for cases with prior CABG was significantly decreased compared with that for cases without prior CABG, as described in the previous report (26). Similarly, in this study, the technical success rate for cases with prior CABG (overall 82.5%; PAA 83.3%; PRA 80.9%) was lower than that for cases without prior CABG (overall 90.6%; PAA 91.6%; PRA 87.9%; overall $p < 0.0001$; PAA $p = 0.001$; PRA $p = 0.099$). Univariate analysis showed prior CABG history was a negative predictor of CTO-PCI success; however, multivariate analysis did not show the same. These findings suggest that an important factor of CTO-PCI for cases with prior CABG history seems to be the existence of suitable collateral for the retrograde approach. For cases without suitable collateral arteries, parallel wire crossing and IVUS-guided wire crossing could contribute to the procedure success as described in the previous report (26). Simultaneously, the dissection re-entry technique is expected to provide better results for such cases.

Recently, some specialists have recommended the use of antegrade subintimal dissection/re-entry strategies as a second- or third-line strategy after the failure of conventional antegrade or retrograde

FIGURE 5 The Distribution of the Crossing Strategies in Cases With Guidewire Success



In cases using only an antegrade approach, single wire crossing was mostly performed. Conversely, the prevalence of parallel wire crossing and IVUS-guided wire crossing was significantly increased in cases using antegrade approach after the retrograde approach failed. Reverse controlled antegrade and retrograde subintimal tracking (reverse CART) was mostly performed in cases using a retrograde approach. IVUS = intravascular ultrasound; STAR = subintimal tracking and re-entry.

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 10, NO. 21, 2017
NOVEMBER 13, 2017:2144–54

TABLE 5 Multivariate Analyses Investigating Possible Predictors of Failed CTO-PCIs

	Overall			PAA			PRA		
	OR	95% CI	p Value	OR	95% CI	p Value	OR	95% CI	p Value
Prior CABG	1.47	0.765–2.715	0.219	1.677	0.780–3.604	0.186			
Prior PCI	1.276	0.928–1.756	0.134	1.135	0.759–1.696	0.588			
Diabetes	1.12	0.850–1.476	0.421	1.429	0.995–2.052	0.053			
eGFR >60 ml/min/1.73 m^2	0.764	0.576–1.012	0.061	0.818	0.565–1.184	0.288			
Reattempt	1.131	0.811–1.577	0.469	0.906	0.552–1.487	0.697			
Target (LAD)	1.26	0.878–1.808	0.211	0.207	0.041–1.052	0.058			
CTO length ≥20 mm	1.42	1.036–1.946	0.029	1.262	0.850–1.874	0.249			
Severe calcification	3.101	2.057–4.675	<0.001	2.837	1.622–4.963	<0.001	3.264	1.739–6.125	<0.001
Tortuosity of CTO lesion	1.972	1.438–2.703	<0.001	1.992	1.365–2.907	<0.001	1.699	1.075–2.686	0.023
Dyslipidemia							0.535	0.322–0.889	0.016
Side branch at proximal cap							2.399	1.524–3.776	<0.001

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

techniques because of the availability of dedicated dissection/re-entry devices (such as the CrossBoss catheter and Stingray balloon and wires [Boston Scientific, Natick, Massachusetts]), which can make the procedure faster and safer (6,10,23,27). Although the success rate of antegrade subintimal dissection/re-entry strategies has been gradually improving (67% to 97.6%), these still carry the risk of perforation, which may not become evident until after stent implantation and periprocedural myocardial infarction because of the occlusion of coronary side branches and collateral circulation. Previous reports have shown a high incidence of procedural complications (myocardial infarction 2.4% to 16%; coronary perforation 2.4% to 14.3%) (27). In the present study, the incidence of MACCEs and other complications was low. One explanation for this low complication rate may be that all of the CTO-PCI procedures were performed without an antegrade subintimal dissection/re-entry strategy.

Multivariate analysis showed that severe lesion calcification was a strong predictor of the failure of CTO-PCIs. The J-CTO score was developed to estimate technical success in CTO-PCI, and lesion calcification was one of the independent predictors for failed procedures (19). We have previously reported that lesion calcification was an independent predictor of failure of the retrograde approach even after successful collateral channel crossing, as in antegrade CTO-PCIs (20). Severe calcification remains an important problem even in CTO-PCI performed by skilled specialists.

STUDY LIMITATIONS. A major disadvantage was the lack of standardized PCI procedures, such as for patient selection and guidewire selection, which depended on the decisions of each specialist. Thus, it lacks approaches that would have more clinical implication for less experienced specialists. Second, all CTO-PCIs were performed by highly skilled, experienced specialists and so the results may not be generalized to the daily clinical practice of less experienced specialists. Third, this study is based on the results of the procedures of the individual operators, not a randomized/multicenter trial. All operators are certified CTO-PCI operators; however, there is a possibility that the difference between the experience and skill among the operators influenced the results.

CONCLUSIONS

This study evaluated the clinical outcomes of primary CTO-PCI approaches taken by highly experienced Japanese CTO-PCI specialists, analyzing these according to the ITT principle. The overall technical success rate was high, and the complication rate was low. In this study, the retrograde approach was frequently chosen as the primary CTO-PCI strategy, especially for more complex CTO lesions. For intermediate CTO lesions, CTO-PCI was mainly performed using only the antegrade technique. Severe lesion calcification remains an important issue in CTO-PCIs.

ACKNOWLEDGMENTS The authors appreciate the great effort for this registry of the late Dr. Kazuaki Mitsudo and dedicate this paper to him. They also appreciate Drs. Harumi Katoh (Department of Cardiology, Clinical Research Center, Kurashiki Central Hospital, Ohara HealthCare Foundation, Okayama, Japan) and Yoshiharu Yamamoto (Clinical Research Center, Kurashiki Central Hospital, Ohara HealthCare Foundation, Okayama, Japan) for managing and analyzing all data for this study. The authors would like to thank Drs. Yasumi Igarashi, Hisayuki Okada, Tsutomu Fujita, Ryohei Yoshikawa, Satoru Otsuji, Yoshihiro Takeda, Kenya Nasu, Takenori Shibata, Yoshihisa Kinoshita, Yuichi Noguchi, Masahiko Ochiai, Satoru Sumitsuji, Shinya Okamoto, Kazuhiro Ahida, Kaname Takizawa, Akitsugu Oida, Yoshihito Yamamoto, Makoto Sekiguchi, Jiro Andoh, Wataru Nagamatsu, Masahisa Yamane, Yoshiki Uehara, Eisho Kyo, Takeshi Serikawa, Fumitake Hosaka, Kenji Kawajiri, Kinzo Ueda, Toru Takahahi, and Shigeru Nakamura for their patients' enrollment in the present study.

ADDRESS FOR CORRESPONDENCE: Dr. Etsuo Tsuchikane, Department of Cardiology, Toyohashi Heart Center, 21-1 Gobutori Oyama-cho Toyohashi, Aichi, Japan 441-8530. E-mail: Tsuchikane@heart-center.or.jp.

PERSPECTIVES

WHAT IS KNOWN? PCI for patients with CTOs, when performed by experienced operators, can enhance the success of the former.

WHAT IS NEW? This is the first study to evaluate the clinical outcomes of primary CTO-PCI approaches considered by highly experienced Japanese CTO-PCI specialists and to analyze them according to the ITT principle.

WHAT IS NEXT? Complex CTO lesion morphology is still an important issue for CTO-PCI procedural success, and further improvement of technologies for medical devices, such as guidewires and catheters, is required to improve the success rate.

REFERENCES

1. 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.

2. Surmely JF, Katoh O, Tsuchikane E, Nasu K, Suzuki T. Coronary septal collaterals as an access for the retrograde approach in the percutaneous treatment of coronary chronic total occlusions. Catheter Cardiovasc Interv 2007;69:826–32.

3. Sianos G, Barlis P, Di Mario C, et al. European experience with the retrograde approach for the recanalisation of coronary artery chronic total occlusions. A report on behalf of the EuroCTO club. EuroIntervention 2008;4:84–92.

4. Tsuchikane E, Katoh O, Kimura M, Nasu K, Kinoshita Y, Suzuki T. 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.

5. 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.

6. Christopoulos G, Menon RV, Karmpaliotis D, et al. The efficacy and safety of the "hybrid" approach to coronary chronic total occlusions: insights from a contemporary multicenter US registry and comparison with prior studies. J Invasive Cardiol 2014;26:427–32.

7. 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.

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. Rathore S, Katoh O, Matsuo H, et al. Retrograde percutaneous recanalization of chronic total occlusion of the coronary arteries: procedural outcomes and predictors of success in contemporary practice. Circ Cardiovasc Interv 2009;2:124–32.

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. 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.

12. Sianos G, Werner GS, Galassi AR, et al. Recanalisation of chronic total coronary occlusions: 2012 consensus document from the EuroCTO club. EuroIntervention 2012;8:139–45.

13. 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.

14. Yamane M, Muto M, Matsubara T, et al. Contemporary retrograde approach for the recanalisation of coronary chronic total occlusion: on behalf of the Japanese Retrograde Summit Group. EuroIntervention 2013;9:102–9.

15. Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. BMJ 1999;319:670–4.

16. Nuesch E, Trelle S, Reichenbach S, et al. The effects of excluding patients from the analysis in randomised controlled trials: meta-epidemiological study. BMJ 2009;339:b3244.

17. Sumitsuji S, Inoue K, Ochiai M, Tsuchikane E, Ikeno F. Fundamental wire technique and current standard strategy of percutaneous intervention for chronic total occlusion with histopathological insights. J Am Coll Cardiol Intv 2011;4:941–51.

18. Werner GS, Ferrari M, Heinke S, et al. Angiographic assessment of collateral connections in comparison with invasively determined collateral function in chronic coronary occlusions. Circulation 2003;107:1972–7.

19. 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.

20. 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.

21. Marenzi G, Assanelli E, Marana I, et al. N-acetylcysteine and contrast-induced nephropathy in primary angioplasty. N Engl J Med 2006;354:2773–82.

22. Tanaka A, Suzuki Y, Suzuki N, et al. Does N-acetylcysteine reduce the incidence of contrast-induced nephropathy and clinical events in patients undergoing primary angioplasty for acute myocardial infarction? Intern Med 2011;50:673–7.

23. Karmpaliotis D, Karatasakis A, Alaswad K, et al. Outcomes with the use of the retrograde approach for coronary chronic total occlusion interventions in a contemporary multicenter US registry. Circ Cardiovasc Interv 2016;9:e003434.

24. 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.

25. Habara M, Tsuchikane E, Muramatsu T, et al. Comparison of percutaneous coronary intervention for chronic total occlusion outcome according to operator experience from the Japanese retrograde summit registry. Catheter Cardiovasc Interv 2016;87:1027–35.

26. Teramoto T, Tsuchikane E, Matsuo H, et al. Initial success rate of percutaneous coronary intervention for chronic total occlusion in a native coronary artery is decreased in patients who underwent previous coronary artery bypass graft surgery. J Am Coll Cardiol Intv 2014;7:39–46.

27. Michael TT, Papayannis AC, Banerjee S, Brilakis ES. Subintimal dissection/reentry strategies in coronary chronic total occlusion interventions. Circ Cardiovasc Interv 2012;5:729–38.

KEY WORDS chronic total occlusion, percutaneous coronary intervention, retrograde approach

APPENDIX For supplemental tables, please see the online version of this paper.