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MINI-FOCUS ISSUE: CHRONIC TOTAL OCCLUSION

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)

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Objectives Our aim was to investigate in-hospital outcomes of percutaneous coronary intervention (PCI) of chronic total occlusion (CTO) using contemporary techniques.

Background Despite its increasing popularity and technical complexity, clinical outcomes of PCI for CTO using contemporary techniques have not been adequately evaluated.

Methods The J-CTO registry (multicenter CTO registry in Japan) is a large scale, multicenter registry enrolling consecutive patients undergoing PCI for CTO from 12 Japanese centers. In-hospital clinical outcomes were evaluated in 498 patients with 528 CTO lesions.

Results Multiple wiring strategies were frequently attempted (parallel wiring 31% and retrograde approach 25%) with relatively long guidewire manipulation time (median 30 min). Utilizing these complex strategies, high procedural success rates (88.6% in the first attempt cases and 68.5% in the retry cases) were accomplished. In-hospital adverse event rates were strikingly low (cardiac death 0.2%, Q-wave myocardial infarction 0.2%, and stroke 0%). Potential disadvantages of these procedures, including a large amount of contrast volume (median 293 ml) and long fluoroscopic time (median 45 min), were not associated with serious clinical sequelae (contrast induced nephropathy 1.2% and radiation dermatitis 0%). Although coronary perforations were documented frequently by angiography (antegrade 7.2% and retrograde 13.6%), clinically significant perforation resulting in cardiac tamponade was rare (0.4%).

Conclusions Most CTO lesions can be safely and successfully treated with PCI utilizing contemporary advanced techniques. Invasiveness and potential risks of these strategies, which have been the greatest concerns of CTO treatment, may be acceptable in the majority of cases considering the actual incidences of related adverse events and the procedural success rates. (J Am Coll Cardiol Intv 2010;3:143–51) © 2010 by the American College of Cardiology Foundation

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Percutaneous coronary intervention (PCI) of chronic total occlusion (CTO) lesions represents a great technical challenge. Because of low procedural success rate (1,2), high restenosis rate (3,4), and high incidence of adverse events (5–7) documented in the early reports of PCI, a large population of patients with CTOs have been managed medically, and such lesions have been the most common reason for referral to bypass surgery rather than PCI (8). However, the benefits of recanalization of CTOs were gradually proven with outcome of improved left ventricular function (9,10) and prolonged survival (5,6). Since the introduction of drug-eluting stents (DES), there has been a striking reduction in restenosis rates (11–13). Consequently, a boost in motivation and interest has taken place for this "last frontier" of PCI in the current clinical arena.

See page 152

Abbreviations and Acronyms

CIN = contrast-induced nephropathy
CTO = chronic total occlusion
DES = drug-eluting stent(s)
eGFR = estimated glomerular filtration rate
GW = guidewire
HD = hemodialysis
MI = myocardial infarction
MLD = minimal lumen diameter
PCI = percutaneous coronary intervention
QCA = quantitative coronary angiography

Recently, techniques for PCI of CTO have dramatically changed. The parallel wiring technique and the retrograde approach have been introduced. These techniques may further improve success rate yet, simultaneously, they potentially prolong procedural time and enhance the risk of complications. Such effects have not been systemically evaluated. Therefore, this study sought to investigate the in-hospital outcomes using the largest available datasets of an ongoing J-CTO (multicenter CTO registry in Japan). The analysis aimed to elucidate the "net" clinical impacts of contemporary PCI technique with in-depth assessments of potential disadvantages.

Methods

Study design and protocol. From April 2006 to November 2007, a multicenter, prospective, nonrandomized registry was conducted in 12 representative Japanese medical centers. All consecutive patients scheduled to undergo PCI for a CTO of a native coronary artery were considered for enrollment, targeting a total of 500 patients. A CTO was defined as an occlusion on angiography with no antegrade filling of the distal vessel other than via collaterals. The duration of the occlusion had to be more than 30 days, estimated from onset of clinical events such as myocardial infarction (MI), sudden onset or worsening of the chest symptoms, or proven by angiography. If the duration of the occlusion was uncertain, but the investigators had no clear reason to date the onset of the CTO at <30 days, the patient was enrolled. Patients who met the following criteria were excluded: 1) bleeding diathesis or coagulation disorder; 2) pregnancy; 3) severe allergy to iodinated contrast material; and 4) Kawasaki's disease or other vasculitis. All procedural and technical details and the choice of devices and anticoagulation regimens were according to the investigator's judgment. Antiplatelet agent regimens consisted of aspirin indefinitely and ticlopidine (200 mg daily, Japanese standard dose) or clopidogrel (75 mg daily) for at least 6 months after the procedure for DES and at least 1 month for bare-metal stents or balloon angioplasty. The study protocols were approved by the institutional review board at each participating center, and all patients provided written informed consent.

Study end points and definitions. The end points evaluated in this study included guidewire (GW) success rate (confirmed by an independent core laboratory), lesion success rate (final % diameter stenosis <50% by quantitative coronary angiography [QCA]), GW manipulation time (time from initial insertion of GW into the coronary lumen to time GW successfully crossing the lesion or GW being pulled out of lumen because of GW failure), contrast volume, fluoroscopic time, contrast-induced nephropathy (CIN) (defined as an absolute increase in serum creatinine concentration from the baseline value of at least 0.5 mg/dl [14]), radiation dermatitis (confirmed by dermatologists), angiographically documented coronary perforation, cardiac death, all-cause death, Q-wave MI or non–Q-wave MI (defined as post-procedural creatine kinase elevation ≥3 times the normal value), stent thrombosis based on Academic Research Consortium definition, target lesion or vessel revascularization, stroke, and major adverse cardiac events (i.e., death, MI, and target vessel revascularization). Chronic kidney disease was defined as not being on maintenance hemodialysis (HD) and an estimated glomerular filtration rate (eGFR) <30 ml/min/1.73 m^2, calculated by the modification of diet in renal disease formula (14).

Qualitative coronary angiography and QCA. The angiograms of the target procedures were sent to an independent core angiographic laboratory at the Tokyo core analysis laboratory located in Tokai University. Qualitative assessment was performed by an expert physician who also usually treated CTO lesions. Coronary perforation was defined as any contrast pool or evidence of contrast leak into cardiac chambers or pericardial space. Perforations were divided into 2 categories by the location of perforation: 1) those in the CTO artery, including CTO site, distal ends, and any portions throughout the CTO vessel; and 2) those within the retrograde channels. QCA was performed by 2 trained angiographic technicians using the automated edge detection system (QCA-CMS version 6.0, Medis, Leiden, the

Table 1. Baseline Patient Characteristics (n = 498)

Age (yrs)	66.9 ± 11.0
>80 yrs old	59 (11.8)
Male sex	406 (81.5)
Symptom of angina/acute MI	351 (70.5)
Heart failure	88 (17.6)
Diabetes	216 (43.3)
Insulin required	63 (12.7)
Hypertension	367 (73.6)
Dyslipidemia on medication	276 (55.4)
eGFR <30 ml/min/1.73 m^2	32 (6.4)
Without hemodialysis	11 (2.2)
With hemodialysis	21 (4.2)
History of CABG	48 (9.6)
History of stroke	9 (1.9)
Peripheral vascular disease	56 (11.2)
LV ejection function (%)	54.7 ± 13.0%
Low LVEF (<40%)	73 (14.7)
Number of diseased arteries	
Triple vessel	113 (22.7)
Double vessel	163 (32.7)
Single vessel	174 (34.9)
History of CABG	48 (9.6)
History of MI	224 (44.9)
Unprotected LM disease	31 (6.2)
Prior PCI	236 (47.3)

Values are mean ± SD or n (%).

CABG = coronary artery bypass grafting; eGFR = estimated glomerular filtration rate; LM = left main; LV = left ventricle; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Netherlands). Occlusion length was measured from the proximal occlusion to the distal retrograde filling from contralateral collaterals using a dual injection technique, start of filling of bridging collaterals to distal vessel reconstruction, or from the length of the lesion visible after the GW crossing. If stents were not used, minimal lumen diameter (MLD) and reference diameter were measured. If stents were implanted, in-stent and in-lesion segments were assessed.

Statistical analysis. Continuous variables were presented as mean ± SD or median and range if appropriate. Discrete variables were expressed as percentages. Chi-square test or Fischer exact test was used for categorical variables, and unpaired Student *t* test and Wilcoxon test were used for continuous variables. A p value <0.05 was considered statistically significant. All statistical analyses were performed with JMP version 8.0 (SAS Institute, Cary, North Carolina).

Results

Patients, lesions, and procedural characteristics. Between April 2006 and December 2007, a total of 498 patients with 528 CTO lesions were enrolled in this study. Baseline patient characteristics are displayed in Table 1. Fifty-nine of 498 patients (11.8%) were >80 years old. The incidence of previous history of heart failure was high (17.6%). Furthermore, high incidences of diabetes (43.3%) and chronic HD (4.2%) were consistent with the report from another Japanese interventional registry (15). The majority (55.4%) of patients had multivessel disease. Baseline lesion characteristics are listed in Table 2. Previous failed attempt of PCI for the same CTO lesion had been undertaken in 10.2% of the lesions. Incidence of the known predictors of CTO failure, including abrupt CTO entry, calcification, bridge

Table 2. Baseline Lesion and Procedural Characteristics (n = 528 Lesions)

Location of CTO	
LAD	190 (36.0)
RCA	234 (44.3)
LCx	101 (19.1)
LM	3 (0.6)
In-stent restenosis	34 (6.4)
Previously failed (retry) lesion	54 (10.2)
Qualitative and quantitative coronary assessment	
Side branches (within 3 mm from entry)	418 (79.2)
CTO entry type, abrupt	204 (38.6)
Calcification	290 (54.9)
Bridge collateral	118 (22.3)
Bending >45°	237 (44.9)
Rentrop grade III collateral	451 (85.4)
Occlusion length (mm)	13.5 ± 13.0
Reference diameter (proximal only) (mm)	2.9 ± 0.7
Approach site (antegrade route)	
Femoral	463 (87.6)
Brachial	21 (4.0)
Radial	44 (8.4)
Sheath size	
6-F	54 (10.2)
7-F	433 (82.0)
8-F	39 (7.4)
Contralateral injection	370 (70.1)
A total number of used GWs	4 (1–10)
Dilation strategies (lesion success case only, n = 457)	
Stent use	445 (97.3)
Drug-eluting stent use	432 (94.5)
Bare-metal stent use	65 (14.2)
POBA	12 (2.6)
Stent length by QCA (mm)	48.6 ± 24.6
Contrast volume	
Total volume (ml)	293 (53–1,097)
CTO procedure completion (ml)	251 (20–1,030)
GW cross (ml)	148 (4–900)
Total fluoroscopic time (min)	45 (1–301)

Values are n (%), mean ± SD, or median (range).

CTO = chronic total occlusion; GW = guidewire; LAD = left anterior descending artery; LCx = left circumflex artery; LM = left main; POBA = plain old balloon angioplasty; QCA = quantitative coronary angiography; RCA = right coronary artery.

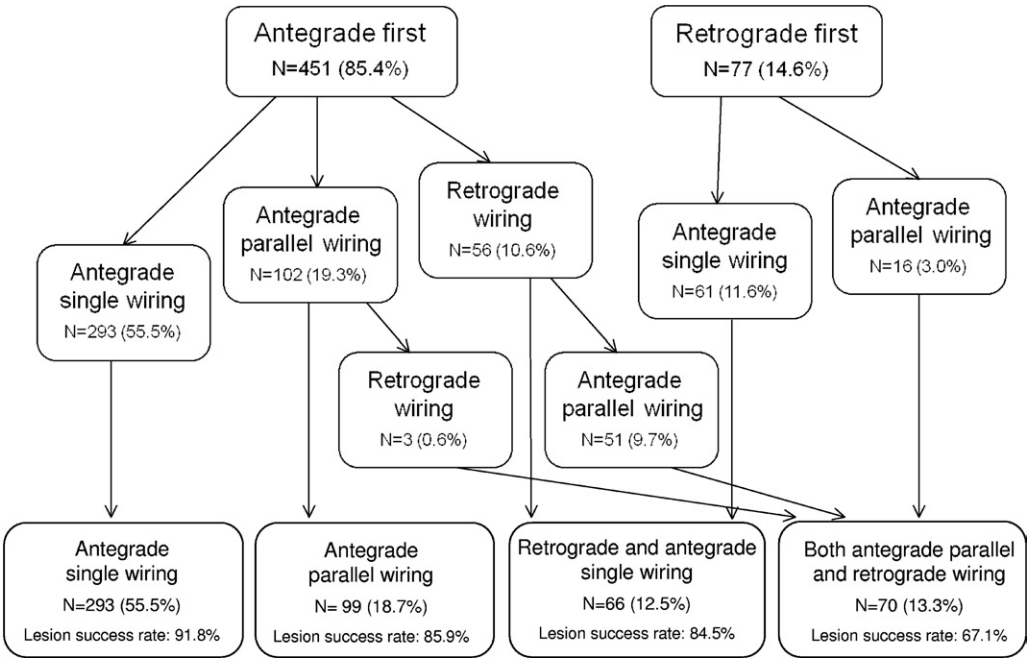

Figure 1. Schematic Representation (Flow Chart) of Selected GW Strategies for PCI of CTOs (n = 528 Lesions)

Lesion success rate was calculated in each strategy category. CTO = chronic total occlusion; GW = guidewire; PCI = percutaneous coronary intervention.

collateral, bending, Rentrop grading, and occlusion length are summarized in Table 2.

The procedural characteristics are also presented in Table 2. The median number of GWs used during the procedures was 4.0 (range 1 to 10). Figure 1 illustrates a flow chart of the selected GW strategies. Almost one-half of the lesions were treated with single wiring, and the rest were done with multiple wiring techniques. An initial retrograde approach was attempted in 14.6% of PCIs for CTOs. Stents were used in the majority (97.3%) of lesions if vessel size allowed it, and a DES was selected in 94.5% of lesions. In the procedural success subgroup, in-lesion reference diameter and MLD were significantly smaller in the nonstented cases compared with the stented cases at post-treatment (2.04 ± 0.53 mm vs. 2.41 ± 0.59 mm, $p < 0.001$ and 1.26 ± 0.54 mm vs. 1.57 ± 0.49 mm, $p < 0.001$). In-stent MLD was 2.21 ± 0.40 mm.

GW and lesion success rate. Overall GW and lesion success rates were extremely high (87.7% and 86.6%, respectively) (Fig. 2). Among these, the success rates of the retry cases (previously attempted but failed) were significantly lower (72.2% and 68.5%), compared with those of first attempt cases (89.5% and 88.6%). Lesion success rates according to each category of selected GW strategy are shown in Figure 1.

Retrograde approaches and success rate. Table 3 displays a detailed assessment of the subgroup treated with the retrograde approach (n = 136, 25.7% of the procedures). In the majority of cases (79.4%) with a retrograde approach, retrograde wiring was started at the very early stage of the procedures. Lesion success rate of the "retrograde first touch" subsets was overall relatively high (79.2%) among the retrograde approach cases. If the retrograde wire crossed over the collateral channel and successfully reached the re-entry side of CTO segments (74.5% of the retrograde

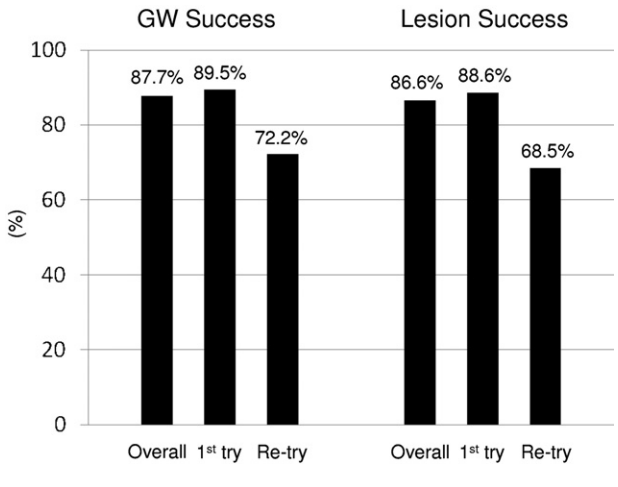

Figure 2. GW Success and Lesion Success Rate (n = 528)

Retry means attempt for previously failed chronic total occlusion lesions. GW = guidewire.

Table 3. Detailed Assessment of Retrograde Approach (n = 136)

	Incidence	Lesion Success Rate
Timings of retrograde wiring		
Retrograde earlier than antegrade	77 (56.6)	79.2
After quick antegrade wiring	31 (22.8)	74.2
After sufficient antegrade wiring	28 (20.6)	67.9
Used retrograde route		
Septal route	87 (63.9)	86.7
Epicardial route	27 (20.2)	78.3
Graft route	21 (15.1)	72.2
Self artery route (bridging collateral)	1 (0.84)	100.0
Advancement of retrograde wire		
Crossed channel, reached re-entry of CTO	101 (74.5)	93.9
Crossed channel, but not reached re-entry	4 (2.73)	33.3
Channels not crossed	31 (22.7)	60.0

Values are n (%) or %.
Abbreviations as in Table 2.

Table 4. Complications and In-Hospital Outcomes

Complications	
Cardiac tamponade	2 (0.4)
Emergent PCI	2 (0.4)
Emergent CABG	0 (0)
Blood transfusion	8 (1.6)
Access site surgery	2 (0.4)
Gastrointestinal bleeding	1 (0.2)
Contrast-induced nephropathy	6 (1.2)
Radiation dermatitis	0 (0)
In-hospital adverse outcomes	
All-cause death	2 (0.4)
Cardiac death	1 (0.2)
Q-wave myocardial infarction	1 (0.2)
Non–Q-wave myocardial infarction	10 (2.1)
Stroke	0 (0)
Stent thrombosis	0 (0)

Values are n (%).
Abbreviations as in Table 1.

attempts), final lesion success rate of this subset was remarkably high (93.9%). All success cases were finalized with antegrade stent and/or balloon delivery.

GW manipulation time and success rate. Distribution of GW manipulation time is shown in Figure 3A. Nearly one-half of the cases were completed within 30 min. Approximately 10% of the procedures took more than 2 h. GW manipulation time was significantly longer in the failure cases compared with the success cases (median 85 min vs. 26 min, respectively; $p < 0.0001$). The GW success rate of each time category is displayed in Figure 3B. Of note, GW success rate decreased nearly time-dependently. The cases that required GW manipulation time of <60 min achieved a high GW success rate (93.3%). However, the success rate decreased to 49.9% for those requiring more than 120 min.

In-hospital complications. Table 4 summarizes complications and in-hospital outcomes. Cardiac death was seen only in 0.2% of cases. Post-procedure creatine phosphokinase was followed in 420 patients (84.4%). Among them, 10 patients satisfied the definition of MI, exceeding 3 times the normal value of creatine phosphokinase. Only 1 case showed Q-wave MI (0.24%), and the other 9 cases were identified as non–Q-wave MI (2.1%) with clinical symptoms in only 1 patient. There was no stroke or stent thrombosis during hospital stay. Significant in-hospital complications, including cardiac tamponade, emergent re-

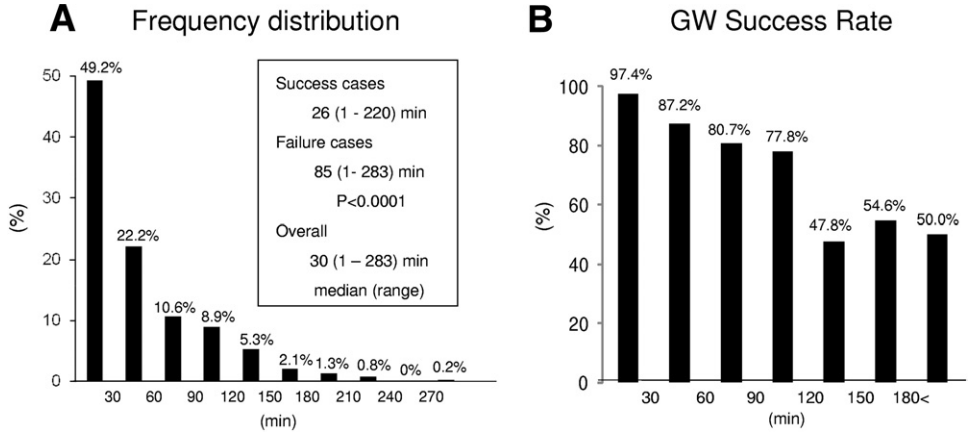

Figure 3. Frequency Distribution of GW Manipulation Time and Corresponding GW Success Rate

Frequency distribution of guidewire (GW) manipulation time **(A)** and GW success rate inversely related to GW manipulation time **(B)**. Nearly one-half of the cases were completed in <30 min. A significant difference was observed between success and failure cases. GW success rate inversely related to GW manipulation time.

vascularization, access site surgery, and gastrointestinal bleeding, rarely occurred.

Fluoroscopic time and contrast volume. Distribution of fluoroscopic time for procedural success and failure is displayed in Figure 4. Similar to GW manipulation time, fluoroscopic times were longer in the failure cases than the success cases (median 60 min vs. 41 min, $p < 0.001$). Despite relatively long fluoroscopic time, none of the cases in this cohort developed radiation dermatitis during the hospital stay (Table 4).

The median of contrast volume required for GW crossing was 148 ml (GW success cases only); this was 251 ml for CTO procedure completion (lesion success cases only) and 293 ml used in total for all procedures including the failed cases (Table 2). Interestingly, in contrast to GW manipulation time and fluoroscopic time, contrast volume was not statistically significantly different between GW success cases and failures (median 285 ml vs. 330 ml, $p = 0.22$) (Fig. 5). Except maintenance HD patients, serial serum creatinine levels could be assessed in 408 patients (85.6%). Despite the use of a relatively large contrast volume, the incidence of CIN was unexpectedly low (1.2%) in the non-HD patients. There was no statistically significant difference in total contrast volume between the 2 groups of patients with or without post-operative CIN (median 290 ml vs. 307 ml, respectively; $p = 0.49$). Importantly, pre-procedural serum creatinine level and eGFR was almost identical between the 2 groups (mean ± SD: 0.91 ± 0.10 mg/dl vs. 0.93 ± 0.32 mg/dl, $p = 0.66$ and 64.3 ±7.8 ml/min/1.73 m^2 vs. 64.9 ± 17.8 ml/min/1.73 m^2, $p = 0.69$). All the patients with CIN had normal pre-procedural creatinine and eGFR levels.

Coronary perforation. By a detailed qualitative assessment of coronary angiography, angiographic coronary perforation was detected in 7.2% (36 of 528) of the cases at the side of the CTO artery. All perforations occurred during GW manipulation. Interestingly, perforations were more frequent in procedures with a retrograde approach (retrograde channels perforation 13.6% [17 of 127]; compared with the CTO artery; $p < 0.001$). Table 5 summarizes specific types of perforation sites and the additional treatment applied for hemostasis. The majority of perforations observed in the CTO artery were detected by contrast staining on angiogram (99.8%), only 0.2% showed blow-out perforation. In contrast, retrograde channel perforation was associated with frequent perforations into cardiac spaces (41.2%), in addition to contrast staining (58.8%). No action was taken in more than 70% of angiographic perforations, and they did not present significant clinical problems. One-third of patients with angiographic perforation required hemostatic procedures. Pericardiocentesis was required only in 2 cases of perforations in the CTO artery (0.2% of the procedures, 3.8% of the perforations); 1 was a blow-out perforation and the other was contrast staining type; both occurred during antegrade GW manipulation. None of the cases with retrograde channel perforation had cardiac tamponade. Even when coronary perforation was detected angiographically during the procedures, final GW success was achieved in 71.7% of patients.

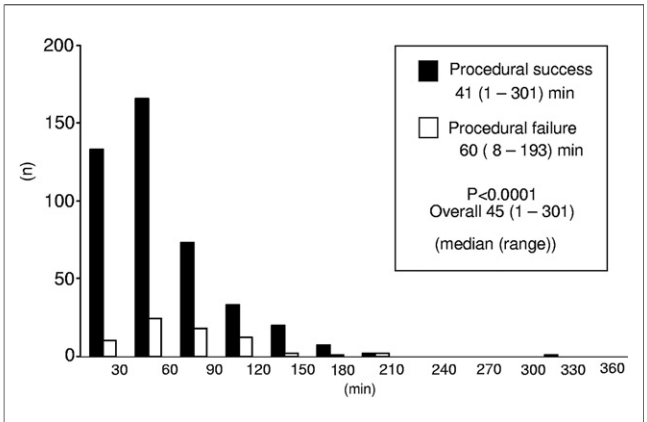

Figure 4. Frequency Distribution of Total Fluoroscopic Time Comparing Procedural Success and Failure

Overall, relatively long fluoroscopic time was required for success in the procedures. A significant difference was observed in the fluoroscopic time between success and failure cases.

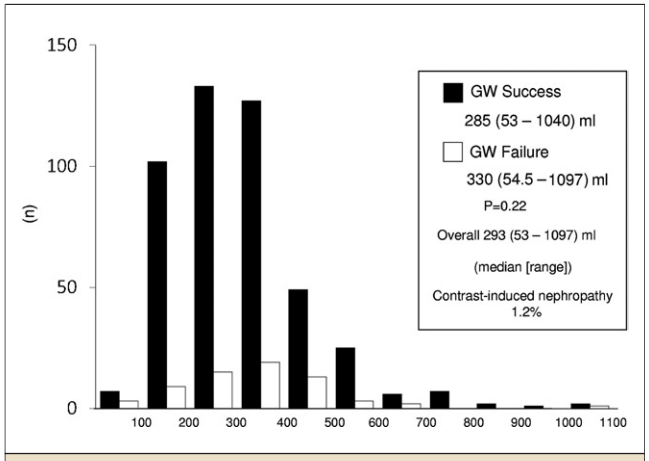

Figure 5. Frequency Distribution of Total Contrast Volume Used During the Procedures

There was no statistically significant difference in contrast volume between success and failure cases. Abbreviations as in Figure 1.

Discussion

Generally, low initial success rate remains to be the biggest issue regarding PCI for CTO. Data from 25 years of experience from the Mayo Clinic indicate that although the initial success rate of PCI of CTO improved from 51% in the balloon angioplasty era to 72% in the early stent era, it reached a plateau of about 72% in the bare-metal stent era and 70% in the DES era (2). Other reports indicate that the

Table 5. Severity of Angiographic Coronary Perforation and Hemostatic Treatment

Perforation in the CTO Artery (n = 36)			Perforation in Retrograde Channel (n = 17)		
Severity	**Actions**	**n (%)**	**Severity**	**Actions**	**n (%)**
Contrast staining n = 35 (99.8%)	Observation	25 (71.4%)	Contrast staining n = 10 (58.8%)	Observation	9 (90.0%)
	Hemostatic procedures	10 (28.6%)		Hemostatic procedure	1 (10.0%)
	Self-fat emboli	4		Ballooning	1
	Ballooning	3	Perforation into cardiac chambers n = 7 (41.2%)	Observation	6 (85.7%)
	Balloon + drainage	1		Hemostatic procedure	1 (14.3%)
	Others	2		Ballooning + coiling	1
Perforation into pericardial space n = 1 (0.2%)	Observation	0 (0%)	Perforation into pericardial space n = 0 (0%)	NA	NA
	Hemostatic procedure	1 (100%)			
	Coiling + drainage	1			

Abbreviations as in Table 2.

rate remains around the high 60% to mid-70% across the studies (1,5,6). Contrary to the expectations, adverse event rates relating to PCI of CTO were found to be comparable to those of PCI for non-CTO lesions (5). However, more complex and aggressive strategies may possibly increase the adverse event rate, which remains to be addressed. In the J-CTO registry, the data demonstrated outstanding outcomes, including one of the highest procedural success rates and the lowest substantial complication rates among the published reports ever.

Historical comparisons and potential benefits of the retrograde approach. Almost 3 years before the J-CTO registry, the CONQUEST (CTO New techniQUE for STandard procedure) registry was conducted by the CTO "specialized" operators at 6 Japanese centers (16). At that time, the parallel wire technique, characterized as manipulation of 2 wires in a back-and-forth sequence until either wire reached the distal exit point of the true lumen, was the last resort. After completion of the CONQUEST registry, a novel GW strategy, the "retrograde approach," was proposed (17); this technique had already been available during the enrollment period of the J-CTO registry.

Interestingly, the proportion of CTO lesions requiring multiple wire strategies were almost identical between the 2 studies (the CONQUEST registry 43.1% vs. the J-CTO registry 44.5%). Considering the increase in the number of the participating operators in the J-CTO registry, the same level of high initial procedural success rate of de novo CTO lesions (the CONQUEST registry 86.2% vs. the J-CTO registry 86.6%) and reduction of contrast volume for target treatment completion (the CONQUEST registry 339 ± 140 ml vs. the J-CTO registry 274 ± 151 ml) is quite meaningful. Reduction of contrast volume might be primarily due to the retrograde GW that plays a role as a "marker" of the distal true lumen. Furthermore, excellent contralateral imaging could be obtained by injecting very small amounts of contrast super-selectively from the collateral channel using a micro-catheter.

The most desirable feature of the retrograde approach is that it engages the distal true lumen, which is the target point of the antegrade wire. Once retrograde GW successfully passes the collateral channels, the next step is to bring the antegrade and retrograde GWs to meet somewhere in the middle. In fact, we had an extremely high success rate of 93.9% in this registry, once such a face-to-face GW positioning was accomplished. Suitable case selection for the retrograde approach remains to be defined.

Disadvantages of PCI for CTO and its clinical impact. Potential disadvantages of CTO treatment include: 1) longer procedural and fluoroscopic times; 2) greater contrast volume; and 3) high incidence of coronary perforation. In this registry, we had a consensus to minimize radiation exposure complications by frequently changing fluoroscopic projection angles during the procedures. Although specific data are not available, such careful attention might possibly have reduced skin complications. A previous study has shown that limiting the total fluoroscopic time or dose area product, or changing the beam angulations is important for controlling the entrance skin dose during prolonged procedures (18). Although no case developed radiation dermatitis during the hospital stay, prolonged careful evaluations should be performed to detect delayed skin problems.

CIN is one of the most serious issues of complex PCI. Since investigators tried to adjust contrast volume based on pre-operative renal function, the incidence of CIN could be minimized to 1.2% in this study. As a consequence, CIN occurred somewhat more frequently in the patients with normal creatinine levels; however, the actual contrast volume used for these patients was not greater than average. Therefore, it may be difficult to anticipate complication of CIN in the pre-operative periods for the contrast volume range of this study. However, continuous efforts should be made to further decrease contrast volume for PCI of CTO.

Angiographic coronary perforation was frequently observed during CTO treatment; however, the most important problem was whether it related to clinical problems like

cardiac tamponade or not. In this registry "clinical perforation" requiring any hemostatic maneuvers occurred in less than 30% of the cases with angiographic perforation. Evaluating the clinical significance of angiographic perforation is critically important, and our goal must be to avoid cardiac tamponade. The incidence of cardiac tamponade in the J-CTO registry was strikingly low at 0.4%, compared with the previous reports (a range of 0.8% to 1.9%) (2,16). Potential hypotheses to explain the decreased incidence of cardiac tamponade in the J-CTO registry are: 1) adequate hemostatic procedures as needed; and 2) reduction of long and aggressive antegrade GW manipulation, thanks to the introduction of retrograde approaches. A surprising finding was that relatively high procedural success rate was achieved even after angiographic detection of coronary perforation. Although a careful evaluation is required, procedural continuation could be considered for many cases with angiographic coronary perforation.

A new paradigm for CTO treatment. In general, PCI procedures for CTO lesions are not always difficult for the following reasons: 1) nearly one-half of the cases were successfully treated with single, antegrade wiring and with GW manipulation time of <30 min, as we observed in this registry; and 2) "true" occlusion length tends to be shorter than we could determine from unilateral diagnostic angiography. In the J-CTO registry, mean occlusion length was relatively short as evaluated by frequent use of guiding catheters for contralateral injection allowing excellent collateral images.

Although the majority of CTO studies indicated initial success rates of approximately 70% (1,2,5,6), we believe that this can be improved up to 80% or 90% by introduction of adjunctive GW strategies as shown in this trial and the CONQUEST trial (16). Our study demonstrated that the clinical impacts of the disadvantages of PCI of CTO on organ damage were fairly small. Furthermore, the efficacy of DES ensures long-term patency of recanalized CTO lesions (11–13). Therefore, it might be possible to consider a "PCI-first strategy for CTO lesions." Further investigation focusing on long-term results as compared with coronary artery bypass grafting surgery would be required to justify the proposed new paradigm for CTO treatment.

Study limitations. Potential limitations of this study should be considered. First, lack of randomization design did not allow any type of comparisons in this study. Second, the operators participating in this registry were limited in the only advanced PCI centers. In general, the outcomes are dependent on basic skills and judgments of the physicians performing the procedures. There must be clear differences between "experienced" operators in the J-CTO registry and less experienced PCI operators. However, continuous efforts and adequate training must fill these technical and/or judgment gaps. Third, some cases with procedural success were finally achieved by the operators' persistent "efforts." Except procedural time, we did not perform any assessments of quantification of these factors, which might cause a bias in the results. Fourth, although this trial was designed to enroll consecutive series of CTO lesions treated in each participating site, there was no means to confirm whether consecutive cases were truly registered in this trial. Furthermore, actual PCI attempt rate among the all CTO lesions could not be addressed, because of lack of the exact numbers of the CTO cases that: 1) were sent to bypass surgery; or 2) were followed medically during the study periods. Fifth, because not all patients received post-procedural blood tests (approximately 85% of the enrolled population had measurements), accurate incidence of CIN or MI could not be assessed. However, since post-procedural blood tests tend to be performed in high-risk patients or in patients with periprocedural problems, the true incidence might not exceed the actual data obtained. Sixth, since radiation dermatitis is most often detected after several weeks, the evaluation period appeared to be insufficient. Although no specific skin problems were additionally reported from the participating sites, conclusive confirmation must be obtained. Finally, in this registry, an occlusion duration of >30 days was used as the definition of CTO, consistent with the previous reports (11,19). Recently, CTO has been commonly defined as >3 months of occlusion duration after several consensus reports (2,7,20). The study protocol was already established before these consensus reports were published. We estimated that a very few cases had occlusion duration of <3 months, which is unlikely to have influenced the overall success rates.

Conclusions

In-hospital analysis of the J-CTO registry showed a high procedural success rate in the real-world consecutive series of patients using complex wiring strategies. This was achieved at the expense of longer fluoroscopy time, a larger volume of contrast material, and elevated risks of coronary perforation; however, such procedural characteristics were not commonly associated with serious clinical sequelae. Overall, the incidence of major cardiac adverse events was very low, comparable to that of general interventional treatments. Invasiveness and potential risks of these aggressive strategies, which have constituted the greatest concerns of CTO treatment, might be acceptable considering the actual incidences of related adverse events and the procedural success rates.

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