JACC: CARDIOVASCULAR INTERVENTIONS VOL. 11, NO. 14, 2018

The Hybrid Approach to Chronic Total Occlusion Percutaneous Coronary Intervention

Update From the PROGRESS CTO Registry

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ABSTRACT

OBJECTIVES The aim of this study was to determine the techniques and outcomes of hybrid chronic total occlusion (CTO) percutaneous coronary intervention (PCI) in a diverse group of patients and operators on 2 continents.

BACKGROUND CTO PCI has been evolving with constant improvement of equipment and techniques.

METHODS Contemporary outcomes of CTO PCI were examined by analyzing the clinical, angiographic, and procedural characteristics of 3,122 CTO interventions performed in 3,055 patients at 20 centers in the United States, Europe, and Russia.

RESULTS The mean age was 65 ± 10 years, and 85% of the patients were men, with high prevalence of diabetes (43%), prior myocardial infarction (46%), prior coronary artery bypass graft surgery (33%), and prior PCI (65%). The CTO target vessels were the right coronary artery (55%), left anterior descending coronary artery (24%), and left circumflex coronary artery (20%). The mean J-CTO (Multicenter Chronic Total Occlusion Registry of Japan) and PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) scores were 2.4 ± 1.3 and 1.3 ± 1.0, respectively. The overall technical and procedural success rate was 87% and 85%, respectively, and the rate of in-hospital major complications was 3.0%. The final successful crossing strategy was antegrade wire escalation in 52.0%, retrograde in 27.1%, and antegrade dissection re-entry in 20.9%; >1 crossing strategy was required in 40.9%. Median contrast volume, air kerma radiation dose, and procedure and fluoroscopy time were 270 ml (interquartile range: 200 to 360 ml), 2.9 Gy (interquartile range: 1.7 to 4.7 Gy), 123 min (interquartile range: 81 to 188 min) and 47 min (interquartile range: 29 to 77 min), respectively.

CONCLUSIONS CTO PCI is currently being performed with high success and acceptable complication rates among various experienced centers in the United States, Europe, and Russia. (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention [PROGRESS CTO]; NCT02061436) (J Am Coll Cardiol Intv 2018;11:1325–35) © 2018 the American College of Cardiology Foundation. Published by Elsevier. All rights reserved.

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ISSN 1936-8798/$36.00 https://doi.org/10.1016/j.jcin.2018.02.036

ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass graft

CCS = Canadian Cardiovascular Society

CTO = chronic total occlusion

IQR = interquartile range

MACE = major adverse cardiac event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

TIMI = Thrombolysis In Myocardial Infarction

The hybrid approach to chronic total occlusion (CTO) percutaneous coronary intervention (PCI) advocates dual coronary injection, careful and structured review of the angiogram, and flexibility (1). Use of all crossing strategies (antegrade wire escalation [2], antegrade dissection re-entry [3-6], and the retrograde approach [7-10]) is encouraged (1), with initial and subsequent choices influenced by the CTO anatomic characteristics and the outcomes of the originally selected approach (1,11-18). Application of the hybrid approach to CTO PCI has been associated with good outcomes in U.S. and European registries, although CTO PCI outcomes in nonselected populations have been less optimal, with a success rate of approximately 60% (19). We examined a contemporary, multicenter CTO PCI registry to determine the techniques and outcomes of hybrid CTO PCI in a diverse group of patients and operators on 2 continents.

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METHODS

We analyzed the clinical, angiographic, and procedural characteristics of 3,122 CTO PCIs performed in 3,055 patients enrolled in the PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; NCT02061436) registry between January 2012 and November 2017 at 18 U.S., 1 European, and 1 Russian center (Online Appendix). Some centers enrolled patients during only part of the study period because of participation in other studies. The study was approved by the Institutional Review Board of each center.

DEFINITIONS. Coronary CTOs were defined as coronary lesions with TIMI (Thrombolysis In Myocardial Infarction) flow grade 0 of at least 3 months' duration. Estimation of the duration of occlusion was clinical, based on the first onset of angina, history of myocardial infarction (MI) in the target vessel territory, or comparison with a prior angiogram. Calcification was assessed by angiography as mild (spots), moderate (involving ≤50% of the reference lesion diameter), or severe (involving >50% of the reference lesion diameter). Moderate proximal vessel tortuosity was defined as the presence of at least 2 bends >70° or 1 bend >90° and severe tortuosity as 2 bends >90° or 1 bend >120° in the CTO vessel. Blunt or no stump was defined as lack of tapering or lack of a funnel shape at the proximal cap. Interventional collateral vessels were defined as collateral vessels considered amenable to crossing by a guidewire and a

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Manuscript received January 16, 2018; revised manuscript received February 12, 2018, accepted February 27, 2018.

microcatheter by the operator. A procedure was defined as "retrograde" if an attempt was made to cross the lesion through a collateral vessel or bypass graft supplying the target vessel distal to the lesion; if not, the procedure was classified as "antegrade only." Antegrade dissection re-entry was defined as antegrade PCI during which a guidewire was intentionally introduced into the subintimal space proximal to the lesion, or re-entry into the distal true lumen was attempted following intentional or inadvertent subintimal guidewire crossing.

Technical success was defined as successful CTO revascularization with achievement of <30% residual diameter stenosis within the treated segment and restoration of TIMI antegrade flow grade 3. Procedural success was defined as the achievement of technical success without any in-hospital complications. In-hospital major adverse cardiac events (MACE) included any of the following adverse events before hospital discharge: death, MI, recurrent symptoms requiring urgent repeat target vessel revascularization with PCI or coronary artery bypass graft (CABG) surgery, tamponade requiring either pericardiocentesis or surgery, and stroke. MI was defined using the third universal definition of MI (type 4a MI) (20). Major bleeding was defined as bleeding causing reduction in hemoglobin >3 g/dl or bleeding requiring transfusion or surgical intervention. The J-CTO (Multicenter Chronic Total Occlusion Registry of Japan) score was calculated as described by Morino et al. (21), the PROGRESS CTO score as described by Christopoulos et al. (22), and the PROGRESS CTO complications score as described by Danek et al. (23).

TABLE 1 Clinical Characteristics of the Study Population, Classified According to Technical Success

	Overall (N = 3,055)	Technical Success (n = 2,657)	Technical Failure (n = 398)	p Value
Age (yrs)	64.80 ± 10.09	64.6 ± 10.15	66.01 ± 9.63	0.0141
Male	85.25	84.69	88.95	0.0378
BMI (kg/m^2)	30.60 ± 6.14	30.50 ± 6.15	31.20 ± 6.02	0.0666
Smoking (current)	26.01	25.37	30.27	0.0561
Diabetes	43.02	43.53	39.65	0.1758
Dyslipidemia	92.20	92.11	92.75	0.6781
Hypertension	90.26	89.61	94.49	0.0044
Family history of CAD	33.35	33.44	32.80	0.8423
CCS angina classification				0.4771
Class ≤1	11.44	11.64	10.15	
Class ≥2	88.56	88.36	89.85	
Myocardial viability performed	24.99	24.28	29.32	0.0783
Prior MI	46.00	44.82	53.75	0.0023
Heart failure	30.56	29.71	36.25	0.0159
Prior valve surgery or procedure	3.17	3.06	3.89	0.4210
Prior PCI	65.29	64.49	70.62	0.0180
Prior CABG surgery	32.49	31.28	40.68	0.0003
Baseline creatinine (mg/dl)	1.01 (0.89–1.22)	1.01 (0.89–1.21)	1.07 (0.90–1.27)	0.1301
Currently on dialysis	2.67	2.50	3.80	0.1633
Prior CVD	11.70	11.51	12.90	0.4567
Prior PAD	15.02	14.53	18.29	0.0709
Chronic lung disease	14.20	13.80	16.81	0.1386
Left ventricular EF (%)	54 (42–60)	55 (44–60)	50 (40–60)	0.0357

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

BMI = body mass index; CABG = coronary artery bypass graft; CAD = coronary artery disease; CVD = cerebrovascular disease; EF = ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; PAD = peripheral arterial disease.

STATISTICAL ANALYSIS. Categorical variables were expressed as percentages and were compared using Pearson's chi-square test or the Fisher exact test. Continuous variables are presented as mean ± SD or as median (interquartile range [IQR]) unless otherwise specified and were compared using the Student's *t*-test and 1-way analysis of variance for normally distributed variables; the Wilcoxon rank sum test and the Kruskal-Wallis test were applied for nonparametric continuous variables as appropriate. Multivariate logistic regression with stepwise backward elimination was performed to examine the independent association between annual CTO PCI volume and procedural outcomes (procedural success and in-hospital MACE). Variables with univariate associations in the present study ($p < 0.05$) were entered into the model, as well as variables that have been previously linked with procedural outcomes of CTO PCI, including age, smoking, peripheral arterial disease, chronic lung disease, history of MI, stroke, PCI or CABG surgery, left ventricular ejection fraction, CTO target vessel, multiple CTO vessels treated during the same procedure, and CTO PCI only. All statistical analyses were performed using JMP version 13.0 (SAS Institute, Cary, North Carolina). A 2-sided p value of 0.05 was considered to indicate statistical significance.

RESULTS

CLINICAL AND ANGIOGRAPHIC CHARACTERISTICS. The baseline clinical features of the study population are summarized in Table 1. Compared with patients who had CTO PCI fail, patients who had successful CTO PCI were younger and less likely to be men and to have hypertension. They were also less likely to have had an MI, congestive heart failure, prior CABG surgery, and prior PCI and had higher left ventricular ejection fraction. Most patients (88.56%) were symptomatic, having at least Canadian Cardiovascular Society (CCS) angina classification class II

TABLE 2 Angiographic Characteristics of Study Lesions, Classified According to Technical Success

	Overall (N = 3,122)	Technical Success (n = 2,711)	Technical Failure (n = 411)	p Value
Target vessel				0.0640
RCA	55.22	54.93	57.14	
LAD	23.81	24.57	18.80	
LCx	19.91	19.47	22.81	
Other	1.06	1.03	1.25	
CTO length (mm)	33.99 ± 24.16	33.43 ± 24.14	37.80 ± 23.99	0.0030
Vessel diameter (mm)	2.85 ± 0.51	2.86 ± 0.51	2.81 ± 0.47	0.1383
Proximal cap ambiguity	35.06	31.98	53.97	<0.0001
Side branch at proximal cap	49.91	47.56	64.14	<0.0001
Blunt stump/no stump	53.69	50.61	72.55	<0.0001
Interventional collateral vessels	56.72	58.80	44.19	<0.0001
Moderate/severe calcification	54.23	52.30	67.02	<0.0001
Moderate/severe tortuosity	34.96	33.43	45.21	<0.0001
In-stent restenosis	16.61	16.13	19.68	0.0878
Previously failed CTO PCI	20.20	19.21	26.70	0.0005
J-CTO score	2.43 ± 1.30	2.34 ± 1.29	3.07 ± 1.13	<0.0001
PROGRESS CTO score	1.32 ± 1.03	1.25 ± 1.01	1.77 ± 1.01	<0.0001
PROGRESS CTO complication score	3.07 ± 1.93	3.00 ± 1.91	3.54 ± 1.97	<0.0001

Values are % or mean ± SD.

CTO = chronic total occlusion; J-CTO = Multicenter Chronic Total Occlusion Registry of Japan; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LM = left main segment; PCI = percutaneous coronary intervention; PROGRESS CTO = Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; RCA = right coronary artery.

TABLE 3 Techniques Used for Chronic Total Occlusion Percutaneous Coronary Intervention in the Study Patients

	Overall (N = 3,122)	Technical Success (n = 2,711)	Technical Failure (n = 411)	p Value
Crossing strategies used				
AWE	81.77	81.15	85.89	0.0204
ADR	31.68	29.69	44.77	<0.0001
Retrograde	38.57	35.96	55.72	<0.0001
First crossing strategy				0.0124
AWE	75.36	75.80	72.51	
ADR	8.39	8.67	6.57	
Retrograde	16.24	15.53	20.92	
Final crossing strategy				<0.0001
AWE	45.89	51.95	5.24	
ADR	18.95	20.96	5.49	
Retrograde	23.97	27.09	2.99	
None	11.19	0.00	86.28	
Balloon-uncrossable lesions	10.62	10.21	29.37	<0.0001
Balloon-undilatable lesions	11.11	10.74	22.22	0.0349
Access site				
Right femoral	78.96	78.46	82.24	0.0798
Left femoral	54.29	53.34	60.58	0.0060
Right radial	32.48	33.12	28.22	0.0481
Left radial	18.67	19.48	13.38	0.0031
Bifemoral approach	51.35	50.42	57.42	0.0082
Biradial approach	14.09	14.90	8.76	0.0009

Values are %.

ADR = antegrade dissection reentry; AWE = antegrade wire escalation.

(CCS class II, 24.97%; CCS class III, 53.93%; CCS class IV, 9.65%), and most had stable (64.33%) or unstable (18.20%) angina.

The angiographic characteristics of the study lesions are presented in Table 2. The CTO target lesions were located in the right coronary artery (55.22%), left anterior descending coronary artery (23.81%), and left circumflex coronary artery (19.91%). Failed CTO PCI was associated with longer lesion length (33.4 ± 24.1 mm vs. 37.9 ± 24.0 mm; p = 0.0030), proximal cap ambiguity (53.97% vs. 31.98%; p < 0.0001), moderate to severe calcification (72.55% vs. 52.30%; p < 0.0001), and tortuosity (45.21% vs. 33.43%; p < 0.0001) or previously failed recanalization attempt (26.70% vs. 19.21%; p = 0.0005). Failed CTO PCI cases also had higher J-CTO scores (2.34 ± 1.29 vs. 3.07 ± 1.13; p < 0.0001), PROGRESS CTO scores (1.25 ± 1.01 vs. 1.77 ± 1.13; p < 0.0001), and PROGRESS CTO complications scores (3.00 ± 1.91 vs. 3.54 ± 1.97; p < 0.0001).

PROCEDURAL OUTCOMES OF THE HYBRID APPROACH. Overall technical and procedural success was 87% and 85%, respectively, and the in-hospital major complications rate was 3.0%. The baseline technical and procedural characteristics are presented in Tables 3 and 4. Antegrade wire escalation was the most commonly used initial approach (in 75%), especially for lower complexity CTOs (J-CTO score 2.28 ± 1.29, PROGRESS CTO score 1.35 ± 1.05), whereas antegrade dissection re-entry (8%; J-CTO score 2.86 ± 1.16, PROGRESS CTO score 1.50 ± 1.07) and the retrograde approach (16%; J-CTO score 3.12 ± 1.07, PROGRESS CTO score 1.33 ± 0.96) were used for more complex lesions (p < 0.0001). The initial approach was successful in 55% of patients, whereas 41% of patients underwent further attempts that were technically successful in 79% (Figure 1).

The final successful crossing strategy was antegrade wire escalation (46%), antegrade dissection re-entry (19%), and the retrograde approach (24%). The success of antegrade wire escalation decreased with lesion complexity, as classified with the J-CTO score (easy [J-CTO score 0], 88%; intermediate [J-CTO score 1], 72%; difficult [J-CTO score 2], 51%; and very difficult [J-CTO score ≥3], 32% to 17%; p < 0.0001) and the PROGRESS CTO score (55%, 43%, 42%, 39%, and 43%, respectively for scores of 0, 1, 2, 3, and 4; p < 0.0001). The retrograde approach was more commonly required for complex lesions, as classified by the J-CTO score (3%, 9%, 20%, and 35% to 44%, respectively for J-CTO scores of 0, 1, 2,

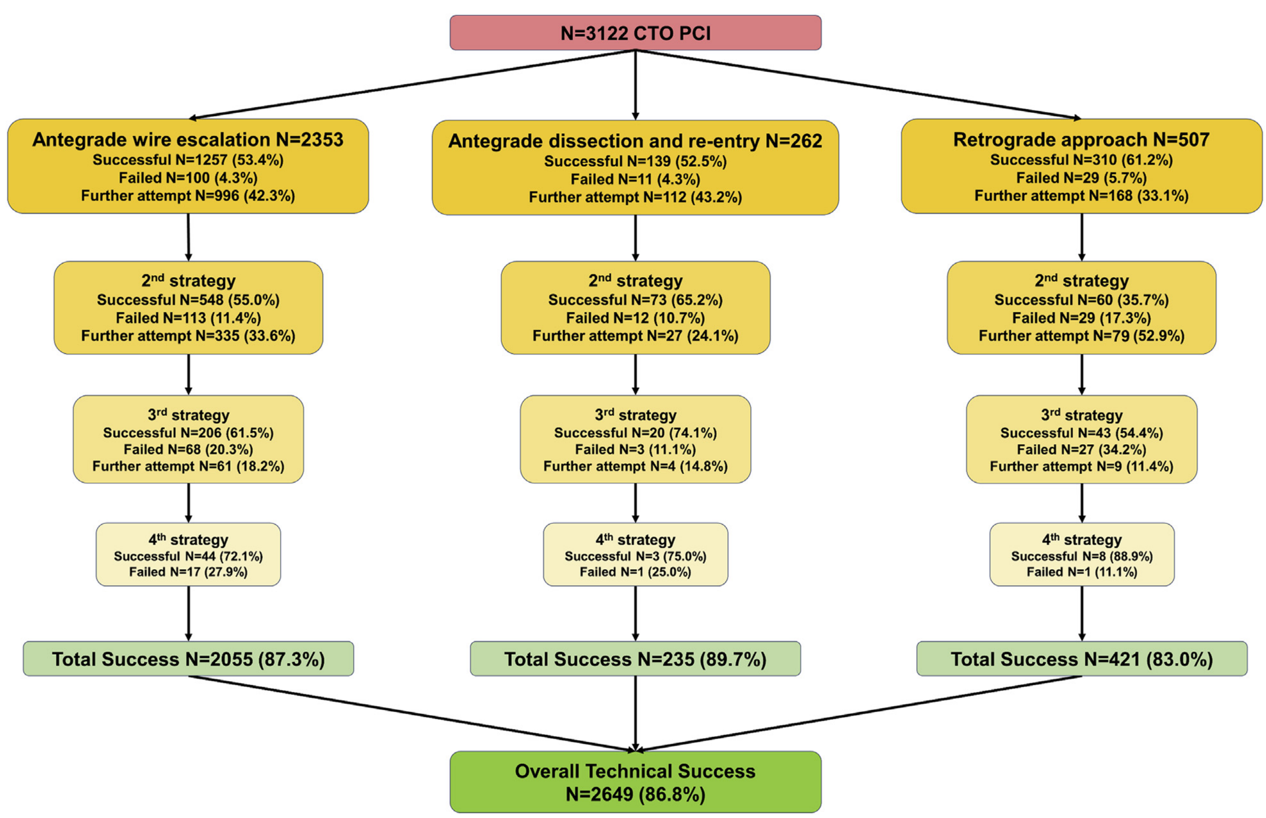
TABLE 4 Procedural Characteristics, Classified According to Percutaneous Coronary Intervention Outcomes and Lesion Complexity (J-CTO Score)

	Overall	Technical Success	Technical Failure	p Value	Easy (0)	Intermediate (1)	Difficult (2)	Very Difficult (≥3)	p Value
Dual injection	70.41	69.57	75.82	0.0260	47.59	64.19	68.70	77.89	<0.0001
Radial access*	37.06	37.70	32.85	0.0577	49.59	39.09	35.83	38.17	0.0030
Femoral access	81.90	81.37	85.40	0.0480	63.27	78.17	82.65	84.09	<0.0001
Procedure time (min)	123 (81–188)	121 (80–184)	140 (85–224)	0.0003	77 (46–117)	92 (58–136)	115 (73–172)	152 (102–217)	<0.0001
Contrast volume (ml)	270 (200–360)	260 (200–350)	300 (220–400)	0.0001	220 (160–300)	250 (190–340)	260 (200–350)	280 (202–385)	<0.0001
Fluoroscopy time (min)	47.0 (28.6–77.0)	45.0 (27.3–73.7)	66.0 (39.0–93.6)	0.0001	27.0 (18.1–39.2)	33.1 (19.3–53.7)	41.9 (27.1–65.7)	63.1 (38.6–93.0)	<0.0001
Patient AK dose (Gy)	2.9 (1.7–4.7)	2.8 (1.6–4.5)	3.9 (2.4–6.0)	0.0001	1.8 (0.9–3.3)	2.1 (1.2–3.5)	2.5 (1.4–4.4)	3.5 (2.1–5.2)	<0.0001
Number of stents†	2.4 ± 1.1	2.4 ± 1.1	2.7 ± 1.6	0.5559	1.8 ± 0.9	2.0 ± 1.0	2.3 ± 1.1	2.8 ± 1.2	<0.0001
Stent length (mm)†	71.8 ± 36.4	71.7 ± 36.3	78.6 ± 47.6	0.6599	48.0 ± 25.2	57.6 ± 31.1	66.5 ± 33.5	85.5 ± 36.3	<0.0001
Non-CTO lesion PCI	28.20	28.39	26.80	0.5611	32.75	32.00	29.19	26.37	0.0786
In-hospital MACE	3.04	2.37	7.54	0.0001	1.36	1.41	3.01	3.11	0.0119
Technical success	86.84	–	–	–	96.90	94.84	89.14	81.26	<0.0001

Values are %, median (interquartile range), or mean ± SD. *Radial access indicates any radial access site use in CTO PCI; including biradial and combined radial-femoral approaches. †In successful cases stents were implanted in 97.10% versus in failed procedures in 4.89% (related to perforation, investment procedure, donor vessel dissection, or stenting but Thrombolysis In Myocardial Infarction flow grade ≥3) ($p < 0.0001$).

AK = air kerma; J-CTO = Multicenter Chronic Total Occlusion Registry of Japan; MACE = major adverse cardiac event(s); PCI = percutaneous coronary intervention.

FIGURE 1 Application of the Hybrid Approach in the Study Patients



Sequence of chronic total occlusion (CTO) crossing techniques used in the study patients and associated technical success. PCI = percutaneous coronary intervention.

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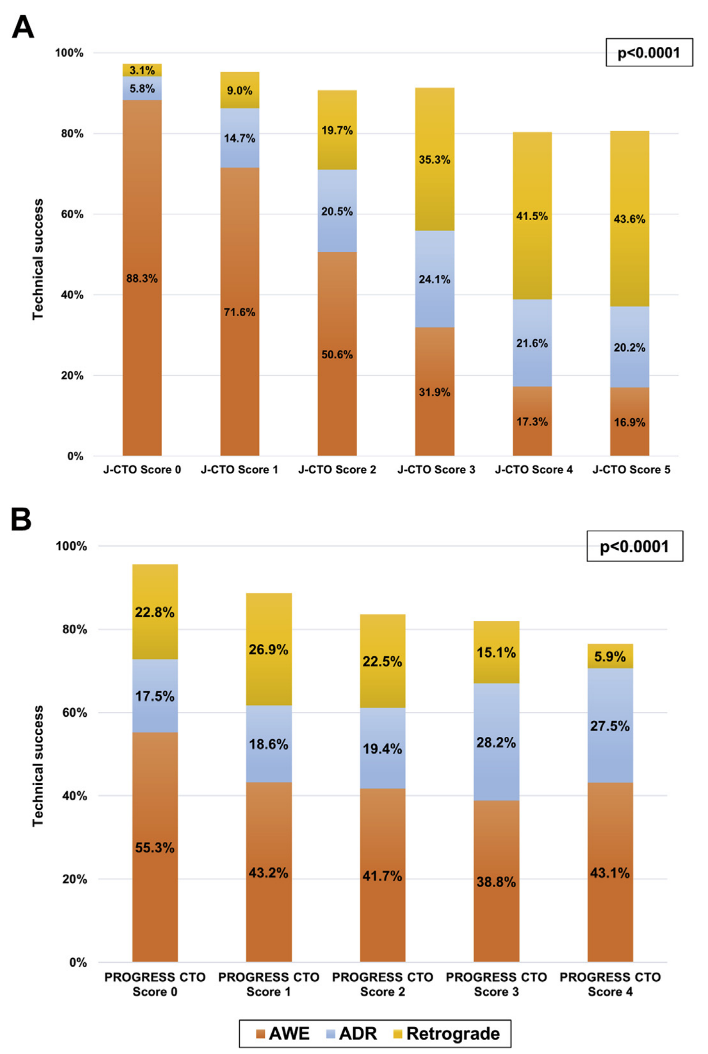
FIGURE 2 Technical Success and Crossing Strategy Use According to J-CTO Score and the PROGRESS CTO Score



Impact of chronic total occlusion (CTO) lesion complexity, as assessed by the J-CTO score **(A)** and PROGRESS CTO score **(B)** on technical success and use of various crossing strategies. ADR = antegrade dissection re-entry; AWE = antegrade wire escalation; J-CTO = Multicenter Chronic Total Occlusion Registry of Japan; PROGRESS CTO = Prospective Global Registry for the Study of Chronic Total Occlusion Intervention.

and ≥3; $p < 0.0001$) but less frequently in lesions with higher PROGRESS CTO score (23%, 27%, 23%, 15%, and 6%; $p < 0.0001$) (**Figures 2A and 2B**).

Dual injection was used in 70% of all cases and was more frequent in failed interventions (76% vs. 70%; $p = 0.026$) and in complex lesions with high J-CTO scores (48% vs. 78%; $p < 0.0001$). Radial access was used in 37% overall, with a biradial approach in 14% and in combination with a femoral approach in 20% of cases. Use of radial access was lower with increasing lesion complexity (easy, 50%; intermediate, 39%; difficult, 36%; very difficult, 38%; $p = 0.003$), whereas the frequency of femoral (63%, 78%, 83%, and 84%; $p < 0.0001$) and bifemoral (28%, 43%, 51%, and 57%; $p < 0.0001$) approaches increased with increasing lesion complexity. Median contrast volume, air kerma radiation dose, and procedural and fluoroscopy time were 270 ml (IQR: 200 to 360 ml), 2.9 Gy (IQR: 1.7 to 4.7 Gy), and 123 min (IQR: 81 to 188 min) and 47.0 min (IQR: 28.6 to 77.0 min), respectively, and were higher for more complex lesions (**Table 4**). Less complex lesions required fewer stents ($p < 0.0001$), but the frequency of non-CTO PCI was higher in those groups and decreased with increasing lesion complexity ($p = 0.08$).

The procedural success and annual CTO PCI volume at the participating sites are shown in Online Figure 1. Higher median annually performed CTO PCI per center was associated with higher procedural success in both univariate and multivariate analysis (**Figure 3**) but not in-hospital MACE.

The incidence of in-hospital MACE was 3.04% (death, 0.85%; acute MI, 1.08%; stroke, 0.26%; emergency CABG surgery, 0.16%; urgent repeat PCI, 0.36%; and pericardial tamponade, 0.85%) and increased with increasing lesion complexity (**Table 4**). The prevalence of in-hospital MACE was higher in failed procedures (7.54% vs. 2.37%; $p < 0.0001$) and with more complex crossing techniques: antegrade wire escalation, antegrade dissection re-entry, or retrograde crossing (1.09% vs. 2.96% vs. 5.61%; $p < 0.0001$). Use of the retrograde approach was associated with higher incidence of complications, as shown in **Figure 4**. Median length of hospital stay was significantly higher in patients with versus without in-hospital MACE (6 days [IQR: 2 to 9 days] vs. 1 day [IQR: 1 to 2 days]); $p < 0.0001$).

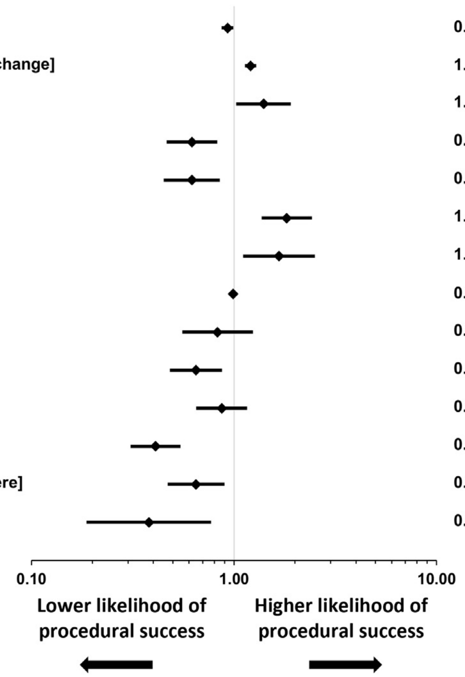
DISCUSSION

To the best of our knowledge, this is the largest study reported to date on CTO PCI using the hybrid approach, demonstrating a high technical success rate (88%) with an acceptable major complication rate (3.0%). These outcomes were achieved despite high lesion complexity and relatively low success of the initially selected CTO crossing strategy (55%) (**Figure 5**).

Previous smaller studies have provided similarly encouraging results. In an earlier report from the PROGRESS CTO registry from 11 U.S. centers, technical success was 91% and in-hospital MACE was 1.7% (11). Wilson et al. (17) reported a 79% initial success rate among 1,156 patients from 7 centers enrolled in the UK Hybrid CTO Registry, with a 90%

FIGURE 3 Baseline Clinical and Angiographic Characteristics and Procedural Success

Variables	OR	CI 95%	p-value
Age [per 10 years change]	0.93	0.872-0.993	0.0310
Annual CTO PCI volume [per 20 unit change]	1.21	1.133-1.289	<0.0001
Adequate distal landing zone	1.40	1.026-1.909	0.0340
Bifurcation at distal cap	0.62	0.460-0.824	0.0011
Calcification [moderate to severe]	0.62	0.452-0.853	0.0033
Interventional collaterals	1.82	1.369-2.423	<0.0001
LAD CTO target vessel	1.67	1.112-2.511	0.0135
Lesion length [per 5 mm change]	0.99	0.980-1.005	<0.0001
Prior CVD	0.83	0.554-1.239	0.3589
Prior HF	0.65	0.481-0.871	0.0041
Prior MI	0.87	0.648-1.158	0.3335
Proximal cap ambiguity	0.41	0.308-0.544	<0.0001
Proximal tortuosity [moderate to severe]	0.65	0.468-0.894	0.0083
≥2 CTO PCI in the same procedure	0.38	0.188-0.772	0.0074



Multivariate analysis of parameters associated with procedural success. CI = confidence interval; CTO = chronic total occlusion; CVD = cerebrovascular disease; HF = heart failure; LAD = left anterior descending coronary artery; MI = myocardial infarction; OR = odds ratio; PCI = percutaneous coronary intervention.

final technical success rate after repeat procedures. The RECHARGE (Registry of Crossboss and Hybrid Procedures in France, the Netherlands, Belgium, and United Kingdom) registry of 1,253 CTO interventions performed in 1,177 patients between 2014 and 2015 at 22 European centers reported an 86% procedural success rate and a 2.6% major in-hospital complication rate (18). Vo et al. (24) reported a single-operator pilot study showing a rapid increase in procedural success despite the low initial CTO PCI experience. At 2 high-volume, experienced centers Pershad et al. (14) showed significant increase in technical (from 79.4% to 95.4%; $p < 0.001$) and procedural (from 77.9% to 88.3%) success rates after implementation of the hybrid algorithm, compared with the pre-implementation period. Furthermore, the Hybrid Video Registry analyzed 194 video-recorded live case demonstrations reporting a high success rate (92.8%), even in highly complex CTOs, with acceptable procedure time and contrast volume (25). As shown in prior studies, higher annual CTO PCI volume was independently associated with higher success rates, reflecting the importance of center and operator experience in optimizing outcomes, especially among complex lesion and patient subgroups (26).

In the present study, we found that technical and procedural success remained high, with reasonably low complication rates, despite expansion of the registry in recent years. Antegrade wire escalation was more commonly applied as the initial crossing approach (74%) for less complex lesions (J-CTO score 2.24 ± 1.24, PROGRESS CTO score 1.32 ± 0.87) and was the most common final crossing strategy (in approximately one-half of the cases). Antegrade dissection re-entry and retrograde techniques were more likely to be used as initial strategy in cases with complex anatomy (J-CTO scores 2.78 ± 1.21 and 3.32 ± 0.98, respectively; PROGRESS CTO scores 1.38 ± 0.93 and 2.00 ± 0.89, respectively) and were the final successful strategies in 22% and 28% of all cases, respectively.

Failure to cross with a guidewire was the most common reason for CTO PCI failure (in 86%). In

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 11, NO. 14, 2018
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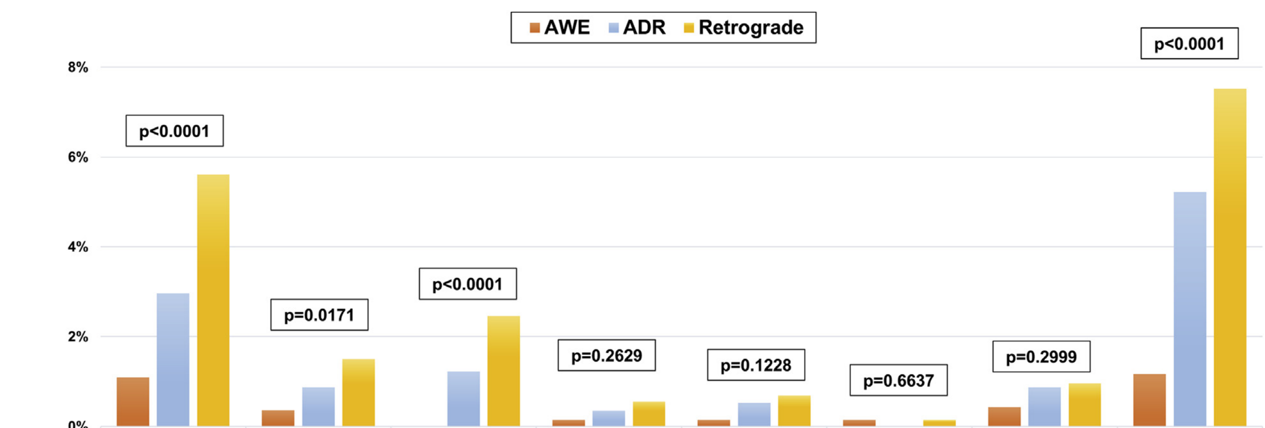
FIGURE 4 **In-Hospital Major Complications Classified According to Final Successful Crossing Strategy**



	MACE overall	Death	Acute MI	Stroke	Re-PCI	Emergency CABG	Pericardial tamponade	Perforation
AWE	1.09%	0.36%	0.00%	0.14%	0.14%	0.14%	0.43%	1.16%
ADR	2.96%	0.87%	1.22%	0.35%	0.52%	0.00%	0.87%	5.22%
Retrograde	5.61%	1.50%	2.46%	0.55%	0.68%	0.14%	0.96%	7.52%

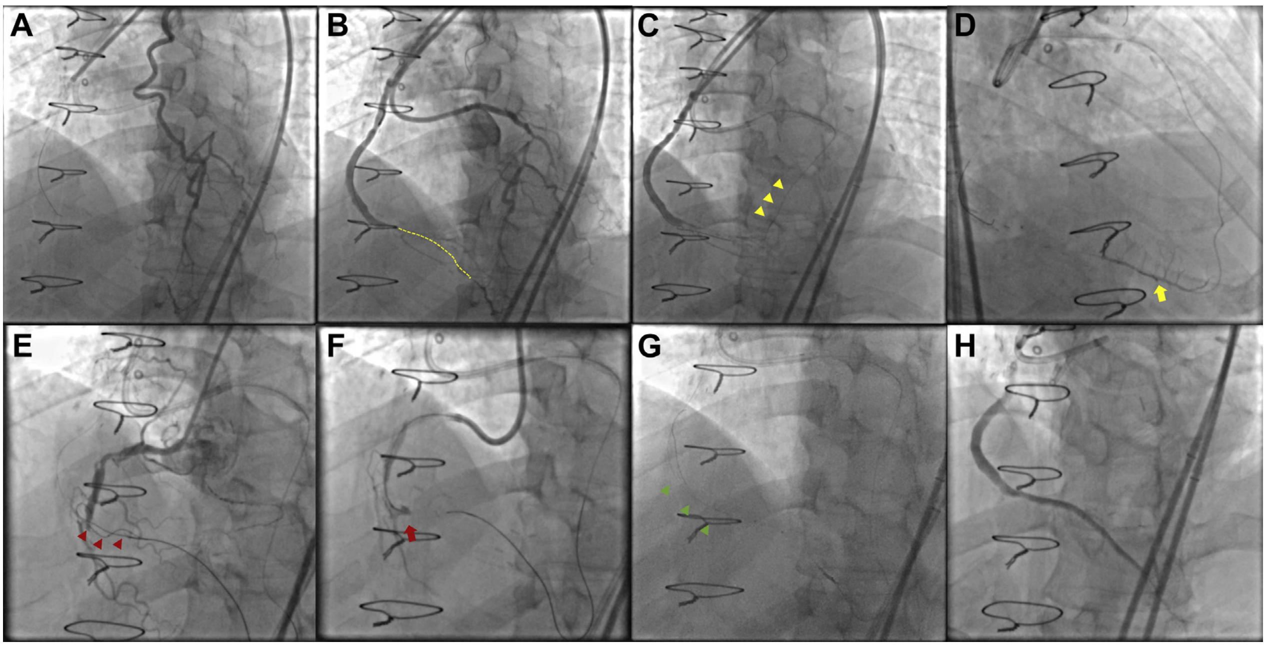
Use of the retrograde approach was associated with higher overall in-hospital major adverse cardiac events (MACE) and risk for perforation. ADR = antegrade dissection and re-entry; AWE = antegrade wire escalation; CABG = coronary artery bypass graft; MI = myocardial infarction; PCI = percutaneous coronary intervention.

13%, the procedure failed despite successful guidewire crossing (Table 3) because of balloon-undilatable lesions (3.9%), inability to deliver stents (2.3%), final TIMI flow grade <3 (1.3%), residual stenosis >30% (1.0%), and procedure-related complications (0.8%; 1 patient with donor vessel thrombosis, 1 patient with aortocoronary dissection, and 1 procedure related death due to pericardial tamponade and subsequent cardiogenic shock). The presence of balloon-uncrossable (29.4% vs. 10.2%; p < 0.0001) and balloon-undilatable lesions (22.2% vs. 10.7; p = 0.0109) was higher in the failed CTO PCI group, highlighting the need for CTO PCI operators to have experience in treating these and other complex lesions, such as severe calcification and bifurcations (27,28).

The overall complication rate was 3%, and complications occurred less frequently in technically successful procedures (2.2% vs. 7.9%; p < 0.0001). The risk for complications was higher in more complex lesions (easy [J-CTO score 0] 1.36% vs. very difficult [J-CTO score ≥3] 3.11%; p = 0.01) and with use of advanced crossing techniques (which were more commonly used for more complex lesions). This highlights the importance of weighing the risks and benefits of the procedure, both during discussions with patients and family (to determine whether CTO PCI should be done) and during the procedure itself: implementing more complex CTO crossing strategies (such as retrograde crossing via epicardial collateral vessels) may predispose to increased risk for complications, which may be justified in some patients because of significant potential benefit, but not in some others.

Despite the encouraging findings of our study and other contemporary registries, the success rates of CTO interventions in unselected patient cohorts remain low. Hannan et al. (29) (New York State PCI Registry, n = 4,030 patients) reported a 61.3% success rate with a 1.07% complication rate (vs. 1.06% for non-CTO PCI cases, p = 0.95). Ramunddal et al. (30) showed a similarly low procedural success rate (54.2%) among 6,442 patients undergoing CTO intervention in SCAAR (Swedish Coronary Angiography and Angioplasty Registry). Habara et al. (31) compared the acute outcomes of 3,229 CTO interventions among 56 high- and low-volume centers in Japan, showing a higher overall success rate at high-volume centers (90.6% vs. 85.6%; p < 0.001), without a significant difference in in-hospital MACE rate (0.45% vs. 0.62%; p = 0.35), attributed mostly to a higher antegrade success rate. Sharma et al. (32) showed that procedural outcomes of CTO interventions among operators who had received proctorship in using the hybrid approach were better (77.5% vs. 62.1%; p < 0.0001), especially in more complex cases (for J-CTO scores ≥2, the corresponding rates were 70.7% and 49.5%, respectively; p = 0.0003) than those who did not receive mentorship. Hence, CTO PCI should be performed by

FIGURE 5 **Clinical Case, Illustrating the Importance of Changing Crossing Strategy to Successfully Recanalize a Challenging Chronic Total Occlusion**



Percutaneous coronary intervention (PCI) of a distal right coronary artery (RCA) chronic total occlusion (CTO) in a patient with Canadian Cardiovascular Society class III angina and 4 prior failed CTO attempts and 2 prior coronary artery bypass graft surgeries. **(A)** Left internal mammary artery (LIMA) injection demonstrating septal and epicardial collateral channels from the left anterior descending coronary artery (LAD) to the RCA. **(B)** Triple coronary injection showing mild disease in the saphenous vein graft (SVG) to the RCA, distal RCA CTO immediately distal to the SVG anastomotic site, and mild disease in previously stented proximal and mid LAD along with competitive flow from the LIMA graft. **(C)** Multiple attempts for septal collateral crossing (using surfing and contrast guided techniques) succeeded in advancing a guidewire to the distal RCA, but a microcatheter could not be advanced over the guidewire. **(D)** Successful contrast-guided epicardial collateral crossing using a Suoh 03 guidewire over a Caravel microcatheter (Asahi Intecc, Nagoya, Japan). **(E)** Several attempts to advance the retrograde guidewire distal to the SVG anastomosis failed, despite using multiple guidewires. **(F)** Multiple attempts to recanalize the native RCA failed, as the antegrade guidewire could not be advanced distal to the SVG anastomosis. **(G)** The reverse controlled antegrade and retrograde tracking and dissection (CART) was successfully used to cross the CTO and advance the retrograde guidewire into the SVG-RCA, followed by guidewire externalization. **(H)** Final angiographic result after stent implantation. The patient had significant symptom alleviation.

experienced operators at dedicated centers to achieve optimal results.

STUDY LIMITATIONS. First, we did not have mid- and long-term follow-up of the study patients. Second, there was no core laboratory assessment of the study angiograms or clinical event adjudication. Third, the procedures were performed at dedicated, high-volume CTO centers by experienced operators, limiting the extrapolation to less experienced operators at low-volume centers.

CONCLUSIONS

CTO PCI can currently be achieved with high success and acceptable complication rates among various operators and patient populations in the United States and Europe, highlighting the need for developing more CTO PCI centers of excellence in order to achieve the best possible clinical outcomes in this challenging patient and lesion group.

ACKNOWLEDGMENTS Study data were collected and managed using Research Electronic Data Capture electronic data capture tools hosted at the Minneapolis Heart Institute Foundation. Research Electronic Data Capture is a secure, Web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

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PERSPECTIVES

WHAT IS KNOWN? Coronary CTO can be challenging to recanalize, with success rates of approximately 60% in unselected, all-comer populations.

WHAT IS NEW? Application of the hybrid approach resulted in a high technical success rate (87%) and an acceptable rate of major in-hospital complications (3%) across a large number of sites and operators in the United States, Europe, and Russia. Changing crossing strategy was required in 41% of cases, with the final success strategy being antegrade wire escalation in 52%, retrograde in 27%, and antegrade dissection re-entry in 21%.

WHAT IS NEXT? Bridging the gap between what is currently achieved and what can be achieved in CTO intervention should be a major focus of upcoming research and education efforts.

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KEY WORDS chronic total occlusion, outcomes, percutaneous coronary intervention, techniques

APPENDIX For a list of centers participating in the present study and a supplemental figure, please see the online version of this paper.