

Development and Validation of a Scoring System for Predicting Periprocedural Complications During Percutaneous Coronary Interventions of Chronic Total Occlusions: The Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS CTO) Complications Score

Barbara Anna Danek, MD; Aris Karatasakis, MD; Dimitri Karpaliotis, MD; Khaldoon Alaswad, MD; Robert W. Yeh, MD; Farouc A. Jaffer, MD, PhD; Mitul P. Patel, MD; Ehtisham Mahmud, MD; William L. Lombardi, MD; Michael R. Wyman, MD; J. Aaron Grantham, MD; Anthony Doing, MD; David E. Kandzari, MD; Nicholas J. Lembo, MD; Santiago Garcia, MD; Catalin Toma, MD; Jeffrey W. Moses, MD; Ajay J. Kirtane, MD; Manish A. Parikh, MD; Ziad A. Ali, MD; Judit Karacsonyi, MD; Bavana V. Rangan, BDS, MPH; Craig A. Thompson, MD, MMSc; Subhash Banerjee, MD; Emmanouil S. Brilakis, MD, PhD

Background—High success rates are achievable for chronic total occlusion (CTO) percutaneous coronary intervention (PCI) using the hybrid approach, but periprocedural complications remain of concern. Although scores estimating success and efficiency in CTO PCI have been developed, there is currently no available score for estimation of the risk for periprocedural complications. We sought to develop a scoring tool for prediction of periprocedural complications during CTO PCI.

Methods and Results—We analyzed data from 1569 CTO PCIs in the Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS CTO) using a derivation and validation sampling ratio of 2:1. Variables independently associated with periprocedural complications in multivariable analysis in the derivation set were assigned points based on their respective odds ratios. Forty-four (2.8%) patients experienced complications. Three factors were independent predictors of complications and were included in the score: patient age >65 years, +3 points (odds ratio, OR=4.85, CI 1.82-16.77); lesion length \geq 23 mm, +2 points (OR=3.22, CI 1.08-13.89); and use of the retrograde approach +1 point (OR=2.41, CI 1.04-6.05). The resulting score showed good calibration and discriminatory capacity in the derivation (Hosmer-Lemeshow χ^2 6.271, $P=0.281$, receiver-operating characteristic [ROC] area=0.758) and validation (Hosmer-Lemeshow χ^2 4.551, $P=0.473$, ROC area=0.793) sets. Score values of 0 to 2, 3 to 4, and \geq 5 were defined as low, intermediate, and high risk of complications (derivation cohort 0.4%, 1.8%, 6.5%, $P<0.001$; validation cohort 0.0%, 2.5%, 6.8%, $P<0.001$).

Conclusions—The PROGRESS CTO complication score is a useful tool for prediction of periprocedural complications in CTO PCI.

Clinical Trial Registration—URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT02061436. (*J Am Heart Assoc.* 2016;5:e004272 doi: 10.1161/JAHA.116.004272)

Key Words: chronic total occlusion • complication • outcome • percutaneous coronary intervention • risk stratification

From the VA North Texas Healthcare System and UT Southwestern Medical Center, Dallas, TX (B.A.D., A.K., J.K., B.V.R., S.B., E.S.B.); Columbia University, New York, NY (D.K., J.W.M., A.J.K., M.A.P., Z.A.A.); Henry Ford Hospital, Detroit, MI (K.A.); Massachusetts General Hospital and Harvard Medical School, Boston, MA (R.W.Y., F.A.J.); VA San Diego Healthcare System and University of California San Diego, San Diego, CA (M.P.P., E.M.); University of Washington, Seattle, WA (W.L.L.); Torrance Memorial Medical Center, Torrance, CA (M.R.W.); Mid America Heart Institute, Kansas City, MO (J.A.G.); Medical Center of the Rockies, Loveland, CO (A.D.); Piedmont Heart Institute, Atlanta, GA (D.E.K., N.J.L.); Minneapolis VA Healthcare System and University of Minnesota, Minneapolis, MN (S.G.); University of Pittsburgh Medical Center, Pittsburgh, PA (C.T.); Boston Scientific, Natick, MA (C.A.T.).

An accompanying Data S1 is available at <http://jaha.ahajournals.org/content/5/10/e004272/DC1/embed/inline-supplementary-material-1.pdf>

Correspondence to: Emmanouil S. Brilakis, MD, PhD, Dallas VA Medical Center (111A), 4500 South Lancaster Road, Dallas, TX 75216. E-mail: esbrilakis@gmail.com

Received July 24, 2016; accepted September 13, 2016.

© 2016 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley Blackwell. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

Chronic total occlusion (CTO) percutaneous coronary intervention (PCI) success rates continue to improve as new techniques and tools develop to address the specific challenges in CTO PCI.¹⁻⁴ The occurrence of periprocedural complications, however, continues to impact risk-benefit considerations, with a rate of 3.1% in a large contemporary meta-analysis.¹ Although scores predicting technical and procedural outcomes in CTO PCI have been developed (such as the Japanese Chronic Total Occlusion [J-CTO] score,⁵ the Prospective Global Registry for the Study of Chronic Total Occlusion Intervention [PROGRESS CTO] score,⁶ and the Clinical and Lesion-related [CL] score⁷), there is currently no specific tool to predict the risk of periprocedural complications in this setting. We sought to develop a scoring system to predict occurrence of periprocedural complications during CTO PCI.

Methods

Patient Population

We examined the clinical, angiographic, and procedural characteristics of 1569 consecutive CTO PCIs in 1569 patients who were included in the PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention, NCT02061436)^{2,6,8-18} between January 2012 and March 2016 at 12 US centers. A list of the contributing centers can be found in Data S1. Procedures were entered retrospectively and prospectively into the database. Some centers only enrolled patients during part of the study period due to participation in other studies. Second CTO PCIs in a single patient were excluded from the analysis, as were procedures without data on technical success, procedural success, or periprocedural complications. The study was approved by the institutional review board of each center. A waiver of informed consent was obtained for this study.

Definitions

Coronary CTOs were defined as coronary lesions with thrombolysis in myocardial infarction (TIMI) grade 0 flow of at least 3 months' duration. Estimation of the duration of occlusion was clinical, based on the first onset of angina, prior history of myocardial infarction in the target vessel territory, or comparison with a prior angiogram. Calcification was assessed by angiography as mild (spots), moderate (involving $\leq 50\%$ of the reference lesion diameter), and severe (involving $> 50\%$ of the reference lesion diameter). Moderate proximal vessel tortuosity was defined as the presence of at least 2 bends $> 70^\circ$ or 1 bend $> 90^\circ$, and severe tortuosity as 2 bends $> 90^\circ$ or 1 bend $> 120^\circ$ 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 collaterals were defined as collaterals considered amenable to crossing by a guidewire and a microcatheter by the operator.

Technical success of CTO PCI was defined as successful CTO revascularization with achievement of $< 30\%$ residual diameter stenosis within the treated segment and restoration of TIMI grade 3 antegrade flow. Procedural success was defined as the combination of technical success with no in-hospital complications. In-hospital complications included any of the following adverse events prior to hospital discharge: death, myocardial infarction, recurrent symptoms requiring urgent repeat target vessel revascularization with PCI or coronary artery bypass graft surgery (CABG), tamponade requiring either pericardiocentesis or surgery, and stroke. Myocardial infarction (MI) was defined using the Third Universal Definition of Myocardial Infarction (type 4 MI).¹⁹ Estimated glomerular filtration rate was calculated using the Modification of Diet in Renal Disease (MDRD) formula.

Score Development

The study population was divided with a ratio of 2:1 using random number generation, resulting in a derivation set of 1065 and a validation set of 504 CTO PCIs. Univariable analysis was performed on the derivation cohort to identify variables associated with the occurrence of in-hospital complications. All variables available in the PROGRESS CTO registry were included in the univariable analysis. Variables associated with complications with $P < 0.10$ were entered into a multivariable model in order to identify independent predictors of complications. Stepwise backward selection was performed until only variables with $P < 0.05$ in the multivariable model remained. These variables were considered independent predictors of complications. Points were assigned to each independent predictor variable based on odds ratio to form a scoring system.

Statistical Analysis

Categorical variables are expressed as percentages and were compared using a Pearson chi-squared test or Fisher exact test. Continuous variables are presented as mean \pm standard deviation or median (interquartile range, IQR) unless otherwise specified and were compared using the t test or Wilcoxon rank-sum test, as appropriate. The calibration of the score was assessed using the Hosmer-Lemeshow chi-squared statistic. The discriminatory capacity was evaluated with receiver-operating characteristic (ROC) curves and with the calculated area-under-the-curve (AUC). Validation was performed by comparing the ROC curves in the derivation and

Table 1. Clinical, Angiographic, Procedural Characteristics, and Outcomes in the Overall Study Population, Derivation Set, and Validation Set

Variable	Overall	Derivation	Validation	P Value
Clinical characteristics				
Age, y	65±10	66±10	65±10	0.35
Age >65 y	50	52	47	0.055
Male	84	84	85	0.57
Body mass index, kg/m ²	31±6	31±6	31±6	0.99
Diabetes mellitus	45	46	42	0.14
Dyslipidemia	95	95	94	0.42
Hypertension	90	90	89	0.57
Prior myocardial infarction	43	43	42	0.88
Prior PCI	66	64	68	0.13
Prior CABG	36	36	35	0.58
Prior heart failure	29	29	27	0.47
Prior valve procedure	3	4	2	0.11
Cerebrovascular disease	11	11	10	0.82
Peripheral arterial disease	17	15	19	0.061
Chronic lung disease	13	13	13	0.77
Current tobacco use	25	24	28	0.054
eGFR, mL/min per 1.73 m ²	72±26	72±25	71±27	0.67
eGFR <60 mL/min per 1.73 m ² or currently on dialysis	32	32	32	0.99
Currently on dialysis	3	3	4	0.31
LV ejection fraction, %	50±14	50±14	50±13	0.80
LV ejection fraction <40%	21	22	20	0.29
Angiographic characteristics				
RCA target	56	56	54	0.53
LAD target	23	23	24	0.72
LCX target	21	20	21	0.72
Proximal segment target	38	38	39	0.83
Lesion length, mm	30 (20-45)	30 (20-40)	30 (20-50)	0.63
Length ≥20 mm	77	77	76	0.92
Length ≥23 mm	66	66	65	0.92
Proximal cap ambiguity	32	31	33	0.62
Side branch at proximal cap	47	48	47	0.75
Blunt/no stump	53	54	52	0.51
Distal cap at bifurcation	32	31	33	0.47
Good distal landing zone	62	63	61	0.55
Interventional collaterals	59	60	57	0.41
Moderate/severe calcification	57	57	57	0.96
Moderate/severe tortuosity	36	36	38	0.45
In-stent restenosis	15	14	17	0.16
Prior CTO PCI attempt	17	15	20	0.020
J-CTO score	2.5±1.2	2.5±1.2	2.6±1.2	0.17
PROGRESS CTO score	1.3±1.0	1.3±1.0	1.4±1.0	0.13

Continued

Table 1. Continued

Variable	Overall	Derivation	Validation	P Value
Procedural characteristics				
Radial access	27	27	27	0.92
Dual injection	72	72	72	0.98
Antegrade wire escalation used	74	74	74	0.94
ADR used	35	35	34	0.65
Retrograde approach used	42	41	43	0.40
IVUS used	44	43	46	0.30
Prophylactic LVAD	2	2	3	0.45
Procedural outcomes				
Technical success	90	90	90	0.82
Procedural success	88	89	87	0.35
Contrast volume, mL	270 (200-370)	270 (200-369)	274 (200-370)	0.67
Fluoroscopy time, minutes	47 (29-77)	46 (28-77)	49 (30-78)	0.41
Patient air kerma dose, Gy	3.2 (2.0-5.2)	3.2 (2-5.3)	3.2 (1.9-5.2)	0.97
Procedure time, minute	129 (88-192)	126 (87-192)	139 (94-199)	0.052
Periprocedural MACE	2.8	2.6	3.2	0.54
Death	0.6	0.7	0.4	0.52
Myocardial infarction	1.0	0.8	1.6	0.12
Re-PCI	0.3	0.2	0.4	0.44
Emergency CABG	0.1	0	0.2	0.15
Stroke	0.3	0.4	0	0.17
Tamponade requiring pericardiocentesis	1.0	0.9	1.0	0.92

Values are % or mean±standard deviation or median (interquartile range). ADR indicates antegrade dissection reentry; CABG, coronary artery bypass grafting; CTO, chronic total occlusion; eGFR, estimated glomerular filtration rate; IVUS, intravascular ultrasound; J-CTO score, Multicenter CTO Registry of Japan score; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; LV, left ventricular; LVAD, left ventricular assist device; MACE, major adverse cardiovascular event; PCI, percutaneous coronary intervention; PROGRESS CTO, Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; RCA, right coronary artery.

validation cohorts. Differences in AUC between curves were tested using the method described by Hanley and McNeil.^{20,21} The Cochran-Armitage test was used to evaluate for trend. All statistical analyses were performed with JMP 12.0 (SAS Institute, Cary, NC), SPSS version 22.0 (IBM Corporation, Armonk, NY), and MedCalc version 16.2.1 (Ostend, Belgium). A 2-sided *P* value of 0.05 was considered statistically significant.

Results

Patient Population and Procedural Outcomes

The study population consisted of 1569 CTO PCIs in 1569 patients. Mean age was 65±10 years; 84% were male; 36% had a history of CABG, and 66% had a prior PCI (Table 1). The right coronary artery was the most common target vessel (56%), followed by the left anterior descending coronary artery (23%) and the left circumflex coronary artery (21%).

Retrograde techniques and collaterals used in the study population are summarized in Table 2. Overall technical success was 90%, and overall procedural success was 88%. Periprocedural complications occurred in 44 patients (2.8%). Sixteen patients experienced myocardial infarction; 15 patients developed tamponade requiring pericardiocentesis; 4 patients had a stroke; 4 patients required urgent repeat PCI; 1 patient required urgent CABG; 9 patients died before discharge from the hospital. Median procedure time was 129 minutes (IQR 88-192), and median fluoroscopy time was 47 minutes (IQR 29-77). Median patient air kinetic energy released per unit mass (kerma) dose was 3.2 Gray (IQR 2.0-5.2), and median contrast volume was 270 mL (IQR 200-370).

Score Derivation

The derivation set included 1065 randomly assigned CTO PCIs, with technical success 90%, procedural success 89%, and periprocedural major adverse cardiovascular events

Table 2. Retrograde Crossing Techniques and Collaterals Used in the Study Cohort

Retrograde Technique Used	%
Retrograde true lumen puncture	26
Kissing wire	1
Just marker	3
Knuckle wire	5
CART	4
Reverse CART	64
Guideliner reverse CART	2
Collateral Channel Used	%
Septal	62
Epicardial	35
SVG	16
LIMA	2

CART indicates controlled antegrade and retrograde subintimal tracking; LIMA, left internal mammary artery; SVG, saphenous vein graft.

(MACE) in 28 patients (2.6%) (Table 1). On univariable analysis in the derivation group, procedures that resulted in MACE were more likely to have been performed in patients over age 65 (85% vs 51%, $P<0.001$), with prior cardiac valve procedure or cardiac valve surgery (14% vs 4%, $P=0.003$), or in patients who required prophylactic use of a percutaneous left ventricular assist device (LVAD, 11% vs 2%, $P=0.002$). Periprocedural complications occurred more frequently in CTO PCIs that involved a CTO ≥ 23 mm in length (88% vs 65%, $P=0.013$), use of the retrograde approach (71% vs 40%, $P=0.001$), or in CTOs with a higher J-CTO score (3.0 ± 1.1 vs 2.5 ± 1.2 , $P=0.012$) (Table 3). Complications tended to occur in patients with prior heart failure (44% vs 29%, $P=0.078$), with a blunt or no stump at the proximal end of the CTO (72% vs 53%, $P=0.066$), and with the presence of interventional collaterals (76% vs 59%, $P=0.089$). The following binary variables that met the threshold of $P<0.10$ were entered into a multivariable model: patient age >65 , prior heart failure, prior valve procedure or surgery, CTO length ≥ 23 mm, blunt or no stump, and use of the retrograde approach (Table 4). Three of these variables were independently associated with the occurrence of periprocedural complications; points were assigned to each variable based on the magnitude of the odds ratio (+3 points for age >65 [OR=4.85, CI 1.82-16.77], +2 points for length ≥ 23 mm [OR=3.22, CI 1.08-13.89], and +1 point for use of the retrograde approach [OR=2.41, CI 1.04-6.05]). These points were summed together to form the PROGRESS CTO complications score (Figure 1). The PROGRESS CTO complications score performed well on receiver-operating characteristics (ROC) curve analysis for prediction of complications (AUC 0.758, 95% CI 0.665-0.850) (Figure 2). The score had

good calibration (Hosmer-Lemeshow $\chi^2=6.271$, $P=0.281$). The score was used to stratify the population into risk groups: low risk (0-2 points), intermediate risk (3-4 points), and high risk (≥ 5 points). The proportions of the study population in each stratum of the score were 34% low risk; 33% intermediate risk; and 34% high risk. In the derivation set, the probability of periprocedural complications in each of these groups was: 0.4%, 1.8%, and 6.5%, respectively (Cochran-Armitage test for trend $P<0.001$).

Score Validation

The validation set included 504 randomly assigned CTO PCIs, in which 16 patients (3.2%) experienced periprocedural complications. There were no significant differences in clinical characteristics, angiographic characteristics, procedural characteristics, or outcomes between the derivation and validation groups, with the exception of prior failed CTO PCI, which occurred more frequently in the validation group than in the derivation group (20% vs 15%, $P=0.020$) (Table 1).

In the validation set and in the whole study cohort, stratification into risk groups using the PROGRESS CTO complications score was similar (test for trend $P<0.001$) (Figure 3). The AUC of the ROC for complications in the validation set was similar to that in the derivation set (0.793 [95% CI 0.682-0.905]) (Figure 2). The score showed good calibration (Hosmer-Lemeshow $\chi^2=4.551$, $P=0.473$). The difference between AUCs in the derivation and validation sets was $\Delta=0.035$ ($P=0.64$).

In addition, the ability of the score to predict the most serious complications (death, stroke, and tamponade requiring pericardiocentesis) was assessed in the derivation and validation set using ROC analysis (AUC=0.833, 95% CI 0.681-0.984); the score showed increasing incidence of these events at each stratum of the score (test for trend in derivation and validation sets $P<0.001$ and $P=0.009$, respectively) (Figure 3).

Sensitivity and specificity of the score analysis were calculated, showing stepwise alterations with change in PROGRESS CTO complications score (Figure 4).

Comparison With Other CTO PCI Scores for Prediction of Complications

The performance of the PROGRESS CTO complications score for predicting occurrence of periprocedural MACE was compared with those of other CTO PCI scores. The J-CTO score, the PROGRESS CTO score, and the CL score were compared with the PROGRESS CTO complications score for prediction of complications in the validation set (Figure 5). The AUCs were: PROGRESS CTO complications score 0.793 (95% CI 0.682-0.905), J-CTO score 0.676 (95% CI 0.560-

Table 3. Univariable Analysis of Clinical, Angiographic, and Procedural Characteristics in the Derivation Set

Variable	Overall	Complications	No Complications	P Value
Clinical characteristics				
Age, y	66±10	72±9	65±10	<0.001
Age >65 y	52	85	51	<0.001
Male	84	86	84	0.81
Body mass index, kg/m ²	31±6	30±5	31±6	0.64
Diabetes mellitus	46	39	46	0.45
Dyslipidemia	95	96	95	0.72
Hypertension	90	89	90	0.88
Prior myocardial infarction	43	56	42	0.17
Prior PCI	64	57	65	0.41
Prior CABG	36	36	36	0.94
Prior heart failure	29	44	29	0.078
Prior valve procedure	4	14	4	0.003
Cerebrovascular disease	11	14	11	0.55
Peripheral arterial disease	15	14	15	0.88
Chronic lung disease	13	22	12	0.13
Current tobacco use	24	14	24	0.23
eGFR, mL/min per 1.73 m ²	72±25	65±21	72±26	0.042
eGFR <60 mL/min per 1.73 m ² or currently on dialysis	32	42	32	0.31
Currently on dialysis	3	7	3	0.17
LV ejection fraction, %	50±14	46±15	50±14	0.27
LV ejection fraction <40%	22	41	22	0.033
Angiographic characteristics				
RCA target	56	63	56	0.49
LAD target	23	15	23	0.29
LCX target	20	22	20	0.82
Proximal segment target	38	43	38	0.60
Lesion length, mm	30 (20-40)	30 (27-56)	30 (20-40)	0.10
Length ≥20 mm	77	88	76	0.15
Length ≥23 mm	66	88	65	0.013
Proximal cap ambiguity	31	40	31	0.34
Side branch at proximal cap	48	56	47	0.40
Blunt/no stump	54	72	53	0.066
Distal cap at bifurcation	31	24	31	0.45
Good distal landing zone	63	52	63	0.25
Interventional collaterals	60	76	59	0.089
Moderate/severe calcification	57	67	57	0.32
Moderate/severe tortuosity	36	37	36	0.87
In-stent restenosis	14	14	14	0.97
Prior CTO PCI attempt	15	21	15	0.38
J-CTO score	2.5±1.2	3.0±1.1	2.5±1.2	0.012
PROGRESS CTO score	1.3±1.0	1.2±1.0	1.3±1.0	0.84

Continued

Table 3. Continued

Variable	Overall	Complications	No Complications	P Value
Procedural characteristics				
Antegrade wire escalation used	26	25	26	0.90
ADR used	35	43	35	0.41
Retrograde approach used	41	71	40	0.001
IVUS used	43	30	43	0.22
Prophylactic LVAD	2	11	2	0.002

Values are % or mean±standard deviation or median (interquartile range). ADR indicates antegrade dissection reentry; CABG, coronary artery bypass grafting; CTO, chronic total occlusion; eGFR, estimated glomerular filtration rate; IVUS, intravascular ultrasound; J-CTO score, Multicenter CTO Registry of Japan score; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; LV, left ventricular; LVAD, left ventricular assist device; MACE, major adverse cardiovascular event; PCI, percutaneous coronary intervention; PROGRESS CTO, Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; RCA, right coronary artery.

0.791), PROGRESS CTO score 0.501 (95% CI 0.379-0.620), and CL score 0.776 (95% CI 0.669-0.884), respectively. The differences in AUCs between the PROGRESS CTO complications score and other scores were J-CTO score $\Delta=0.117$ ($P=0.15$); PROGRESS CTO score $\Delta=0.292$ ($P<0.001$); and CL score $\Delta=0.017$ ($P=0.83$).

Discussion

Our study demonstrates that a simple, 3-component score can be used to determine the risk for periprocedural complications during CTO PCI. To the best of our knowledge, this is the first score specifically designed to predict complications during CTO PCI and may be of great value for procedural planning and discussion with the patient.

Several scores have been developed to predict the efficiency and success of CTO PCI,⁵⁻⁷ such as the CL score, which uses a combination of 6 clinical and angiographic characteristics to predict procedural failure.⁷ Although

procedural failure is sometimes related to a complication,¹³ procedural outcomes may be related to distinct baseline characteristics. There is an association between technical outcome and complications (technical success among patients who experienced periprocedural complications was 64% vs 91% in those without complications), as some of the factors that may contribute to technical failure (angiographic factors such as calcification; clinical factors such as patient age) may also predispose to procedural complications. However, technical outcome is not known during planning for CTO PCI and thus was not included in the PROGRESS CTO complications score.

Although a failed attempt at CTO PCI is undesirable, some would consider a periprocedural complication potentially more undesirable. Hence, use of a simple, validated score

Table 4. Multivariate Logistic Regression in the Derivation Set

Variable	Odds Ratio	95% CI	P Value	Points
Age >65 y	4.85	1.82 to 16.77	0.001	+3
Prior heart failure			NS	
Prior valve procedure			NS	
Length ≥ 23 mm	3.22	1.08 to 13.89	0.035	+2
Blunt/no stump			NS	
Retrograde approach used	2.41	1.04 to 6.05	0.041	+1

CI indicates confidence interval; NS, statistically nonsignificant.

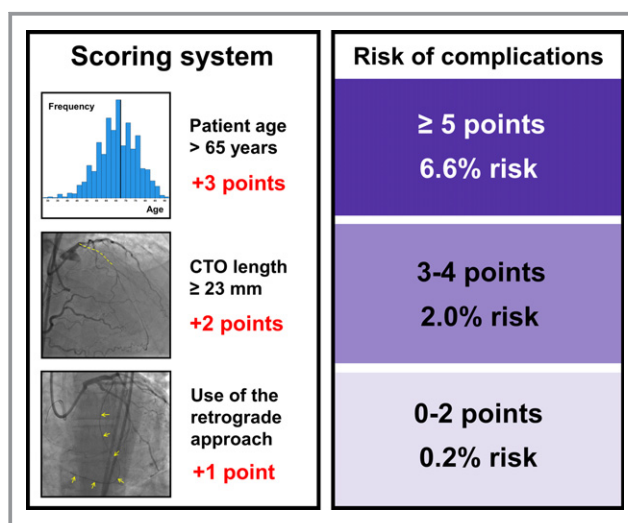


Figure 1. The PROGRESS CTO complications score. Summary of the PROGRESS CTO complications scoring system and risk groups for the overall cohort (validation cohort+derivation cohort). PROGRESS CTO indicates Prospective Global Registry for the Study of Chronic Total Occlusion Intervention.

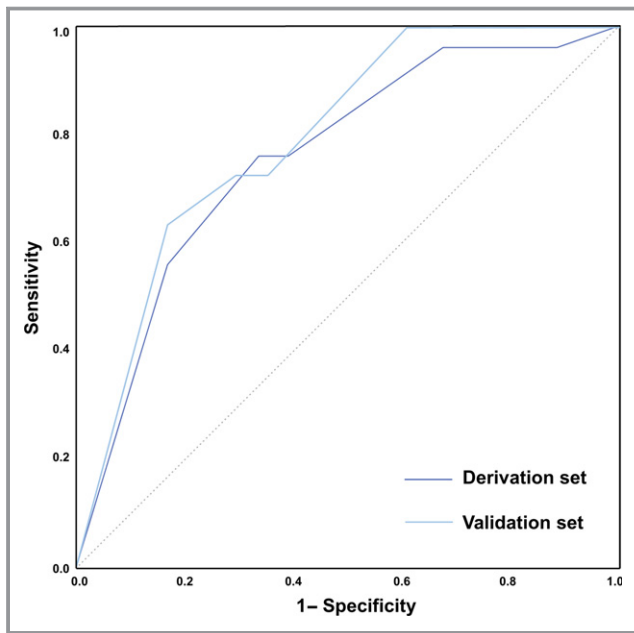


Figure 2. Comparison of the PROGRESS CTO complications score in the derivation and validation sets. The areas under the curves for the derivation and validation sets are 0.758 (95% CI 0.665-0.850) and 0.793 (95% CI 0.682-0.905), respectively. PROGRESS CTO indicates Prospective Global Registry for the Study of Chronic Total Occlusion Intervention.

specific for complications (in addition to scores predicting success and efficiency) can significantly aid physician and patient decision making by allowing accurate determination of the risk/benefit ratio for each procedure.²² In the context of other clinical factors, such a score could also help operators decide how aggressively to pursue angiographic success. Ultimately, an integrated approach that balances the desire for success with the risk for complications is critical for CTO PCI (or any PCI).

Older age was the most important predictor for complications in our study: the incidence of complications was 7% in patients aged >75 years versus 4% in patients aged 66 to 75 years versus 1% in patients aged ≤65 years ($P<0.001$). This finding is consistent with prior studies^{10,23,24} and is likely related to more complex coronary anatomy with increasing age, higher prevalence of tortuosity and calcification, higher prevalence of prior CABG, and possibly lower tolerance to inadvertent guidewire exits. Older patients are more likely to have diffuse aortic atheroma, predisposing them to strokes during coronary intervention. Moreover, older patients tend to have more comorbidities and likely have less reserve to tolerate a complication. Despite the association of age with the above comorbidities, age itself was a strong independent predictor of complications,

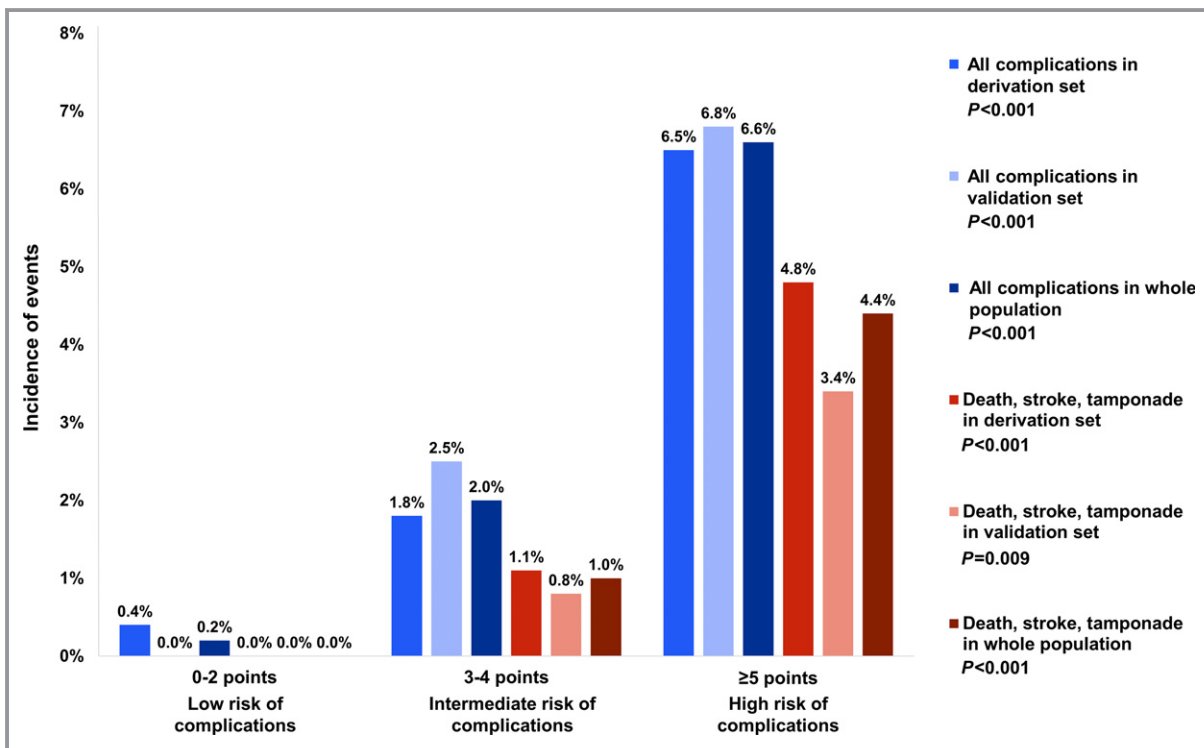


Figure 3. Incidence of periprocedural complications in strata of the PROGRESS CTO complications score. The incidence of all complications is represented by the blue bars; the incidence of the most serious complications (death, stroke, and tamponade requiring pericardiocentesis) is represented by the red bars. Differences in the incidence of events among strata were statistically significant in the derivation set, the validation set, and the whole study population. PROGRESS CTO indicates Prospective Global Registry for the Study of Chronic Total Occlusion Intervention.

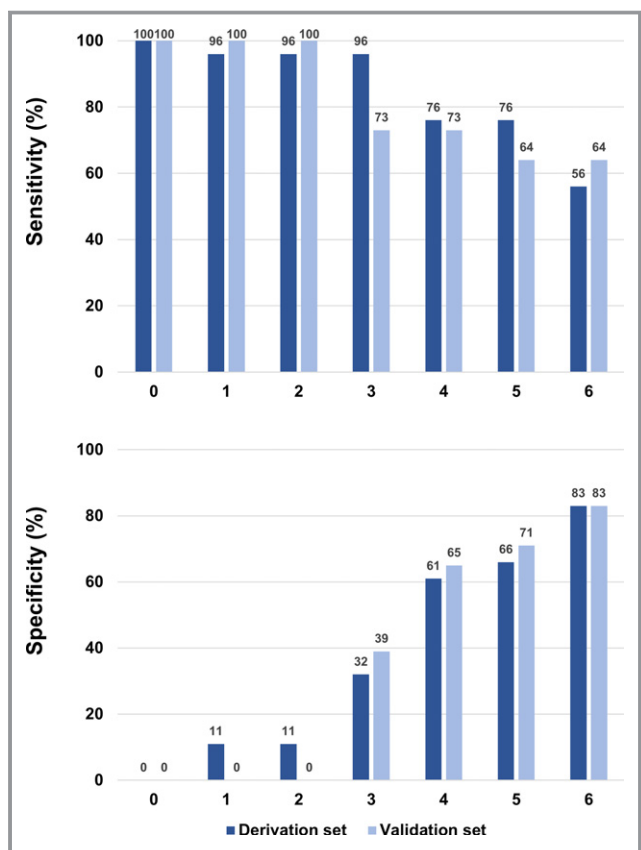


Figure 4. Sensitivity and specificity of the PROGRESS CTO complications score in the derivation and validation sets. PROGRESS CTO indicates Prospective Global Registry for the Study of Chronic Total Occlusion Intervention.

indicating that these factors act synergistically to increase the risk of adverse outcomes.

CTO length was an independent predictor of complications, a finding that is in line with the CL score (≥ 20 mm length predictive of procedural failure)⁴ and other studies.^{13,25} Longer lesion length may increase the complexity of the procedure and the need for advanced (and potentially more hazardous) crossing strategies, such as antegrade dissection/reentry and the retrograde approach.

Use of the retrograde approach was an independent predictor of complications in our cohort.²⁶ Although judicious use of retrograde techniques is important for high technical success^{27,28} and is integral to the hybrid algorithm,²⁹ this specialized and potentially complex technique does carry increased risk for complications, such as donor vessel or collateral injury³⁰ and donor vessel territory ischemia with increased risk for myocardial infarction.³¹⁻³³ Device entrapment in collateral vessels may also occur.³⁴ The retrograde approach also requires longer activated clotting time (ACT, >350 seconds) targets, potentially increasing the risk for bleeding.

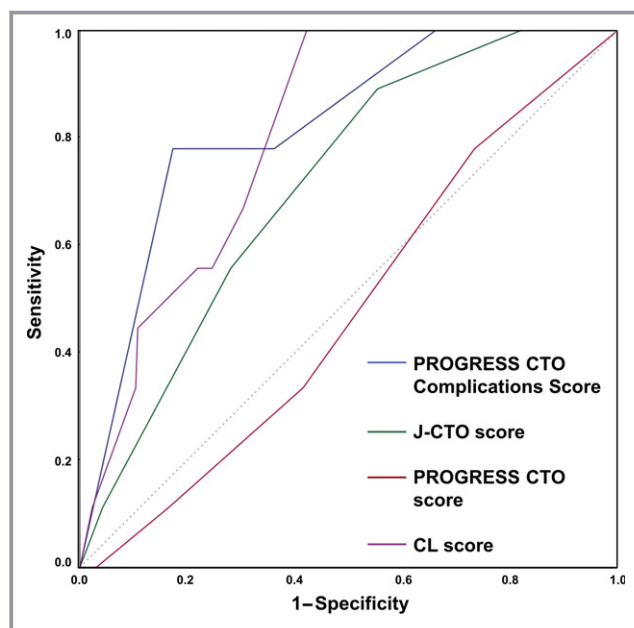


Figure 5. Comparison of the PROGRESS CTO complications score with other scoring systems. The PROGRESS CTO complications score is compared with the J-CTO score, the PROGRESS CTO score, and the CL score in the validation set. The areas under the curves (AUCs) were PROGRESS CTO complications score 0.793 (95% CI 0.682-0.905), J-CTO score 0.676 (95% CI 0.560-0.791), PROGRESS CTO score 0.501 (95% CI 0.379-0.620), and CL score 0.776 (95% CI 0.669-0.884), respectively. The differences in AUCs between the PROGRESS CTO complications score and other scores were as follows: J-CTO score $\Delta=0.117$, $P=0.15$; PROGRESS CTO score $\Delta=0.292$, $P<0.001$; and CL score $\Delta=0.017$, $P=0.83$. PROGRESS CTO indicates Prospective Global Registry for the Study of Chronic Total Occlusion Intervention.

The PROGRESS CTO complications score performed better than the J-CTO and PROGRESS CTO score for predicting periprocedural MACE; however, the CL score (which was developed for predicting procedural success) performed comparably to the PROGRESS CTO complications score (difference in AUC 0.015), although it contains twice as many (6) input variables.

Limitations

Our study is limited by the observational design as well as by lack of independent angiographic and clinical event adjudication. Because quantitative coronary angiographic analysis was not performed, evaluation of angiographic characteristics may be subject to operator bias. Long-term follow-up data were not available for the entire study cohort; thus, no conclusions can be drawn about long-term risk of major adverse cardiac events or the impact of periprocedural complications on longer-term outcomes. The scoring model was developed using only cases with complete data, without imputation for missing values. The PROGRESS CTO registry contains data

about procedures performed at high-volume centers by highly experienced operators; as a result, conclusions drawn about this study cohort may not be broadly generalizable. Although only centers that contributed at least 40 cases are included in the analysis, some of these centers had more than 1 operator. Only variables collected as part of the registry were analyzed; some lesion and procedural characteristics that were not assessed could potentially be associated with the risk for complications. Additionally, data on contrast-induced nephropathy were not collected. Because the incidence of complications was relatively low in our overall cohort (2.8%), our study may have limited power to identify predictors of complications. However, it is expected that in a larger cohort (or a cohort with higher incidence of complications), higher model diagnostic accuracy would result in increased statistical significance of the score components. External independent validation is needed to confirm these findings.

Conclusions

A simple score consisting of 1 clinical characteristic (age >65 years), 1 angiographic characteristic (CTO length \geq 23 mm), and 1 procedural characteristic (use of the retrograde approach) may be useful to predict the occurrence of in-hospital complications during CTO PCI. This tool can be used to assess patient risk and inform clinical decision-making.

Acknowledgments

Study data were collected and managed using REDCap electronic data capture tools hosted at University of Texas Southwestern Medical Center. REDCap (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.

Sources of Funding

Research reported in this publication was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health under award number UL1-RR024982. The content is solely the responsibility of the authors and does not necessarily represent the official view of the NIH.

Disclosures

Dr Karpaliotis reports speaker's fees from Abbott Vascular and MEDTRONIC; and consultant fees/honoraria from Asahi

and Boston Scientific. Dr Alaswad reports consultant fees/honoraria from Asahi, Terumo, and Boston Scientific; and speaker's fees from Abbott Vascular. Dr Yeh reports a Career Development Award (1K23HL118138) from the National Heart, Lung, and Blood Institute; and consultant fees/honoraria from Boston Scientific and Gilead Sciences. Dr Jaffer reports consultant fees/honoraria from Abbott Vascular and Boston Scientific; and research grants from National Institutes of Health (HL-R01-108229), Kowa Ltd, Merck, and Siemens. Dr Mahmoud reports advisory board/consulting fees from Medtronic and Corindus; speaker's fees from Medtronic, Corindus, and Abbott Vascular; educational program fees from Abbott Vascular; and clinical events committee fees from St. Jude. Dr Wyman reports consultant fees/honoraria from Boston Scientific, Abbott Vascular, and Asahi. Dr Grantham reports consultant fees/honoraria from Abbott Vascular, Asahi, and Boston Scientific; and research grants from Boston Scientific, Asahi, Abbott Vascular, Medtronic, and Bridgepoint Medical. Dr Kandzari reports consultant fees/honoraria from Boston Scientific, Medicines Company, and Medtronic. Dr Lembo reports consultant fees/honoraria from Abbott Vascular, Boston Scientific, and Medtronic. Dr Garcia reports consulting fees from Medtronic and Surmodics. Dr Kirtane reports research grants from Boston Scientific, Medtronic, Abbott Vascular, Abiomed, St. Jude Medical, GlaxoSmithKline, and Eli Lilly. Dr Moses reports research grants from Abiomed. Dr Ali reports consultant fees/honoraria from St. Jude Medical, and AstraZeneca Pharmaceuticals; ownership interest/partnership/principal in Shockwave Medical and VitaBx Inc; and research grants from Medtronic and St. Jude Medical. Dr Rangan reports research grants from InfraRedX and Spectranetics. Dr Thompson reports salary from Boston Scientific. Dr Banerjee reports research grants from Gilead and the Medicines Company; consultant/speaker honoraria from Covidien and Medtronic; ownership in MDCARE Global (spouse); intellectual property in HygeiaTel. Dr Brilakis reports consultant fees/honoraria from Abbott Vascular, Asahi, Boston Scientific, Elsevier, Somahlution, St. Jude, and Terumo; research grants from Boston Scientific, and InfraRedX; and salary from Medtronic (spouse). The remaining authors have no disclosures to report.

References

1. Patel VG, Brayton KM, Tamayo A, Mogabgab O, Michael TT, Lo N, Alomar M, Shorrock D, Cipher D, Abdullah S, Banerjee S, Brilakis ES. Angiographic success and procedural complications in patients undergoing percutaneous coronary chronic total occlusion interventions: a weighted meta-analysis of 18,061 patients from 65 studies. *JACC Cardiovasc Interv.* 2013;6:128–136.
2. Christopoulos G, Karpaliotis D, Alaswad K, Yeh RW, Jaffer FA, Wyman RM, Lombardi WL, Menon RV, Grantham JA, Kandzari DE, Lembo N, Moses JW, Kirtane AJ, Parikh M, Green P, Finn M, Garcia S, Doing A, Patel M, Bahadorani J, Tarar MN, Christakopoulos GE, Thompson CA, Banerjee S, Brilakis ES.

- Application and outcomes of a hybrid approach to chronic total occlusion percutaneous coronary intervention in a contemporary multicenter US registry. *Int J Cardiol.* 2015;198:222–228.
3. Galassi AR, Sianos G, Werner GS, Escaned J, Tomasello SD, Boukhris M, Castaing M, Buttner JH, Bufe A, Kalnins A, Spratt JC, Garbo R, Hildick-Smith D, Elhadad S, Gagnor A, Lauer B, Bryniarski L, Christiansen EH, Thuesen L, Meyer-Gessner M, Goktekin O, Carlino M, Louvard Y, Lefevre T, Lismanis A, Gelev VL, Serra A, Marza F, Di Mario C, Reifart N; Euro CTO Club. Retrograde recanalization of chronic total occlusions in Europe: procedural, in-hospital, and long-term outcomes from the multicenter ERCOT registry. *J Am Coll Cardiol.* 2015;65:2388–2400.
 4. Tanaka H, Morino Y, Abe M, Kimura T, Hayashi Y, Muramatsu T, Ochiai M, Noguchi Y, Kato K, Shibata Y, Hiasa Y, Doi O, Yamashita T, Morimoto T, Hinohara T, Fujii T, Mitsudo K. Impact of J-CTO score on procedural outcome and target lesion revascularisation after percutaneous coronary intervention for chronic total occlusion: a substudy of the J-CTO Registry (Multicentre CTO Registry in Japan). *EuroIntervention.* 2016;11:981–988.
 5. Morino Y, Abe M, Morimoto T, Kimura T, Hayashi Y, Muramatsu T, Ochiai M, Noguchi Y, Kato K, Shibata Y, Hiasa Y, Doi O, Yamashita T, Hinohara T, Tanaka H, Mitsudo K; J-CTO Registry Investigators. 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. *JACC Cardiovasc Interv.* 2011;4:213–221.
 6. Christopoulos G, Kandzari DE, Yeh RW, Jaffer FA, Karpaliotis D, Wyman MR, Alaswad K, Lombardi W, Grantham JA, Moses J, Christakopoulos G, Tarar MN, Rangan BV, Lembo N, Garcia S, CIPHER D, Thompson CA, Banerjee S, Brilakis ES. 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. *JACC Cardiovasc Interv.* 2016;9:1–9.
 7. Alessandrino G, Chevalier B, Lefevre T, Sanguineti F, Garot P, Untersee H, Hovasse T, Morice MC, Louvard Y. A clinical and angiographic scoring system to predict the probability of successful first-attempt percutaneous coronary intervention in patients with total chronic coronary occlusion. *JACC Cardiovasc Interv.* 2015;8:1540–1548.
 8. Alaswad K, Menon RV, Christopoulos G, Lombardi WL, Karpaliotis D, Grantham JA, Marso SP, Wyman MR, Pokala NR, Patel SM, Kotsia AP, Rangan BV, Lembo N, Kandzari D, Lee J, Kalynych A, Carlson H, Garcia SA, Thompson CA, Banerjee S, Brilakis ES. Transradial approach for coronary chronic total occlusion interventions: insights from a contemporary multicenter registry. *Catheter Cardiovasc Interv.* 2015;85:1123–1129.
 9. Christopoulos G, Karpaliotis D, Alaswad K, Lombardi WL, Grantham JA, Rangan BV, Kotsia AP, Lembo N, Kandzari DE, Lee J, Kalynych A, Carlson H, Garcia S, Banerjee S, Thompson CA, Brilakis ES. The efficacy of “hybrid” percutaneous coronary intervention in chronic total occlusions caused by in-stent restenosis: insights from a US multicenter registry. *Catheter Cardiovasc Interv.* 2014;84:646–651.
 10. Christopoulos G, Karpaliotis D, Wyman MR, Alaswad K, McCabe J, Lombardi WL, Grantham JA, Marso SP, Kotsia AP, Rangan BV, Garcia SA, Lembo N, Kandzari D, Lee J, Kalynych A, Carlson H, Thompson CA, Banerjee S, Brilakis ES. Percutaneous intervention of circumflex chronic total occlusions is associated with worse procedural outcomes: insights from a multicenter US registry. *Can J Cardiol.* 2014;30:1588–1594.
 11. Christopoulos G, Menon RV, Karpaliotis D, Alaswad K, Lombardi W, Grantham A, Patel VG, Rangan BV, Kotsia AP, Lembo N, Kandzari D, Carlson H, Garcia S, Banerjee S, Thompson CA, Brilakis ES. 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;26:427–432.
 12. Christopoulos G, Menon RV, Karpaliotis D, Alaswad K, Lombardi W, Grantham JA, Michael TT, Patel VG, Rangan BV, Kotsia AP, Lembo N, Kandzari DE, Lee J, Kalynych A, Carlson H, Garcia S, Banerjee S, Thompson CA, Brilakis ES. Application of the “hybrid approach” to chronic total occlusions in patients with previous coronary artery bypass graft surgery (from a contemporary multicenter US registry). *Am J Cardiol.* 2014;113:1990–1994.
 13. Sapontis J, Christopoulos G, Grantham JA, Wyman RM, Alaswad K, Karpaliotis D, Lombardi WL, McCabe JM, Marso SP, Kotsia AP, Rangan BV, Christakopoulos GE, Garcia S, Thompson CA, Banerjee S, Brilakis ES. Procedural failure of chronic total occlusion percutaneous coronary intervention: insights from a multicenter US registry. *Catheter Cardiovasc Interv.* 2015;85:1115–1122.
 14. Christopoulos G, Wyman RM, Alaswad K, Karpaliotis D, Lombardi W, Grantham JA, Yeh RW, Jaffer FA, CIPHER DJ, Rangan BV, Christakopoulos GE, Kypros MA, Lembo N, Kandzari D, Garcia S, Thompson CA, Banerjee S, Brilakis ES. Clinical utility of the Japan-Chronic Total Occlusion score in coronary chronic total occlusion interventions: results from a multicenter registry. *Circ Cardiovasc Interv.* 2015;8:e002171.
 15. Karacsonyi J, Karatasakis A, Karpaliotis D, Alaswad K, Yeh RW, Jaffer FA, Wyman MR, Lombardi WL, Grantham JA, Kandzari DE, Lembo N, Moses JW, Kirtane AJ, Parikh MA, Green P, Finn M, Garcia S, Doing A, Patel M, Bahadorani J, Martinez Parachini JR, Resendes E, Rangan BV, Ungi I, Thompson CA, Banerjee S, Brilakis ES. Effect of previous failure on subsequent procedural outcomes of chronic total occlusion percutaneous coronary intervention (from a contemporary multicenter registry). *Am J Cardiol.* 2016;117:1267–1271.
 16. Christakopoulos GE, Tarar MN, Brilakis ES. The impact of percutaneous coronary intervention of chronic total occlusions on left ventricular function and clinical outcomes. *J Thorac Dis.* 2015;7:1107–1110.
 17. Nguyen-Trong PK, Rangan BV, Karatasakis A, Danek BA, Christakopoulos GE, Martinez-Parachini JR, Resendes E, Ayers CR, Luna M, Abdullah S, Kumbhani DJ, Addo T, Grodin J, Banerjee S, Brilakis ES. Predictors and outcomes of side-branch occlusion in coronary chronic total occlusion interventions. *J Invasive Cardiol.* 2016;28:168–173.
 18. Amsavelu S, Christakopoulos GE, Karatasakis A, Patel K, Rangan BV, Stetler J, Roesle M, Resendes E, Grodin J, Abdullah S, Banerjee S, Brilakis ES. Impact of crossing strategy on intermediate-term outcomes after chronic total occlusion percutaneous coronary intervention. *Can J Cardiol.* 2016; pii: S0828-282X(16)00060-X. doi: 10.1016/j.cjca.2016.01.020. [Epub ahead of print].
 19. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Joint ESC/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Katus HA, Lindahl B, Morrow DA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasche P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghide M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S. Third universal definition of myocardial infarction. *Circulation.* 2012;126:2020–2035.
 20. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology.* 1982;143:29–36.
 21. McNeil BJ, Hanley JA. Statistical approaches to the analysis of receiver operating characteristic (ROC) curves. *Med Decis Making.* 1984;4:137–150.
 22. Brilakis E. *Manual of Coronary Chronic Total Occlusion Interventions.* Waltham, MA: Elsevier Inc; 2014.
 23. Safley DM, House JA, Marso SP, Grantham JA, Rutherford BD. Improvement in survival following successful percutaneous coronary intervention of coronary chronic total occlusions: variability by target vessel. *JACC Cardiovasc Interv.* 2008;1:295–302.
 24. Andre R, Dumonteil N, Lhermusier T, Lairez O, Van Rothen J, Fournier P, Elbaz M, Carrie D, Boudou N. In-hospital and long-term outcomes after percutaneous coronary intervention for chronic total occlusion in elderly patients: a consecutive, prospective, single-centre study. *Arch Cardiovasc Dis.* 2016;109:13–21.
 25. Noguchi T, Miyazaki MS, Morii I, Daikoku S, Goto Y, Nonogi H. Percutaneous transluminal coronary angioplasty of chronic total occlusions. Determinants of primary success and long-term clinical outcome. *Catheter Cardiovasc Interv.* 2000;49:258–264.
 26. Karpaliotis D, Karatasakis A, Alaswad K, Jaffer FA, Yeh RW, Wyman RM, Lombardi WL, Grantham JA, Kandzari DE, Lembo NJ, Doing A, Patel M, Bahadorani JN, Moses JW, Kirtane AJ, Parikh M, Ali ZA, Kalra S, Nguyen-Trong PK, Danek BA, Karacsonyi J, Rangan BV, Roesle MK, Thompson CA, Banerjee S, Brilakis ES. 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:pil. e003434.
 27. Karpaliotis D, Michael TT, Brilakis ES, Papayannis AC, Tran DL, Kirkland BL, Lembo N, Kalynych A, Carlson H, Banerjee S, Lombardi W, Kandzari DE. Retrograde coronary chronic total occlusion revascularization: procedural and in-hospital outcomes from a multicenter registry in the United States. *JACC Cardiovasc Interv.* 2012;5:1273–1279.
 28. Brilakis ES, Grantham JA, Thompson CA, DeMartini TJ, Prasad A, Sandhu GS, Banerjee S, Lombardi WL. The retrograde approach to coronary artery chronic total occlusions: a practical approach. *Catheter Cardiovasc Interv.* 2012;79:3–19.
 29. Brilakis ES, Grantham JA, Rinfret S, Wyman RM, Burke MN, Karpaliotis D, Lembo N, Pershad A, Kandzari DE, Buller CE, DeMartini T, Lombardi WL, Thompson CA. A percutaneous treatment algorithm for crossing coronary chronic total occlusions. *JACC Cardiovasc Interv.* 2012;5:367–379.
 30. Hashidomi H, Saito S. Dilation of the septal collateral artery and subsequent cardiac tamponade during retrograde percutaneous coronary intervention using a microcatheter for chronic total occlusion. *J Interv Cardiol.* 2011; 24:73–76.

31. Lo N, Michael TT, Moin D, Patel VG, Alomar M, Papayannis A, Cipher D, Abdullah SM, Banerjee S, Brilakis ES. Periprocedural myocardial injury in chronic total occlusion percutaneous interventions: a systematic cardiac biomarker evaluation study. *JACC Cardiovasc Interv.* 2014;7:47–54.
32. Werner GS, Coenen A, Tischer KH. Periprocedural ischaemia during recanalisation of chronic total coronary occlusions: the influence of the transcollateral retrograde approach. *EuroIntervention.* 2014;10:799–805.
33. Stetler J, Karatasakis A, Christakopoulos GE, Tarar MN, Amsavelu S, Patel K, Rangan BV, Roesle M, Resendes E, Grodin J, Abdullah S, Banerjee S, Brilakis ES. Impact of crossing technique on the incidence of periprocedural myocardial infarction during chronic total occlusion percutaneous coronary intervention. *Catheter Cardiovasc Interv.* 2016;88:1–6.
34. Utsunomiya M, Kobayashi T, Nakamura S. Case of dislodged stent lost in septal channel during stent delivery in complex chronic total occlusion of right coronary artery. *J Invasive Cardiol.* 2009;21:E229–E233.

SUPPLEMENTAL MATERIAL

Data S1. Contributing centers included in present analysis (>40 cases contributed each)

Appleton Cardiology, Appleton, Wisconsin;

Columbia University, New York, New York;

Henry Ford Hospital, Detroit, Michigan;

Massachusetts General Hospital, Boston, Massachusetts;

Medical Center of the Rockies, Loveland, Colorado;

Piedmont Heart Institute, Atlanta, Georgia;

PeaceHealth St. Joseph Medical Center, Bellingham, Washington;

St. Luke's Health System's Mid-America Heart Institute, Kansas City, Missouri;

Torrance Medical Memorial Medical Center, Torrance, California;

University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania;

University of California Health System and VA San Diego Healthcare System, San Diego, California; and

VA North Texas Healthcare System, Dallas, Texas.