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# 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

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**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  $\chi^2$  6.271,  $P=0.281$ , receiver-operating characteristic [ROC] area=0.758) and validation (Hosmer-Lemeshow  $\chi^2$  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

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

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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.<sup>1-4</sup> The occurrence of periprocedural complications, however, continues to impact risk-benefit considerations, with a rate of 3.1% in a large contemporary meta-analysis.<sup>1</sup> Although scores predicting technical and procedural outcomes in CTO PCI have been developed (such as the Japanese Chronic Total Occlusion [J-CTO] score,<sup>5</sup> the Prospective Global Registry for the Study of Chronic Total Occlusion Intervention [PROGRESS CTO] score,<sup>6</sup> and the Clinical and Lesion-related [CL] score<sup>7</sup>), 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)<sup>2,6,8-18</sup> 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).<sup>19</sup> 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
<b>Clinical characteristics</b>				
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 <sup>2</sup>	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 <sup>2</sup>	72±26	72±25	71±27	0.67
eGFR <60 mL/min per 1.73 m <sup>2</sup> 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
<b>Angiographic characteristics</b>				
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
<b>Procedural characteristics</b>				
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
<b>Procedural outcomes</b>				
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.<sup>20,21</sup> 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  $\geq 23$  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 ( $3.0\pm 1.1$  vs  $2.5\pm 1.2$ ,  $P=0.012$ ) (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  $\geq 23$  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  $\geq 23$  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 ( $\geq 5$  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
<b>Clinical characteristics</b>				
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 <sup>2</sup>	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 <sup>2</sup>	72±25	65±21	72±26	0.042
eGFR <60 mL/min per 1.73 m <sup>2</sup> 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
<b>Angiographic characteristics</b>				
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
<b>Procedural characteristics</b>				
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 Δ=0.117 (P=0.15); PROGRESS CTO score Δ=0.292 (P<0.001); and CL score Δ=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,<sup>5-7</sup> such as the CL score, which uses a combination of 6 clinical and angiographic characteristics to predict procedural failure.<sup>7</sup> Although

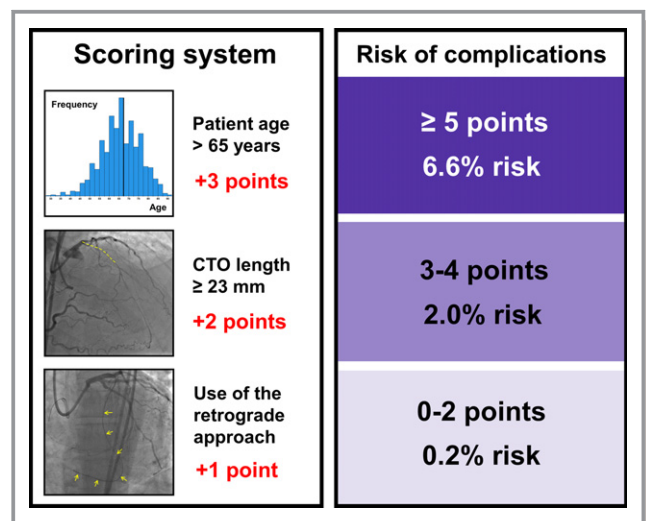
procedural failure is sometimes related to a complication,<sup>13</sup> procedural outcomes may be related to distinct baseline characteristics. There is an association between technical outcome and complications (technical success among patients who experienced periprocedural complications was 64% vs 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

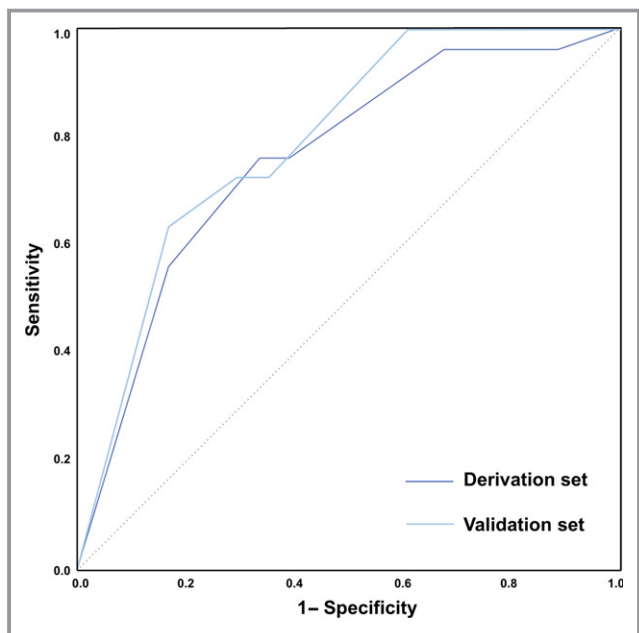
Variable	Odds Ratio	95% CI	P Value	Points
Age >65 y	4.85	1.82 to 16.77	0.001	+3
Prior heart failure			NS	
Prior valve procedure			NS	
Length ≥23 mm	3.22	1.08 to 13.89	0.035	+2
Blunt/no stump			NS	
Retrograde approach used	2.41	1.04 to 6.05	0.041	+1

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.

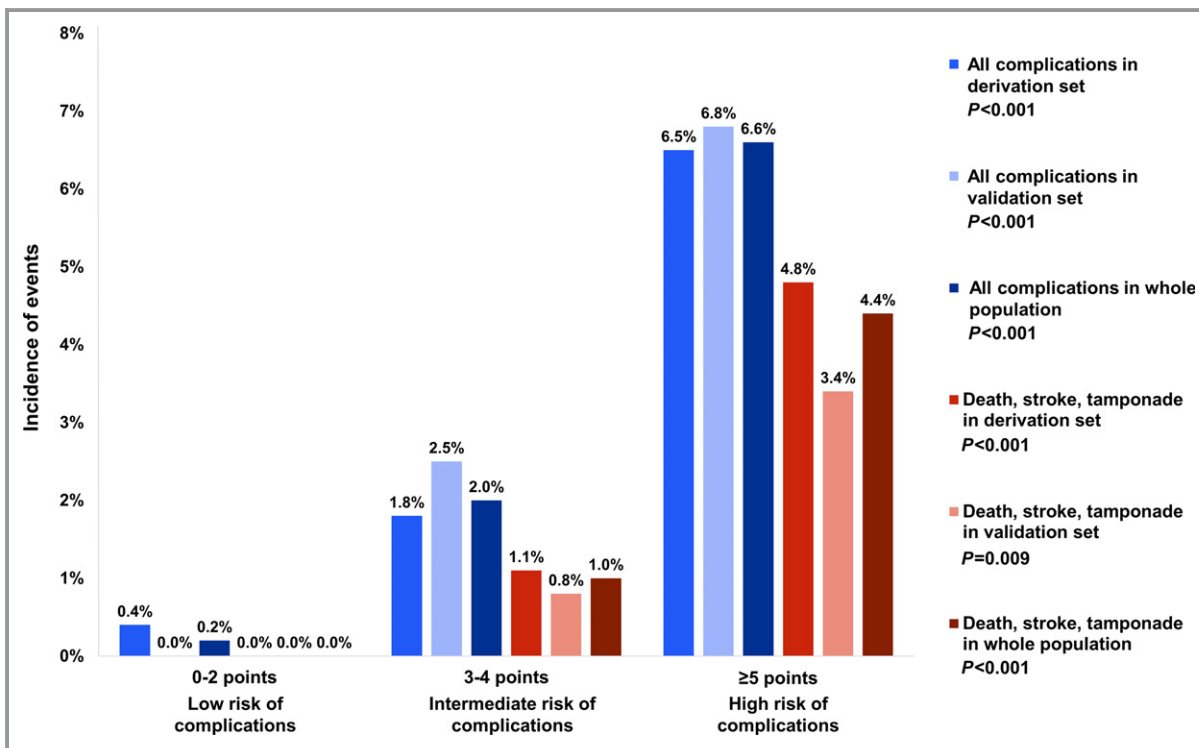




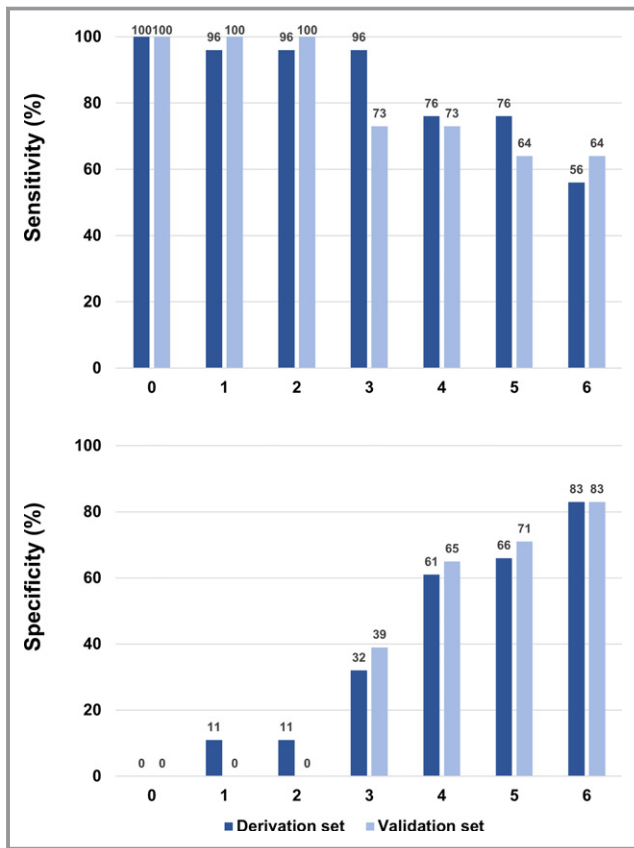
**Figure 2.** Comparison of the PROGRESS CTO complications score in the derivation and validation sets. The areas under the curves for the derivation and validation sets are 0.758 (95% CI 0.665-0.850) and 0.793 (95% CI 0.682-0.905), respectively. PROGRESS CTO indicates Prospective Global Registry for 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.<sup>22</sup> 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<sup>10,23,24</sup> 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.

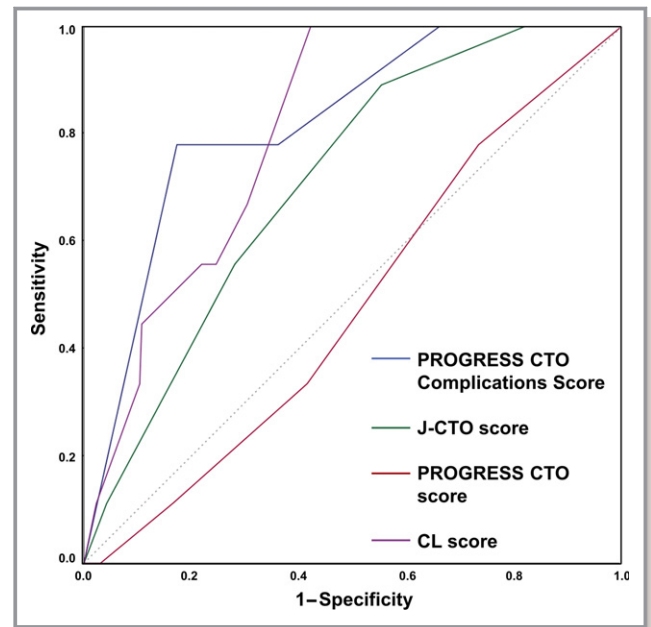


**Figure 4.** Sensitivity and specificity of the PROGRESS CTO complications score in the derivation and validation sets. PROGRESS CTO indicates Prospective Global Registry for the Study of Chronic Total Occlusion Intervention.

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 ( $\geq 20$  mm length predictive of procedural failure)<sup>4</sup> and other studies.<sup>13,25</sup> 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.<sup>26</sup> Although judicious use of retrograde techniques is important for high technical success<sup>27,28</sup> and is integral to the hybrid algorithm,<sup>29</sup> this specialized and potentially complex technique does carry increased risk for complications, such as donor vessel or collateral injury<sup>30</sup> and donor vessel territory ischemia with increased risk for myocardial infarction.<sup>31-33</sup> Device entrapment in collateral vessels may also occur.<sup>34</sup> 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.

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## 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.