

## CLINICAL RESEARCH

### CORONARY

# 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

Georgios Christopoulos, MD,\* David E. Kandzari, MD,† Robert W. Yeh, MD, MBA,‡ Farouc A. Jaffer, MD, PhD,‡ Dimitri Karpaliotis, MD,§ Michael R. Wyman, MD,|| Khaldoon Alaswad, MD,¶ William Lombardi, MD,# J. Aaron Grantham, MD,\*\* Jeffrey Moses, MD,§ Georgios Christakopoulos, MD,\* Muhammad Nauman J. Tarar, MD,\* Bavana V. Rangan, BDS, MPH,\* Nicholas Lembo, MD,† Santiago Garcia, MD,†† Daisha Cipher, PhD,‡‡ Craig A. Thompson, MD, MMSc,§§ Subhash Banerjee, MD,\* Emmanouil S. Brilakis, MD, PhD\*

### ABSTRACT

**OBJECTIVES** This study sought to develop a novel parsimonious score for predicting technical success of chronic total occlusion (CTO) percutaneous coronary intervention (PCI) performed using the hybrid approach.

**BACKGROUND** Predicting technical success of CTO PCI can facilitate clinical decision making and procedural planning.

**METHODS** We analyzed clinical and angiographic parameters from 781 CTO PCIs included in PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) using a derivation and validation cohort (2:1 sampling ratio). Variables with strong association with technical success in multivariable analysis were assigned 1 point, and a 4-point score was developed from summing all points. The PROGRESS CTO score was subsequently compared with the J-CTO (Multicenter Chronic Total Occlusion Registry in Japan) score in the validation cohort.

**RESULTS** Technical success was 92.9%. On multivariable analysis, factors associated with technical success included proximal cap ambiguity (beta coefficient [b] = 0.88), moderate/severe tortuosity (b = 1.18), circumflex artery CTO (b = 0.99), and absence of "interventional" collaterals (b = 0.88). The resulting score demonstrated good calibration and discriminatory capacity in the derivation (Hosmer-Lemeshow chi-square = 2.633; p = 0.268, and receiver-operator characteristic [ROC] area = 0.778) and validation (Hosmer-Lemeshow chi-square = 5.333; p = 0.070, and ROC area = 0.720) subset. In the validation cohort, the PROGRESS CTO and J-CTO scores performed similarly in predicting technical success (ROC area 0.720 vs. 0.746, area under the curve difference = 0.026, 95% confidence interval = -0.093 to 0.144).

**CONCLUSIONS** The PROGRESS CTO score is a novel useful tool for estimating technical success in CTO PCI performed using the hybrid approach. (J Am Coll Cardiol Intv 2016;9:1-9) © 2016 by the American College of Cardiology Foundation.

**ABBREVIATIONS  
AND ACRONYMS****AUC** = area under the curve**CABG** = coronary artery bypass  
graft surgery**CTO** = chronic total occlusion**LCX** = left circumflex**PCI** = percutaneous coronary  
intervention**ROC** = receiver-operator  
characteristic**TIMI** = Thrombolysis In  
Myocardial Infarction

Chronic total occlusion (CTO) percutaneous coronary intervention (PCI) can be challenging, with variable success rates (1-3). Identifying clinical and angiographic characteristics associated with procedural failure could lead to improvement of patient selection and possibly an increase of overall success of CTO PCI. In the J-CTO (Multicenter Chronic Total Occlusion Registry in Japan) study, 5 variables (occlusion length  $\geq 20$  mm, blunt stump, CTO calcification, CTO tortuosity, and prior failed attempt) were combined to create a 5-point score, which could be used to predict successful guidewire crossing within the first 30 min (4). The J-CTO score demonstrated a dose-response relationship with the study's endpoint and had good discriminatory ability. However, it was not associated with CTO PCI success rates in a Canadian single-operator CTO PCI registry that used the hybrid approach (5).

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The hybrid approach differs from the crossing approach used in the J-CTO registry, as it encourages rapid switch between various crossing strategies aiming for efficient, safe, and effective CTO PCI crossing (6). Moreover, prior failure is a subjective factor that is heavily dependent on the expertise of the CTO operator who attempted the procedure. In the

present study, we attempted to develop a novel, parsimonious, and easy-to-use score to allow estimation of the likelihood of technical success among CTO PCI procedures performed using the hybrid approach.

**METHODS**

**PATIENT POPULATION.** We reviewed the clinical and angiographic records of consecutive patients who were included in PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) (NCT02061436) (7-12) between January 2012 and January 2015 at 7 U.S. centers with significant expertise in CTO PCI: Appleton Cardiology, Appleton, Wisconsin; Massachusetts General Hospital, Boston, Massachusetts; Piedmont Heart Institute, Atlanta, Georgia; St. Joseph Medical Center, Bellingham Washington; St. Luke's Health System's Mid-America Heart Institute, Kansas City, Missouri; Torrance Memorial Medical Center, Torrance, California; and VA North Texas Healthcare System, Dallas, Texas. Procedures were prospectively and retrospectively entered into the database. No specific baseline clinical or angiographic criteria were used to justify or exclude study enrollment. The study was approved by the institutional review board of each center.

**DEFINITIONS.** Coronary CTOs were defined as coronary lesions with Thrombolysis In Myocardial Infarction (TIMI) flow grade 0 of at least 3-month

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duration. Estimation of the occlusion duration was on the basis of first onset of anginal symptoms, prior history of myocardial infarction in the target vessel territory, or comparison with a prior angiogram. “Interventional collaterals” were defined as collaterals that were amenable to crossing with a guidewire and a microcatheter according to the judgment of 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 antegrade TIMI flow grade 3. The J-CTO score was calculated as described by Morino et al. (4).

**SCORE DERIVATION.** We separately performed analyses in population subsets that were used for derivation (2/3 random sampling rate, 521 lesions) and validation (1/3 random sampling rate, 260 lesions). Univariable analysis was performed to identify clinical and angiographic variables associated with technical failure. We performed an all-inclusive analysis of the clinical and angiographic characteristics that are available in the PROGRESS CTO registry. Variables with a strong ( $p < 0.05$ ) association then entered a multivariable model. The multivariable analysis was used to identify independent predictors of technical failure. The effect size was quantified by the beta (b) coefficient and the strength of association was demonstrated with the chi-square statistic and p value. Independent predictors were selected on the basis of strength of association ( $p < 0.10$ ) in context with clinical evidence from prior published scientific data. The b coefficients of the independent predictors were then used to estimate the number of points that would be assigned to a specific factor. Subsequently, all points accrued were summed to create the scoring index.

**STATISTICAL ANALYSIS.** Continuous data were summarized as mean  $\pm$  SD (normally distributed data) or median and interquartile range (IQR) (non-normally distributed data) and compared using the *t* test or Wilcoxon rank-sum test, as appropriate. Categorical data were presented as frequencies or percentages and compared using chi-square or Fisher exact test, as appropriate. The calibration of the score was assessed with the Hosmer-Lemeshow chi-square statistic and the lack of fit tests. The discriminatory capacity was evaluated with the receiver-operator characteristic (ROC) curves and with the calculated area under the curve (AUC) (13). The PROGRESS CTO score was validated with comparison of the ROC curves in the derivation and validation cohorts. Subsequently, the score and the score elements were separately re-evaluated in 1,000 bootstrapped samples of the study population. Bootstrapped

**TABLE 1 Baseline Demographic and Angiographic Characteristics in the Derivation Set (n = 521 Lesions)**

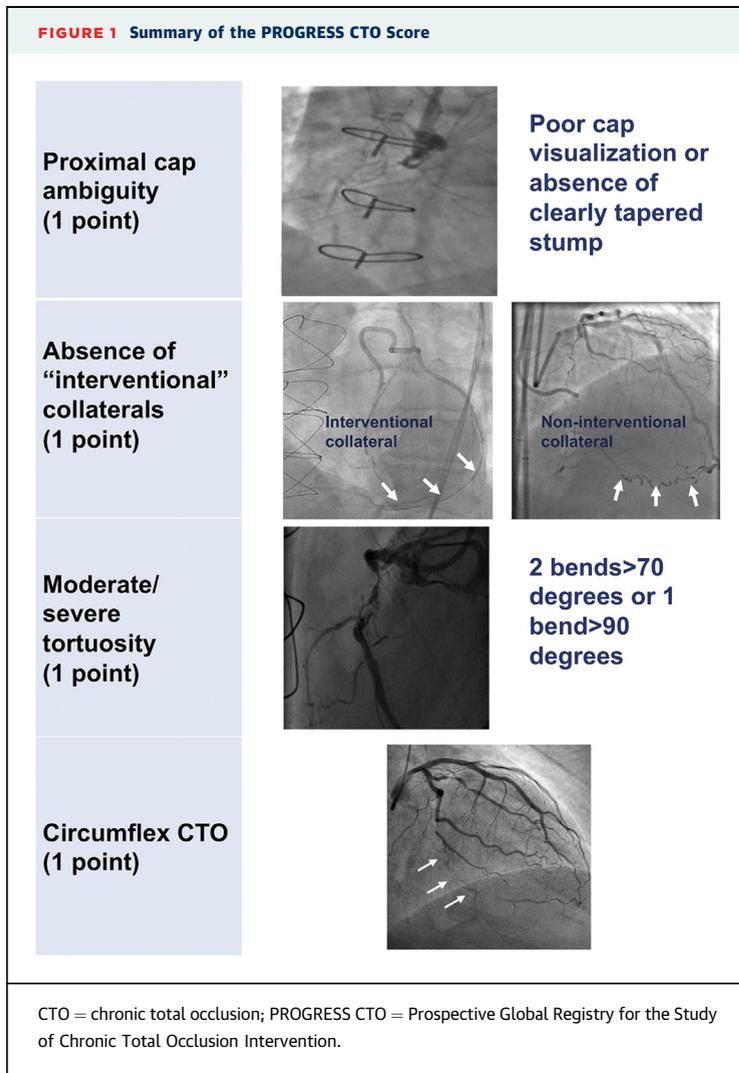
	Technical Success (n = 482)	Technical Failure (n = 39)	p Value
Age, yrs	65 $\pm$ 10	66 $\pm$ 11	0.57
Male	85	89	0.63
BMI, kg/m <sup>2</sup>	31 $\pm$ 6	30 $\pm$ 5	0.69
EF	50 $\pm$ 14	49 $\pm$ 15	0.78
Dyslipidemia	94	100	0.24
Hypertension	89	92	0.79
Current smoking	33	44	0.19
Prior MI	40	57	0.06
CHF	28	25	0.69
Prior PCI	66	84	0.023
Prior CABG	34	46	0.13
Dialysis	2	0	0.99
PVD	16	14	0.99
COPD	12	8	0.53
Target vessel			
RCA	60	53	0.001
LAD	23	8	
LCX	17	39	
Occlusion length, mm	37 $\pm$ 25	42 $\pm$ 23	0.27
Vessel diameter, mm	2.8 $\pm$ 0.5	2.7 $\pm$ 0.4	0.12
Proximal cap ambiguity	26	52	0.006
Side branch at proximal cap	42	58	0.12
Good distal opacification	50	38	0.24
Distal cap at bifurcation	29	38	0.34
Good distal landing zone	59	54	0.68
Collateral filling			
Ipsilateral	16	23	
Contralateral	54	62	0.29
Both	28	12	
None	2	4	
No interventional collaterals	35	58	0.034
Moderate or severe calcification*	56	59	0.67
Moderate or severe tortuosity†	31	56	0.005
In-stent restenosis	13	18	0.32
Prior attempt	16	24	0.22

Values are mean  $\pm$  SD or %. \*Defined as any evident calcification within the CTO segment, excluding spot calcification. †Defined as 2 bends >70° or 1 bend >90°.  
 BMI = body mass index; CABG = coronary artery bypass grafting; CHF = chronic heart failure; CTO = chronic total occlusion; CVD = cerebrovascular disease; EF = ejection fraction; LAD = left anterior descending artery; LCX = left circumflex artery; MI = myocardial infarction; PCI = percutaneous coronary intervention; PVD = peripheral vascular disease; RCA = right coronary artery.

**TABLE 2 Multivariable Analysis in the Derivation Subset (n = 521)**

	OR for Technical Failure (95% CI)	Chi-Square	p Value	b Coefficient	Points
No interventional collaterals	2.40 (0.92-6.55)	3.16	0.076	0.88	1
Proximal cap ambiguity	3.86 (1.49-10.43)	7.62	0.006	1.35	1
Moderate or severe tortuosity	3.25 (1.22-9.28)	5.63	0.021	1.18	1
LCX CTO	2.69 (1.00-7.14)	4.00	0.046	0.99	1
Prior PCI	1.64 (0.54-6.13)	0.69	0.391	0.25	0

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

**FIGURE 1** Summary of the PROGRESS CTO Score

b coefficients with their respective confidence intervals (CIs) were reported. Finally, comparison with the J-CTO score was performed in the validation cohort. Statistical analyses were performed with JMP version 11.0 (SAS Institute, Cary, North Carolina) and SPSS version 22.0 (IBM Corporation, Armonk, New York). A p value <0.05 was considered statistically significant.

## RESULTS

### PATIENT POPULATION AND PROCEDURAL OUTCOMES.

The study cohort consisted of 781 CTO PCI procedures performed in 762 patients. Mean age was  $65 \pm 10$  years, and most of the patients were men (87%) with frequent history of prior coronary artery bypass graft surgery (CABG) (35%), prior myocardial infarction (41%), and prior PCI (66%). The most common CTO PCI target vessel was the right coronary artery (59%), followed by the left anterior descending artery (21%)

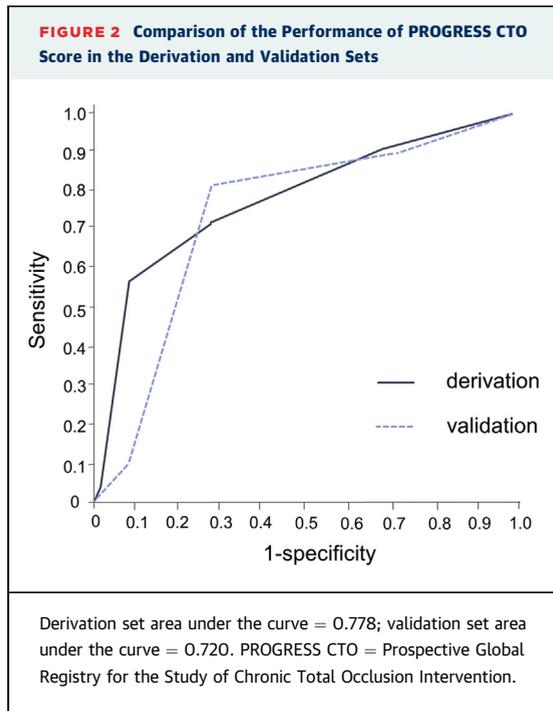
**TABLE 3** Clinical and Angiographic Characteristics in the Derivation and Validation Subsets

	Derivation Set (n = 521)	Validation Set (n = 260)	p Value
Age, yrs	65 ± 10	66 ± 10	0.23
Male	85	89	0.12
BMI, kg/m <sup>2</sup>	31 ± 6	30 ± 6	0.39
EF	50 ± 14	51 ± 13	0.24
Dyslipidemia	95	95	0.91
Hypertension	89	90	0.62
Current smoking	34	30	0.18
Prior MI	42	38	0.42
CHF	28	24	0.33
Prior PCI	67	65	0.62
Prior CABG	35	36	0.71
Dialysis	2	2	0.86
PVD	16	18	0.47
COPD	11	12	0.93
Target vessel			
RCA	59	61	0.93
LAD	22	21	
LCX	19	18	
Occlusion length, mm	37 ± 25	34 ± 25	0.15
Vessel diameter, mm	2.8 ± 0.5	2.8 ± 0.5	0.73
Proximal cap ambiguity	30	28	0.96
Side branch at proximal cap	43	42	0.76
Good distal opacification	50	52	0.63
Distal cap at bifurcation	30	34	0.39
Good distal landing zone	59	56	0.56
Collateral filling			
Ipsilateral	17	16	
Contralateral	55	58	0.88
Both	27	24	
None	2	2	
No interventional collaterals	37	36	0.78
Moderate or severe calcification	56	61	0.25
Moderate or severe tortuosity	33	33	0.88
In-stent restenosis	13	10	0.35
Prior attempt	17	18	0.71

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

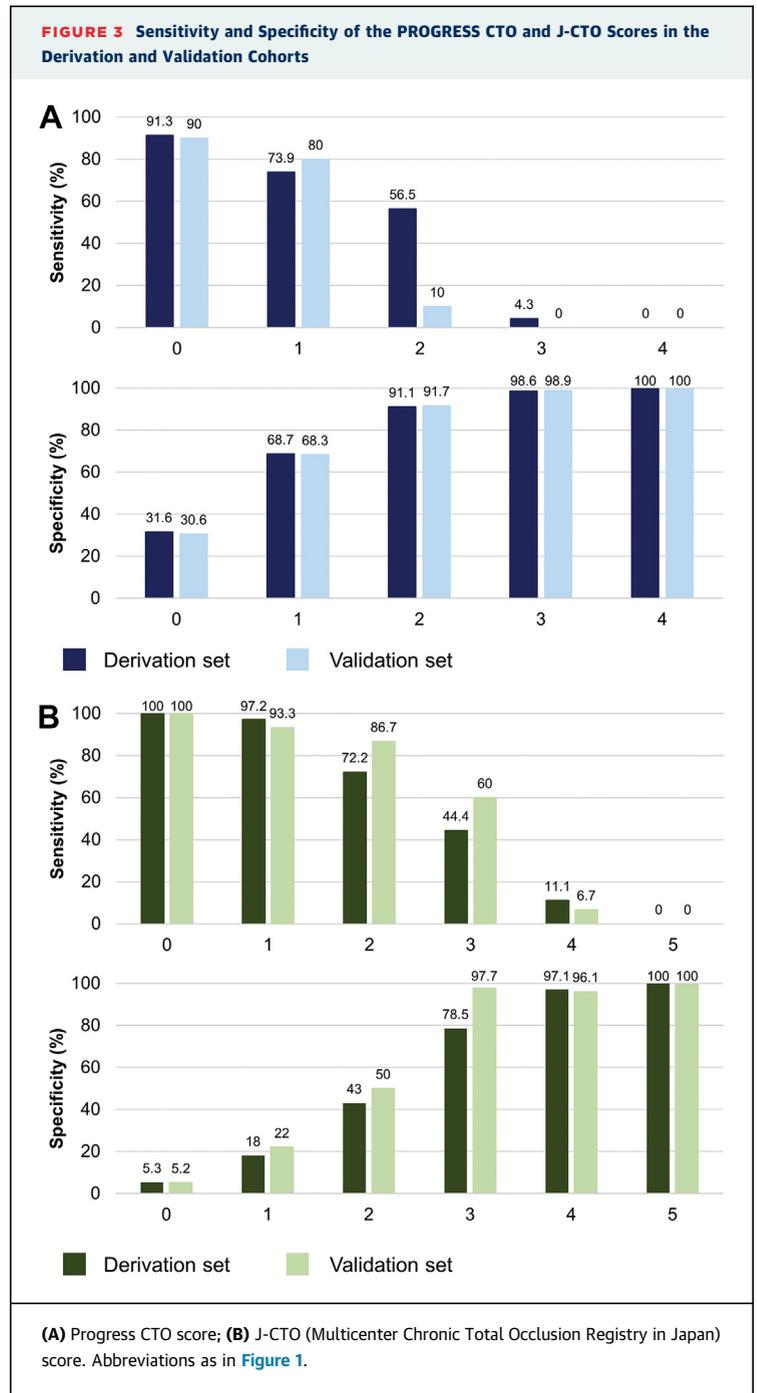
and the left circumflex artery (LCX) (19%). Technical success was achieved in 726 procedures (92.9%). The mean J-CTO score among successful versus failed CTO PCIs was  $2.5 \pm 1.2$  versus  $3.3 \pm 1.0$ , respectively ( $p < 0.001$ ). Median procedure and fluoroscopy time was 114 min (IQR: 79 to 166.5 min) and 42 min (IQR: 25 to 69 min), respectively. Median patient air kerma dose and contrast volume were 3.5 Gray (IQR: 2.0 to 5.7 Gray) and 250 ml (IQR: 190 to 350 ml), respectively.

**SCORE DERIVATION AND VALIDATION.** The derivation subset included 521 CTO PCIs, of which technical success was achieved in 482 (92.5%). As compared

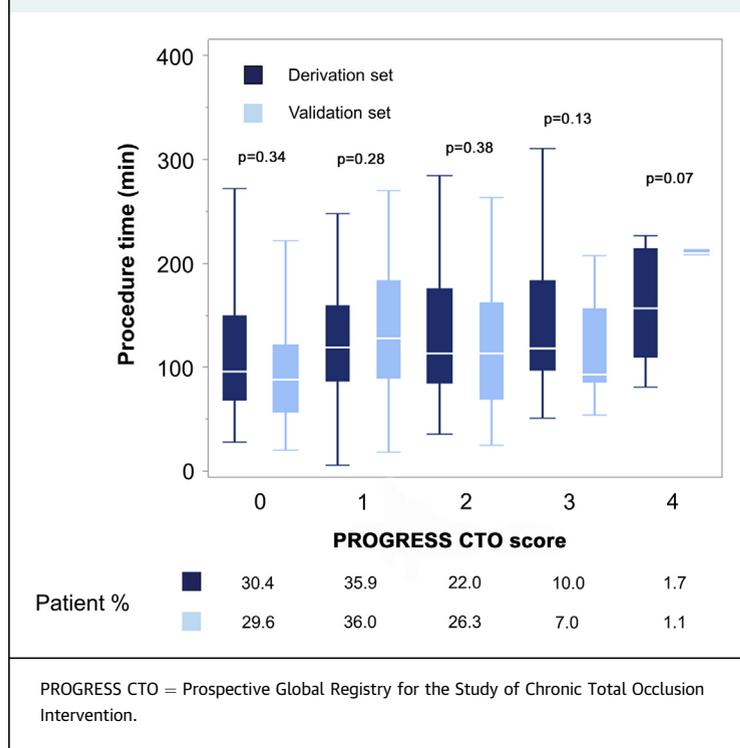


with successful procedures, failed procedures were more likely to be performed among patients with prior PCI (84% vs. 66%;  $p < 0.023$ ), proximal cap ambiguity (52% vs. 26%;  $p = 0.006$ ), lack of interventional collaterals (58% vs. 35%;  $p = 0.034$ ), moderate or severe tortuosity (56% vs. 31%;  $p = 0.005$ ), and LCX as the target vessel (39% vs. 17%;  $p < 0.001$ ) (Table 1). These variables were included in the multivariable analysis, and results are demonstrated on Table 2. Four of the 5 parameters (proximal cap ambiguity, lack of interventional collaterals, LCX PCI, and moderate/severe tortuosity) remained independently associated with technical failure. As the magnitude of their effect was similar (b coefficient range = 0.88 to 1.35), 1 point was assigned to each of the variables selected, creating the PROGRESS CTO score (Figure 1).

Clinical and angiographic characteristics were equally distributed between the derivation and validation subsets (Table 3). The PROGRESS CTO score's AUCs in the derivation and validation cohorts were 0.778 and 0.720, respectively (AUC difference = 0.058, 95% CI: -0.125 to 0.241) (Figure 2). Hosmer-Lemeshow chi-square values in derivation and validation cohorts were chi-square = 2.633 ( $p = 0.268$ ) and chi-square = 5.333 ( $p = 0.070$ ), respectively. The score was successful in predicting technical success with stepwise alterations in sensitivity and specificity for each PROGRESS CTO point (Figure 3A). Procedural time demonstrated only a moderate increase relative



to higher scores (Figure 4). Bootstrapped b coefficients for the score elements were as follows: lack of interventional collaterals: 0.836 (95% CI: 0.021 to 1.608;  $p = 0.032$ ); proximal cap ambiguity: 1.451 (95% CI: 0.693 to 2.380;  $p = 0.001$ ); tortuosity: 0.659 (95% CI: -0.097 to 1.493;  $p = 0.080$ ); LCX intervention: 0.955 (95% CI: 0.094 to 1.754;  $p = 0.011$ ). Collinearity diagnostics, including tolerance and

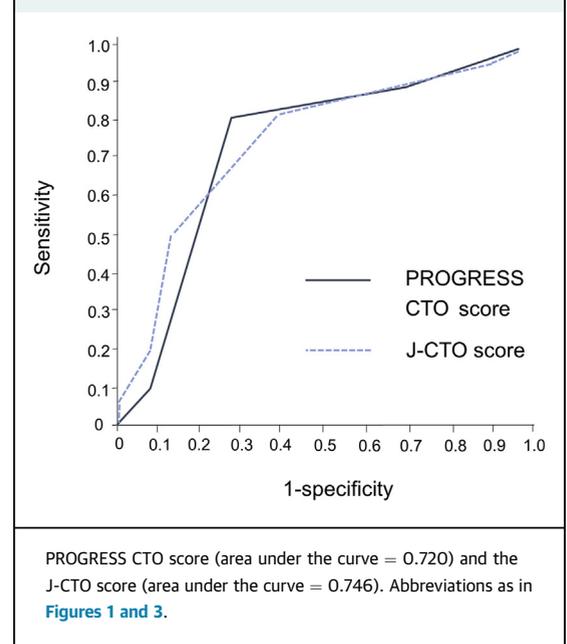
**FIGURE 4** Box Plot of Total Procedure Time in Each PROGRESS CTO Score Stratum in the Derivation and Validation Sets

variance inflation factor statistics, indicated no evidence of multicollinearity. The PROGRESS CTO score's relationship with technical failure was also confirmed with bootstrapping: b coefficient: 0.931 (95% CI: 0.597 to 1.342;  $p = 0.001$ ).

**COMPARISON WITH J-CTO SCORE TO PREDICT TECHNICAL SUCCESS.** We compared the PROGRESS CTO score with the J-CTO score in the validation subset (Figure 5). The AUC was 0.720 for the PROGRESS CTO score and 0.746 for the J-CTO score (AUC difference: 0.026; 95% CI: -0.093 to 0.144). Similar predicting accuracy was noted for each stratum of both scores (Figures 3A and 3B). However, the J-CTO score demonstrated better discriminatory ability in the lower scores (J-CTO sensitivity 93.3% to 100% and specificity 5.2% to 22.0% vs. PROGRESS CTO sensitivity 80.0% to 90.0% and specificity 30.6% to 68.3% for scores 0 to 1) in the validation dataset.

## DISCUSSION

Our study shows that the PROGRESS CTO score can be an effective tool in predicting the likelihood of CTO PCI technical success and guide clinical decision-making. The PROGRESS CTO score had similar predictive ability as the J-CTO score, but is simpler with 4 rather than 5 factors and does not include the prior

**FIGURE 5** Receiver-Operator Characteristic Curves of the PROGRESS CTO and J-CTO Scores in the Validation Dataset

CTO PCI failure, which can be unreliable given different skillsets at different CTO PCI centers and among various operators. Additionally, unlike the J-CTO score that was developed to predict procedural efficiency (i.e., guidewire crossing within 30 min), the PROGRESS CTO score was specifically developed to predict technical failure (12), which is a more clinically important endpoint.

The "hybrid" CTO crossing algorithm is commonly used to guide selection of CTO PCI crossing strategy in the U.S. and increasingly around the world (6). The "hybrid" algorithm assesses 4 key angiographic CTO characteristics (proximal cap ambiguity, quality of the vessel distal to the occlusion, lesion length, and presence of adequate collateral vessels) to determine the subsequent crossing strategy (antegrade wiring, dissection and re-entry, and retrograde). Three of those 4 characteristics were included in the PROGRESS CTO score, namely proximal cap ambiguity, tortuosity (surrogate for distal vessel quality), and presence of interventional collaterals. Lesion length was not independently associated with procedural success, likely because novel crossing techniques (such as antegrade or retrograde dissection and re-entry) may allow for rapid and safe crossing of long occlusion segments.

Several angiographic and clinical parameters have been associated with CTO PCI success, such as prior CABG (14,15), calcification, lesion length, and tortuosity (16). Success is also heavily dependent on operator

experience and expertise (17). Experienced operators can currently achieve >85% success rates, even in complex patient subgroups, such as patients with prior CABG and in-stent restenosis (8,11). All operators contributing cases to the PROGRESS CTO registry were experienced, high-volume CTO PCI operators who performed procedures using a standardized CTO crossing approach.

The retrograde approach to CTO PCI (18,19) is an important complement to the antegrade crossing approaches, especially in cases where the proximal cap is poorly visualized or in challenging lesions where antegrade crossing has failed (6,20). Absence of “interventional” collaterals, that is, collaterals suitable for the retrograde approach, deprives the operator of an alternative crossing strategy and contributes to the likelihood of technical failure. In centers with significant experience, the retrograde approach can be performed with high efficacy rates and a favorable efficiency and safety profile (21-26).

The J-CTO score’s primary outcome measure was CTO PCI efficiency (guidewire crossing time <30 min); the PROGRESS score used final angiographic success as the primary endpoint. Although the discriminatory capacity of the PROGRESS and the J-CTO scores was similar, the PROGRESS CTO score has 2 key advantages: 1) it includes key variables of the widely utilized hybrid algorithm that are not included in the J-CTO score (proximal cap ambiguity and presence of interventional collaterals; as well as circumflex CTO target vessel); and 2) it does not include a parameter of questionable value (prior CTO PCI failure, as the success or failure of the prior procedure heavily depends on the experience of the operator who performed that procedure). These differences may reflect recent advances in CTO PCI, such as expanded use of antegrade dissection/re-entry (27-29) and the retrograde approach (24,26,30,31) that may allow more efficient and successful crossing of complex and long CTOs. The lower success rates for circumflex CTO target vessel is likely related to increased tortuosity of this vessel and the less frequent presence of “interventional” collaterals (9).

**STUDY LIMITATIONS.** PROGRESS CTO is an observational registry without adjudication of clinical events by a clinical events committee. Quantitative coronary angiographic analysis was not performed, and therefore, assessment of angiographic characteristics was susceptible to operator-related bias. In particular, characterization of a collateral vessel as “interventional collateral” is subjective and depends heavily on operator experience. Even among the best CTO

operators, only approximately 70% to 80% of collateral vessels attempted are successfully crossed with a guidewire and a microcatheter (32). Moreover, if an operator is unable to wire a collateral, he or she might be more likely to code it as a “noninterventional” collateral. No long-term follow-up of the CTO patients was available. All procedures were performed by seasoned operators with significant CTO PCI training limiting extrapolation of the study results to less experienced centers and operators. The low failure rate (7.1%) in the derivation cohort may limit the power of univariable and multivariable analyses, due to paucity of observations in the failure group. However, it is expected that in case of a higher failure rate, the increase in model diagnostic accuracy would also increase statistical significance of the score components. Validation of the PROGRESS CTO score in an external dataset would further strengthen our findings. Our analysis did not account for correlation in the limited number of patients (n = 17, 2%) who had PCI of 2 CTO lesions during the same procedure. However, reiteration of the analysis after excluding these lesions did not significantly change the PROGRESS CTO score derivation. Finally, guidewire crossing time was not available, and total procedure time was used as a measure of procedural efficiency, which is related to multiple factors in addition to guidewire crossing time.

## CONCLUSIONS

Evaluation of 4 baseline angiographic characteristics (proximal cap ambiguity, absence of retrograde collaterals, moderate or severe tortuosity, and LCX CTO) can be used to determine the likelihood of technical success with CTO PCI. The PROGRESS CTO score is a simple tool that can be used in clinical practice to predict CTO PCI success and guide clinical decision-making.

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**REPRINT REQUESTS AND CORRESPONDENCE:** Dr. Emmanouil S. Brilakis, Dallas VA Medical Center (111A), 4500 South Lancaster Road, Dallas, Texas 75216. E-mail: [esbrilakis@gmail.com](mailto:esbrilakis@gmail.com).

## PERSPECTIVES

**WHAT IS KNOWN?** Currently there are limited tools for predicting the likelihood of success of CTO PCI.

**WHAT IS NEW?** We developed the PROGRESS CTO score for predicting technical success of CTO PCI. The score includes 4 variables: proximal cap ambiguity, moderate/severe tortuosity, circumflex artery CTO, and

absence of "interventional" collaterals. The PROGRESS CTO score demonstrated good calibration and discriminatory capacity and performed similar to the J-CTO score in predicting technical success.

**WHAT IS NEXT?** Clinical application and external validation of the PROGRESS-CTO score are needed to further refine its clinical utility.

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