7-25-2022

Predicting Periprocedural Complications in Chronic Total Occlusion Percutaneous Coronary Intervention: The PROGRESS-CTO Complication Scores

Bahadir Simsek

Spyridon Kostantinis

Judit Karacsonyi

Khaldoon Alaswad
Henry Ford Health, kalaswa1@hfhs.org

Oleg Krestyaninov

See next page for additional authors

Recommended Citation

Simsek B, Kostantinis S, Karacsonyi J, Alaswad K, Krestyaninov O, Khelimskii D, Davies R, Rier J, Goktekin O, Gorgulu S, ElGuindy A, Chandwaney RH, Patel M, Abi Rafeh N, Karmpaliotis D, Masoumi A, Khatri JJ, Jaffer FA, Doshi D, Poommipanit PB, Rangan BV, Sanvodal Y, Choi JW, Elbarouni B, Nicholson W, Jaber WA, Rinfret S, Koutouzis M, Tsiafoutis I, Yeh RW, Burke MN, Allana S, Mastrodemos OC, and Brilakis ES. Predicting Periprocedural Complications in Chronic Total Occlusion Percutaneous Coronary Intervention: The PROGRESS-CTO Complication Scores. JACC Cardiovasc Interv 2022; 15(14):1413-1422.

Authors

Bahadir Simsek, Spyridon Kostantinis, Judit Karacsonyi, Khaldoon Alaswad, Oleg Krestyaninov, Dmitrii Khelimskii, Rhian Davies, Jeremy Rier, Omer Goktekin, Sevket Gorgulu, Ahmed ElGuindy, Raj H. Chandwaney, Mitul Patel, Nidal Abi Rafeh, Dimitrios Karmpaliotis, Amirali Masoumi, Jaikirshan J. Khatri, Farouc A. Jaffer, Darshan Doshi, Paul B. Poommipanit, Bavana V. Rangan, Yader Sanvodal, James W. Choi, Basem Elbarouni, William Nicholson, Wissam A. Jaber, Stephane Rinfret, Michael Koutouzis, Ioannis Tsiafoutis, Robert W. Yeh, M. Nicholas Burke, Salman Allana, Olga C. Mastrodemos, and Emmanouil S. Brilakis

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 15, NO. 14, 2022

PUBLISHED BY ELSEVIER

NEW RESEARCH PAPERS

FOCUS ON CHRONIC TOTAL OCCLUSIONS

Predicting Periprocedural Complications in Chronic Total Occlusion Percutaneous Coronary Intervention

The PROGRESS-CTO Complication Scores

Bahadir Simsek, MD,[a] Spyridon Kostantinis, MD,[a] Judit Karacsonyi, MD, PhD,[a] Khaldoon Alaswad, MD,[b] Oleg Krestyaninov, MD,[c] Dmitrii Khelimskii, MD,[c] Rhian Davies, MD,[d] Jeremy Rier, DO,[d] Omer Goktekin, MD,[e] Sevket Gorgulu, MD,[f] Ahmed ElGuindy, MD,[g] Raj H. Chandwaney, MD,[h] Mitul Patel, MD,[i] Nidal Abi Rafeh, MD,[j] Dimitrios Karmpaliotis, MD, PhD,[k] Amirali Masoumi, MD,[k] Jaikirshan J. Khatri, MD,[l] Farouc A. Jaffer, MD, PhD,[m] Darshan Doshi, MD, MS,[m] Paul B. Poommipanit, MD,[n] Bavana V. Rangan, BDS, MPH,[a] Yader Sandoval, MD,[o] James W. Choi, MD,[p] Basem Elbarouni, MD,[q] William Nicholson, MD,[r] Wissam A. Jaber, MD,[r] Stephane Rinfret, MD, SM,[r] Michael Koutouzis, MD, PhD,[s] Ioannis Tsiafoutis, MD,[s] Robert W. Yeh, MD,[t] M. Nicholas Burke, MD,[a] Salman Allana, MD,[a] Olga C. Mastrodemos, BA,[a] Emmanouil S. Brilakis, MD, PhD[a]

ABSTRACT

BACKGROUND Chronic total occlusion (CTO) percutaneous coronary intervention (PCI) is associated with increased risk of periprocedural complications. Estimating the risk of complications facilitates risk-benefit assessment and procedural planning.

OBJECTIVES This study sought to develop risk scores for in-hospital major adverse cardiovascular events (MACE), mortality, pericardiocentesis, and acute myocardial infarction (MI) in patients undergoing CTO PCI.

METHODS The study analyzed the PROGRESS-CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; NCT02061436) and created risk scores for MACE, mortality, pericardiocentesis, and acute MI. Logistic regression prediction modeling was used to identify independently associated variables, and models were internally validated with bootstrapping.

RESULTS The incidence of periprocedural complications among 10,480 CTO PCIs was as follows: MACE 215 (2.05%), mortality 47 (0.45%), pericardiocentesis 83 (1.08%), and acute MI 66 (0.63%). The final model for MACE included ≥65 years of age (1 point), moderate-severe calcification (1 point), blunt stump (1 point), antegrade dissection and re-entry (ADR) (1 point), female (2 points), and retrograde (2 points); the final model for mortality included ≥65 years of age (1 point), left ventricular ejection fraction ≤45% (1 point), moderate-severe calcification (1 point), ADR (1 point), and retrograde (1 point); the final model for pericardiocentesis included ≥65 years of age (1 point), female (1 point), moderate-severe calcification (1 point), ADR (1 point), and retrograde (2 points); the final model for acute MI included prior coronary artery bypass graft surgery (1 point), atrial fibrillation (1 point), and blunt stump (1 point). The C-statistics of the models were 0.74, 0.80, 0.78, 0.72 for MACE, mortality, pericardiocentesis, and acute MI, respectively.

CONCLUSIONS The PROGRESS-CTO complication risk scores can facilitate estimation of the periprocedural complication risk in patients undergoing CTO PCI. (J Am Coll Cardiol Intv 2022;15:1413–1422) © 2022 by the American College of Cardiology Foundation.

ISSN 1936-8798/$36.00 https://doi.org/10.1016/j.jcin.2022.06.007

ABBREVIATIONS AND ACRONYMS

ADR = antegrade dissection and re-entry

AUC = area under the receiver-operating characteristic curve

AW = antegrade wiring

CABG = coronary artery bypass grafting

CTO = chronic total occlusion

LVEF = left ventricular ejection fraction

MACE = major adverse cardiovascular event(s)

PCI = percutaneous coronary intervention

ROC = receiver-operating characteristic

Chronic total occlusion (CTO) percutaneous coronary intervention (PCI) is associated with an increased risk of complications.[1,2] Assessment of the procedural risks and benefits is essential for patient counseling and procedural planning. While several scores have been developed to assess the likelihood of technical success in CTO PCI,[3-6] there are only a few tools that assess the risk of complications.[7,8] We analyzed a large multicenter CTO PCI registry to update the previously developed PROGRESS-CTO complications score,[7] and to develop separate risk scores for in-hospital mortality, pericardiocentesis, and acute myocardial infarction (MI).

SEE PAGE 1423

METHODS

The PROGRESS-CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; NCT02061436) includes CTO PCI procedures performed at 40 centers from the United States, Canada, Greece, Turkey, Egypt, Russia, and Lebanon between 2012 and 2022. The Research Electronic Data Capture database was used for data collection and management.[9,10]

DEFINITIONS. CTOs were defined as the absence of antegrade flow through the lesion with a presumed or documented duration of ≥3 months with Thrombolysis In Myocardial Infarction (TIMI) flow grade 0 according to the definition of the CTO Academic Research Consortium.[11]

Technical success was defined as the successful recanalization of the CTO vessel with <30% residual stenosis and final TIMI flow grade 3. Major adverse cardiovascular events (MACE) were defined as the composite of death, MI, stroke, urgent repeat revascularization (re-PCI or surgery), or pericardiocentesis. Procedural success was defined as technical success in the absence of in-hospital MACE. MI was defined using the Third Universal Definition of Myocardial Infarction (type 4a MI).[12]

Calcification was assessed by angiography and classified as mild (spots), moderate and severe, defined as ≤50% and ≥50% calcification compared with reference lesion diameter, respectively.

For risk calculation purposes, antegrade wiring (AW) was defined as the absence of use of either antegrade dissection and re-entry (ADR) or retrograde crossing attempts. If AW and ADR were both used, the case was classified as ADR. If a retrograde strategy was used, the crossing strategy was defined as retrograde.

The study was approved by the Institutional Review Board of each site.

STATISTICAL ANALYSIS. Continuous variables were presented as mean ± SD and compared using the independent *t* test or Mann-Whitney *U* test, as appropriate. Categorical variables were presented as absolute numbers and percentages and compared using the chi-square or Fisher exact test, as appropriate. Univariable logistic regression was performed to identify associations between variables and outcomes (MACE, mortality, pericardiocentesis, acute MI). Variables that had a *P* value of <0.10 in the univariable analysis and considered clinically or angiographically plausible predictors of MACE, mortality, pericardiocentesis, or acute MI were tested in the multivariable logistic regression with a backward elimination approach starting with variables that

From the [a]Center for Coronary Artery Disease, Minneapolis Heart Institute and Minneapolis Heart Institute Foundation, Minneapolis, Minnesota, USA; [b]Division of Cardiology, Henry Ford Hospital, Detroit, Michigan, USA; [c]Meshalkin Siberian Federal Biomedical Research Center, Ministry of Health of Russian Federation, Novosibirsk, Russian Federation; [d]Division of Cardiology, WellSpan York Hospital, York, Pennsylvania, USA; [e]Division of Cardiology, Memorial Bahcelievler Hospital, Istanbul, Turkey; [f]Division of Cardiology, Acibadem Kocaeli Hospital, Izmit, Turkey; [g]Division of Cardiology, Aswan Heart Center, Aswan, Egypt; [h]Division of Cardiology, Oklahoma Heart Institute, Tulsa, Oklahoma, USA; [i]Division of Cardiology, University of California San Diego, San Diego, California, USA; [j]Division of Cardiology, North Oaks Health System, Hammond, Louisiana, USA; [k]Gagnon Cardiovascular Institute, Morristown Medical Center, New Jersey, USA; [l]Division of Cardiology, Cleveland Clinic Foundation, Cleveland, Ohio, USA; [m]Division of Cardiology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA; [n]Division of Cardiology, University Hospitals, Case Western Reserve University, Cleveland, Ohio, USA; [o]Department of Cardiovascular Medicine, Mayo Clinic, Rochester, Minnesota, USA; [p]Cardiology Division, Baylor Heart and Vascular Institute, Department of Internal Medicine, Baylor University Medical Center, Dallas, Texas, USA; [q]Section of Cardiology, St. Boniface Hospital, University of Manitoba, Winnipeg, Manitoba, Canada; [r]Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, USA; [s]Second Cardiology Department, Red Cross General Hospital, Athens, Greece; and the [t]Richard A. and Susan F. Smith Center for Outcomes Research in Cardiology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received March 17, 2022; revised manuscript received June 14, 2022, accepted June 14, 2022.

had the highest *P* value separately in each model. All dropped variables that were considered clinically or angiographically plausible were then individually added to investigate any other potential confounders by checking the change in the beta coefficients in the multivariable regression model. The Hosmer-Lemeshow test was used to test goodness-of-fit, with $P > 0.05$ considered a good fit. The discriminative capacity of the model was illustrated with the receiver-operating characteristic (ROC) curve, with an area under the ROC curve (AUC) 0.70 to 0.80 and 0.80 to 0.90 considered to have an acceptable and excellent discrimination, respectively. Internal validation was performed with bootstrapping 1,000 samples from the dataset. A calculator incorporating the variables in the final prediction model was created (Supplemental Appendix) by calculating the probability of event (P) with the logistic regression equation: $\ln(P/(1-P)) = \beta_0 + \beta_1 \cdot x_1 + \ldots + \beta_z \cdot x_z$. To ease clinical use and for risk score assignment, age and left ventricular ejection fraction (LVEF) were transformed into categorical variables and binary risk scores were provided. Risk scores were created from the full prediction model by assigning weighted points to the beta coefficients in the final models.

Statistical analyses were performed using Stata v17.0 (StataCorp).

RESULTS

BASELINE CHARACTERISTICS AND PROCEDURAL OUTCOMES. Among 10,487 CTO PCIs, in-hospital MACE occurred in 215 (2.05%), mortality in 47 (0.45%), pericardiocentesis in 83 (1.08%), and acute MI in 66 (0.63%) (Supplemental Figure 1). Patients who experienced MACE were older (age 68 ± 11 years vs 64 ± 10 years; $P < 0.001$), more likely to be women (27% vs 19%; $P = 0.004$), and to have a history of heart failure (40% vs 29%; $P = 0.001$), a history of chronic lung disease (20% vs 14%; $P = 0.032$), moderate-severe calcification (67% vs 46%; $P < 0.001$), higher J-CTO score (2.9 ± 1.1 vs 2.4 ± 1.3; $P < 0.001$), and "lower" successful crossing with antegrade wiring (26% vs 55%; $P < 0.001$). Technical success was significantly higher in patients without MACE (87% vs 66%; $P < 0.001$) (Table 1).

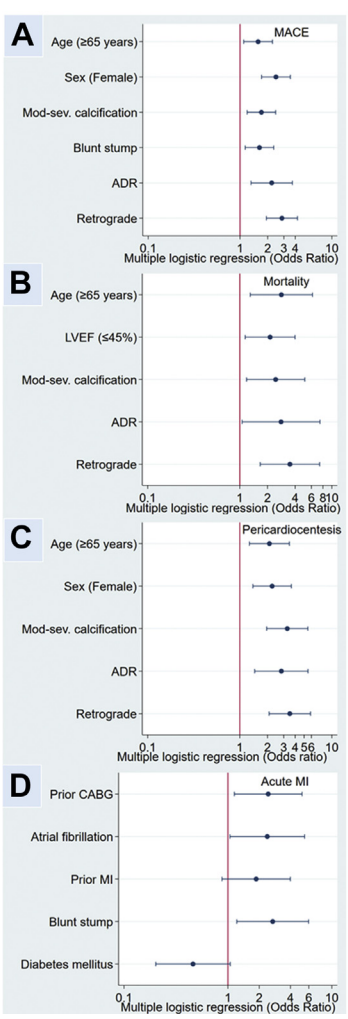
RISK PREDICTION MODELS. Major adverse cardiovascular events. On univariable logistic regression, age, female sex, atrial fibrillation, LVEF, proximal cap ambiguity, moderate-severe

TABLE 1 Clinical, Angiographic, and Procedural Characteristics of Patients With and Without In-Hospital Major Adverse Cardiovascular Events

Characteristics/Variables	Major In-Hospital Adverse Cardiovascular Events (n = 215)	No Major In-Hospital Adverse Cardiovascular Events (n = 10,272)	*P* Value
Age, y	68 ± 11 (192)	64 ± 10 (9,191)	<0.001
Male	142 (73.00)	7,628 (81.00)	0.004
LVEF, %	49 ± 15 (170)	50 ± 13 (8,097)	0.0789
BMI, kg/m^2	30 ± 6 (173)	30 ± 6 (8,584)	0.250
Technical (angiographic) success	142 (66.00)	8,906 (87.00)	<0.001
J-CTO score	2.9 ± 1.1 (203)	2.4 ± 1.3 (9,661)	<0.001
PROGRESS-CTO score	1.4 ± 1.0 (150)	1.3 ± 1.0 (7,911)	0.067
Hypertension	177 (93.00)	8,227 (89.00)	0.152
Diabetes mellitus	71 (38.00)	3,894 (43.00)	0.149
Smoking			0.026
Current/recent (within 1 y)	34 (19.00)	2,341 (26.00)	
Past (>1 y ago)	83 (46.00)	3,321 (37.00)	
Never	65 (36.00)	3,244 (36.00)	
Baseline creatinine, mg/dL	1.3 ± 1.1 (170)	1.2 ± 0.9 (8,374)	0.127
Atrial fibrillation	24 (19.00)	808 (12.00)	0.027
Prior heart failure	73 (40.00)	2,540 (29.00)	0.001
Prior myocardial infarction	86 (48.00)	3,925 (45.00)	0.459
Prior percutaneous coronary intervention	131 (64.00)	5,812 (62.00)	0.603
Prior coronary artery bypass grafting	65 (31.00)	2,750 (29.00)	0.512
Dyslipidemia	170 (89.00)	7,952 (87.00)	0.324
RHC during CTO PCI	23 (21.00)	214 (3.50)	<0.001
LV assist device used	44 (25.00)	315 (3.70)	<0.001
Cerebrovascular disease	25 (13.00)	907 (10.00)	0.146
Chronic lung disease	37 (20.00)	1,288 (14.00)	0.032
On dialysis at baseline	6 (3.20)	218 (2.40)	0.507
Length of hospital stay, d	4 (2-7) (140)	1 (1-1) (7,616)	<0.001
CTO target vessel			0.793
Left main artery	2 (0.96)	47 (0.48)	
LAD	53 (25.00)	2,556 (26.00)	
LCX	46 (22.00)	1,881 (19.00)	
RCA	104 (50.00)	5,138 (53.00)	
SVG	0 (0)	12 (0.10)	
Other	3 (1.40)	150 (1.50)	
CTO lesion length >20 mm	131 (77.00)	5,733 (66.00)	0.005
Moderate or severe calcification (CTO lesion)	138 (67.00)	4,318 (46.00)	<0.001
Orbital atherectomy	3 (1.40)	86 (0.80)	0.377
Rotational atherectomy	20 (9.30)	338 (3.30)	<0.001
IVUS/OCT	90 (55.00)	3,935 (47.00)	0.059
Successful crossing strategy			<0.001
AW	56 (26.00)	5,600 (55.00)	
ADR	30 (14.00)	1,327 (13.00)	
Retrograde	74 (34.00)	1,902 (19.00)	
None	55 (26.00)	1,298 (13.00)	

Values are mean ± SD (n), n (%), or median (IQR) (n). ADR = antegrade dissection and re-entry; AW = antegrade wiring; BMI = body mass index; CTO = chronic total occlusion; IVUS = intravascular ultrasound; J-CTO = Japan-CTO; LAD = left anterior descending artery; LCX = left circumflex artery; LV = left ventricular; LVEF = left ventricular ejection fraction; OCT = optical coherence tomography; PCI = percutaneous coronary intervention; PROGRESS-CTO = Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; RCA = right coronary artery; RHC = right heart catheterization; SVG = saphenous vein graft.

FIGURE 1 PROGRESS-CTO Complication Risk Scores



	Odds ratio	95% CI	p-value	Score
Age (≥65 years)	1.57	1.10-2.26	0.014	1
Sex (Female)	2.46	1.72-3.53	<0.001	2
Mod-sev. calcification	1.71	1.20-2.44	0.003	1
Blunt stump	1.63	1.14-2.33	0.008	1
ADR	2.21	1.32-3.72	0.003	1
Retrograde	2.86	1.94-4.22	<0.001	2

	Odds ratio	95% CI	p-value	Score
Age (≥65 years)	2.83	1.30-6.16	0.009	1
LVEF (≤45%)	2.13	1.14-3.98	0.017	1
Mod-sev. calcification	2.45	1.18-5.08	0.016	1
ADR	2.81	1.06-7.43	0.038	1
Retrograde	3.51	1.67-7.37	0.001	1

	Odds ratio	95% CI	p-value	Score
Age (≥65 years)	2.10	1.27-3.46	0.004	1
Sex (Female)	2.25	1.39-3.63	0.001	1
Mod-sev. calcification	3.28	1.96-5.49	<0.001	1
ADR	2.83	1.45-5.51	0.002	1
Retrograde	3.50	2.08-5.87	<0.001	2

	Odds ratio	95% CI	p-value	Score
Prior CABG	2.44	1.15-5.17	0.020	1
Atrial fibrillation	2.39	1.05-5.47	0.039	1
Prior MI	1.87	0.88-3.99	NS	-
Blunt stump	2.70	1.22-5.98	0.014	1
Diabetes mellitus	0.46	0.20-1.05	NS	-

Multiple logistic regression analyses and attributed risk scores for the PROGRESS-CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) **(A)** major adverse cardiovascular events (MACE), **(B)** mortality, **(C)** pericardiocentesis, and **(D)** acute myocardial infarction (MI) risk scores. ADR = antegrade dissection and re-entry; CABG = coronary artery bypass grafting; LVEF = left ventricular ejection fraction; mod-sev. = moderate-severe.

calcification, moderate-severe proximal vessel tortuosity, ADR, retrograde strategy, and blunt stump were associated with MACE with a *P* value <0.10.

A multivariable logistic regression model to predict MACE was built with these variables, and the final model was created as described in the Methods. The final model included: 1) age (continuous); 2) sex (male/female); 3) moderate-severe calcification (yes/no); 4) crossing strategy (AW/ADR/retrograde); and 5) stump (blunt/tapered) (**Figure 1A**). The PROGRESS-CTO in-hospital MACE risk calculator for clinical use was created with these variables (Supplemental Appendix). The PROGRESS-CTO MACE score showed acceptable performance on the ROC curve (AUC: 0.74; 95% CI: 0.70-0.78) (**Figure 2A**). The Hosmer-Lemeshow test indicated good fitness (*P* = 0.231), and internal validation with bootstrapping of 1,000 samples demonstrated a good agreement with the model (observed AUC: 0.72; 95% bias-corrected CI: 0.68-0.76).

We validated the "old" PROGRESS-CTO complications score in the current dataset and compared it with the updated PROGRESS-CTO MACE score. The AUC for the old PROGRESS-CTO complications score in the current dataset was 0.67 (95% CI: 0.63-0.70), and the updated MACE score had better performance compared with the old score (AUC: 0.74 vs 0.67; *P* = 0.0002). At 2% MACE cutoff, compared with the old score, in the updated MACE score, 38 (27%) of 141 were reclassified higher and 6 (4%) of 141 were reclassified lower in the event group. In the nonevent group, 938 (14%) of 6,860 were reclassified higher and 394 (6%) of 6,860 were reclassified lower (net reclassification improvement: 0.15; 95% CI: 0.13-0.16; *P* = 0.0018).

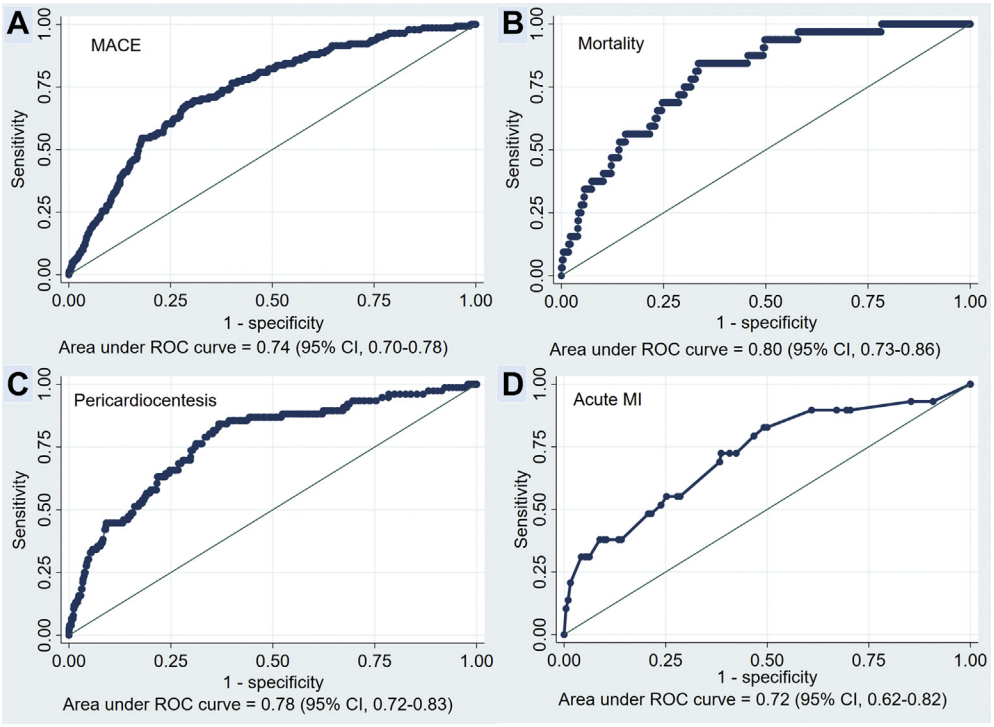
Age was dichotomized (<65 years and ≥65 years) and risk points were assigned to each variable based on the magnitude of OR (+1 for >65 years of age, +2 for female sex, +1 for moderate-severe calcification, +1 for blunt stump, +1 for ADR, +2 for retrograde) (**Figure 1A**).

For each PROGRESS-CTO MACE risk score, the corresponding MACE percentage risk and the proportion of patients falling in that category in the PROGRESS-CTO registry were calculated (**Figures 3A to 3B, Central Illustration**). The calculated risk percentages for MACE based on the PROGRESS-CTO MACE score ranged from 0.43% to 11.73% for MACE; 42% of patients had PROGRESS-CTO MACE score of 2 to 3, corresponding to a MACE risk of 1.10% to 2.60%.

Mortality. On univariable logistic regression, age, LVEF, prior coronary artery bypass grafting (CABG) surgery, moderate-severe calcification, ADR, and retrograde strategy were associated with a periprocedural death, with a *P* value <0.10.

The final model included: 1) age (continuous); 2) LVEF (continuous); 3) moderate-severe calcification (yes/no); and 4) crossing strategy (AW-ADR-retrograde) (**Figure 1B**). The PROGRESS-CTO mortality risk calculator for clinical use was created with these variables (Supplemental Appendix). The PROGRESS-CTO mortality risk score showed an excellent performance with an AUC of 0.80 (95% CI: 0.73-0.86) (**Figure 2B**). The Hosmer-Lemeshow test indicated good fit (*P* = 0.85), and internal validation with bootstrapping of 1,000 samples demonstrated a good

FIGURE 2 **Area Under the ROC Curve for the Complication Risk Scores**



Area under the receiver-operating characteristic (ROC) curve for the **(A)** MACE, **(B)** mortality, **(C)** pericardiocentesis, and **(D)** acute MI risk models. Abbreviations as in Figure 1.

agreement with the model (observed e: 0.71; 95% bias-corrected CI: 0.63-0.81).

Age (<65 years and ≥65 years) and LVEF (≤45% and >45%) were dichotomized and risk points were assigned to each variable based on the magnitude of OR (+1 for >65 years of age, +1 for LVEF ≤45%, +1 for moderate-severe calcification, +1 for ADR, and +1 for retrograde) (Figure 1B).

For each PROGRESS-CTO mortality risk score, the corresponding mortality percentage risk and the proportion of patients falling in that category in the PROGRESS-CTO registry were calculated (Figures 3C to 3D). The calculated risk percentages for mortality based on the PROGRESS-CTO mortality score ranged from 0.05% to 2.42% for mortality, and 63% of patients had PROGRESS-CTO mortality score of 1 or 2, corresponding to a mortality risk of 0.10% to 0.50%.

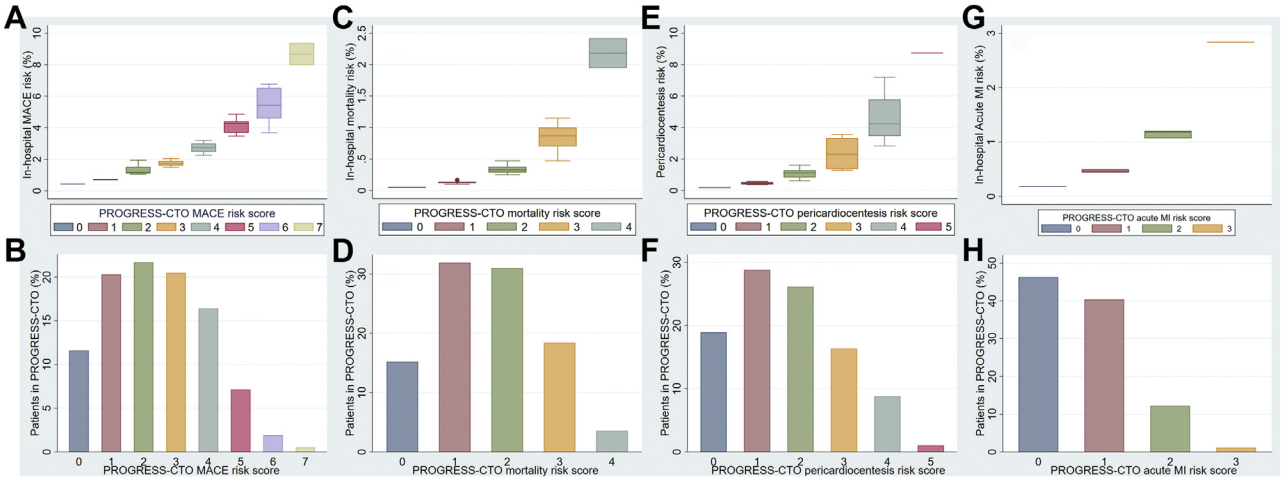
Pericardiocentesis. Patients with prior CABG were excluded from the pericardiocentesis risk prediction model, and the final model was based on 7,672 CTO PCI cases and 83 (1.10%) perforations.

On univariable logistic regression, age, female sex, blunt stump, moderate-severe calcification, ADR, and the retrograde approach were associated with the need for pericardiocentesis, with a *P* value <0.10. The final model included: 1) age (continuous); 2) sex (male/female); 3) moderate-severe calcification (yes/no); and 4) crossing strategy (AW-ADR-retrograde) (Figure 1C). The PROGRESS-CTO pericardiocentesis risk calculator for clinical use was created with these variables (Supplemental Appendix). The PROGRESS-CTO pericardiocentesis risk score had acceptable performance with an AUC of 0.78 (95% CI: 0.72-0.83) (Figure 2C). The Hosmer-Lemeshow test indicated good fitness ($P = 0.10$), and internal validation with bootstrapping of 1,000 samples demonstrated a good agreement with the model (observed AUC: 0.78; 95% bias-corrected CI: 0.72-0.83).

Age (<65 years and ≥65 years) was dichotomized and risk points were assigned to each variable based on the magnitude of OR (+1 for >65 years of age, +1 for female sex, +1 for moderate-severe calcification, +1 for ADR, and +2 for retrograde) (Figure 1C).

For each PROGRESS-CTO pericardiocentesis risk score, the corresponding pericardiocentesis percentage risk and the proportion of patients falling in

FIGURE 3 PROGRESS-CTO Complication Risk Scores and Corresponding Risk Percentages



The PROGRESS-CTO complication risk scores and corresponding risk percentage and percentage of patients in the respective risk group within the PROGRESS-CTO registry for **(A, B)** MACE, **(C, D)** mortality, **(E, F)** pericardiocentesis, and **(G, H)** acute MI. The boxplots represent the risk percentage interval for a given PROGRESS-CTO complication score (from **top to bottom**: maximum, quartile 3, median, quartile 1, minimum). The risk for a given complication score is not a single number but an interval based on the variables the final score is summed—variables with different beta coefficients might be given the same score (eg, score of 1 each, rather than 1 and 1.3) for ease of use; however, this does not correspond to exactly the same risk. Abbreviations as in Figure 1.

that category in the PROGRESS-CTO registry were calculated (Figures 3E to 3F). The calculated risk percentages for pericardiocentesis based on the PROGRESS-CTO mortality score ranged from 0.18% to 8.74% for pericardiocentesis, and 55% of patients had PROGRESS-CTO pericardiocentesis score of 1 or 2, corresponding to a pericardiocentesis risk of 0.40% to 1.60%.

Acute MI. On univariable logistic regression analysis; age, atrial fibrillation, LVEF, diabetes mellitus, prior PCI, prior CABG, proximal cap ambiguity, stump, moderate-severe calcification, and CTO length were associated with a periprocedural MI, with a P value <0.10.

The final model included: 1) prior CABG; 2) atrial fibrillation; 3) prior MI; 4) stump; and 5) diabetes mellitus (Figure 1D). The PROGRESS-CTO acute MI risk calculator for clinical use was created with these variables (Supplemental Appendix). The PROGRESS-CTO acute MI risk score showed acceptable performance, as shown by the AUC (0.72; 95% CI: 0.62-0.82) (Figure 2D). The Hosmer-Lemeshow test indicated good fit ($P = 0.51$), and internal validation with bootstrapping of 1,000 samples demonstrated good agreement with the model (bias-corrected AUC: 0.72; 95% CI: 0.65-0.80).

Risk points were assigned to each variable based on the magnitude of OR (+1 for prior CABG, +1 for atrial fibrillation, +1 for blunt stump) (Figure 1D).

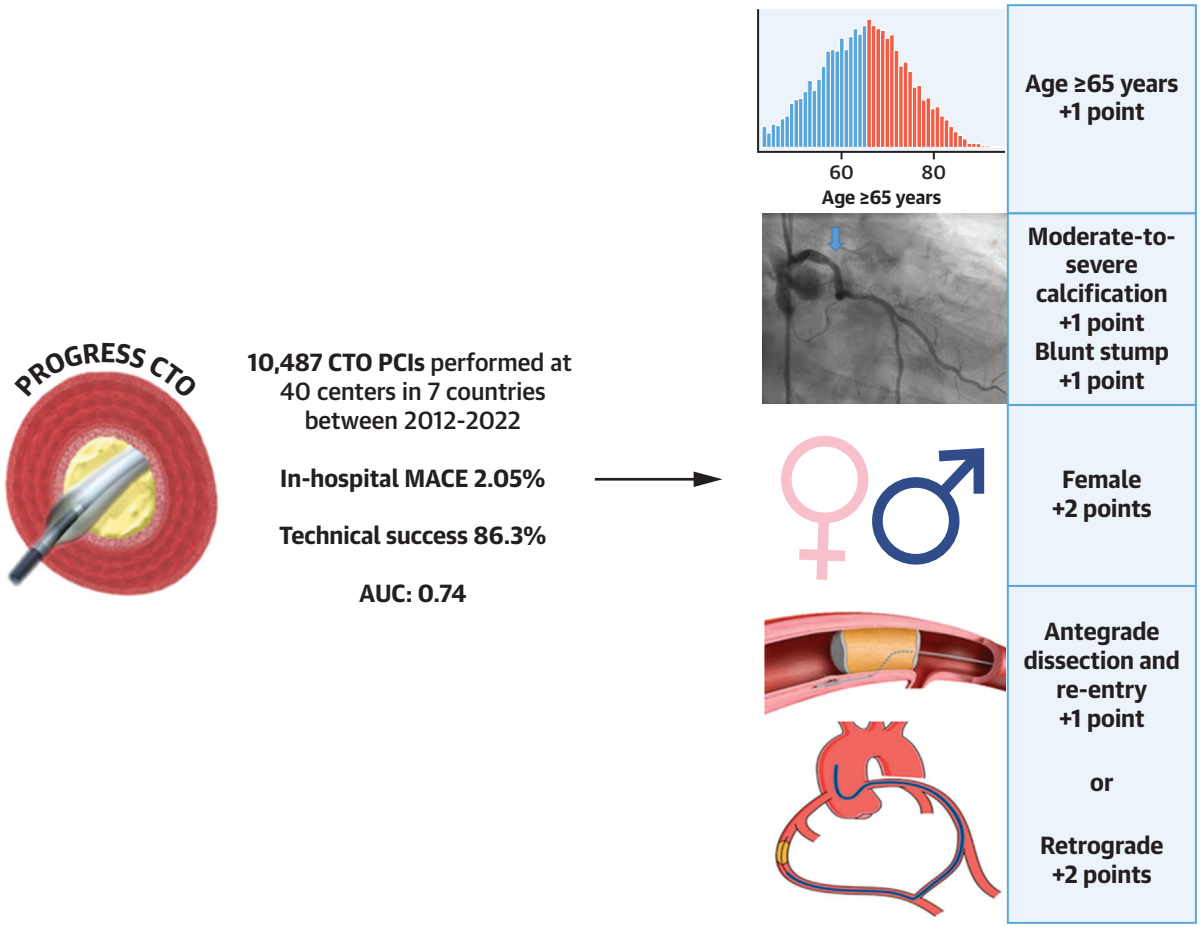
For each PROGRESS-CTO acute MI risk score, the corresponding acute MI percentage risk and the proportion of patients falling in that category in the PROGRESS-CTO registry were calculated (Figures 3G to 3H). The calculated risk percentages for acute MI based on the PROGRESS-CTO acute MI risk score ranged from 0.18% to 2.83% for acute MI, and 87% of patients had PROGRESS-CTO acute MI risk score of 0 or 1, corresponding to an acute MI risk of 0.18% to 0.50%.

DISCUSSION

Our study identified risk factors for MACE, mortality, pericardiocentesis, and acute MI in patients undergoing CTO PCI, and created 4 internally validated risk scores and accompanying risk percentages with acceptable to excellent discrimination.

Several scores have been developed to date to predict technical success rates (the CL-SCORE [Clinical and Lesion-related]),[5] successful guidewire crossing of a CTO lesion within 30 minutes (J-CTO [Japan-CTO] score),[4] and technical success or failure (ORA [Ostial location, Rentrop grade <2, Age ≥75 years], E-CTO [operator Experience CTO], Ellis; RECHARGE [Registry of CrossBoss and Hybrid procedures in FrAnce, the NetheRlands, BelGium and UnitEd Kingdom]; W-CTO [Weighted CTO], PROGRESS-CTO, and CASTLE-CTO [CABG, Age, Stump anatomy, Tortuosity degree,

CENTRAL ILLUSTRATION The PROGRESS-CTO In-Hospital MACE Risk Score



Simsek B, et al. J Am Coll Cardiol Intv. 2022;15(14):1413–1422.

PROGRESS-CTO in-hospital MACE risk score. AUC = area under the receiver-operating characteristic curve; CTO = chronic total occlusion; MACE = major adverse cardiovascular event(s); PCI = percutaneous coronary intervention; PROGRESS-CTO = Prospective Global Registry for the Study of Chronic Total Occlusion Intervention.

Length of occlusion, Extent of calcification-CTO] scores) scores.[3,6,13-17] However, only 2 scores, the PROGRESS-CTO complications score[7] and the coronary perforation (OPEN-CLEAN [CABG, CTO Length, EF < 50%, Age, CalcificatioN] score),[8] have been developed to assess the risk of complications.

The PROGRESS-CTO complications score was developed 6 years ago to facilitate estimation of the risk of any of the following adverse events prior to hospital discharge: death, MI, recurrent symptoms requiring urgent repeat target vessel revascularization with PCI or CABG, tamponade requiring either pericardiocentesis or surgery, and stroke.[7] The score was based on a derivation set of 1,065 and a validation set of 504 CTO PCIs and included 3 variables (age, lesion length, and use of the retrograde approach).

The most recent American College of Cardiology/American Heart Association/Society for Coronary Angiography and Interventions guidelines for coronary artery revascularization downgraded the indication for CTO PCI from Class 2a to 2b. While expert operators can achieve technical success rates exceeding 85%, limiting MACE is essential, considering that the main indication for CTO PCI is alleviation of symptoms.[18,19] To address this need, we updated our MACE risk score based on the outcomes of >10,000 CTO PCIs and created separate complication scores allowing estimation of the risk of multiple complications (MACE, mortality, pericardiocentesis, and acute MI). The updated MACE score had significantly better AUC and net reclassification improvement. We also provided risk percentage intervals

(**Figures 3A to 3B**) corresponding to each score and the proportion of patients falling in each of the risk scores within the PROGRESS-CTO registry, and provided calculators with continuous outcomes (eg, age, LVEF) to allow individualized risk calculation.

Older age, moderate-severe calcification, and the use of ADR or the retrograde approach were independently associated with higher risk of MACE, death, and pericardiocentesis. This finding is consistent with other studies and older age is also included in the ORA and CASTLE scores.[3,13] Older patients are more likely to have complex coronary anatomy and high prevalence of comorbidities that could lead to complications.[20] CTO lesion length was associated with higher MACE rates in the initial PRORESS-CTO complications score,[7] and is part of the CL, J-CTO, Ellis, RECHARGE, W-CTO, E-CTO, and CASTLE-CTO scores; however, the latter scores were designed to estimate the likelihood of technical success or failure, whereas our scores were created to assess the risk of complications. While in the OPEN-CLEAN perforation score, CTO length was found to be associated with increased perforation risk,[8] our current analysis did not show any independent association between CTO length and risk of complications. We identified female sex as an independent risk factor for MACE and pericardiocentesis. This finding is similar to other studies in which women were shown to have higher perforation and bleeding rates.[21,22]

Our analysis revealed an independent association between moderate-severe lesion calcification and worse MACE, mortality, and pericardiocentesis. Lesion calcification is incorporated in the CL, J-CTO, RECHARGE, W-CTO, and CASTLE scores. Coronary calcification can hinder CTO crossing as well as equipment delivery and lesion expansion, especially when combined with tortuosity.[23] Heavily calcified lesions often require multiple modalities for lesion modification, such as intravascular lithotripsy and atherectomy, and are associated with multiple complications, such as perforation.[24]

We also found an independent association between blunt stump and MACE risk. In our analysis, blunt stump was associated with a 63% higher risk of MACE. Lesions with blunt stump often require higher penetration force guidewires or require retrograde crossing, which could be associated with higher complication rates.[18] Stump anatomy is also included in the CL, J-CTO, RECHARGE, W-CTO, E-CTO, and CASTLE scores.[3-5,14,16,17]

Our analysis showed that compared with AW, the use of ADR or retrograde strategies are independently associated with higher risk of MACE, death, and pericardiocentesis risk. While use of the retrograde approach significantly increased the success rate of CTO PCI, it is also associated with higher complication rates.[25] The retrograde approach should, therefore, not be the initial crossing strategy, if feasible.

STUDY LIMITATIONS. First, the PROGRESS-CTO registry is subject to the limitations of observational studies. Second, we do not have independent angiographic and clinical event adjudication. Third, biomarkers for MI were not systematically collected after CTO PCI, which could underestimate the MI rate. Fourth, the cases from which the models were built were performed between 2012 and 2022, which could create heterogeneity. Fifth, not all standard statistical conventions were followed (10:1 events per variable ratio), and as such the MI and mortality models may be overfitted. Therefore, there is a need for replication in other patient series. Sixth, operators in PROGRESS-CTO registry are highly experienced, potentially limiting extrapolation of the results to all CTO PCI practices. Seventh, long-term follow-up data are not available for the entire cohort.

CONCLUSIONS

Using 8 variables (age, sex, calcification status, stump, LVEF, prior CABG, atrial fibrillation, crossing strategy), we created the PROGRESS-CTO MACE, PROGRESS-CTO mortality, PROGRESS-CTO pericardiocentesis, and PROGRESS-CTO acute MI risk scores that showed acceptable to excellent discrimination for event prediction. These tools can be used to assess periprocedural complication risk and guide patient counseling and procedural planning but need validation in independent datasets.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors are grateful for the philanthropic support of our generous anonymous donors, and the philanthropic support of Drs. Mary Ann and Donald A. Sens, Mrs. Diane and Dr Cline Hickok, Mrs. Wilma and Mr. Dale Johnson, Mrs. Charlotte and Mr. Jerry Golinvaux Family Fund, the Roehl Family Foundation, and the Joseph Durda Foundation. The generous gifts of these donors to the Minneapolis Heart Institute Foundation's Science Center for Coronary Artery Disease helped support this research project. Dr Alaswad has served as a consultant and speaker for Boston Scientific, Abbott Cardiovascular, Teleflex, and CSI. Dr Davies has received honoraria from Boston Scientific, Medtronic, Siemens Healthineers, and Shockwave Medical. Dr ElGuindy has received consulting honoraria from Medtronic, Boston Scientific, Asahi Intecc, and Abbott; proctorship fees from Medtronic, Boston Scientific, Asahi Intecc, and Terumo; and educational grants from Medtronic. Dr Patel has received consulting honoraria from Abbott, Medtronic, Terumo, and Cardiovascular Systems. Dr Abi Rafeh has served as a CTO proctor and consultant for Boston Scientific and Abbott Vascular. Dr Karmpaliotis has received honoraria from Boston Scientific and Abbott Vascular; and owns equity in Saranas, Soundbite, and Traverse Vascular. Dr Khatri has received personal

honoraria for proctoring and speaking from Abbott Vascular, Asahi Intecc, Terumo, and Boston Scientific. Dr Jaffer has performed sponsored research for Canon, Siemens, Shockwave, Teleflex, Mercator, and Boston Scientific; has served as a consultant for Boston Scientific, Siemens, Magenta Medical, IMDS, Asahi Intecc, Biotronik, Philips, and Intravascular Imaging; owns equity interest in Intravascular Imaging and DurVena; and his employer (Massachusetts General Hospital) has licensing arrangements with Terumo, Canon, and Spectrawave, for which Dr Jaffer has right to receive royalties. Dr Doshi has served on the Speakers Bureau for Abbott Vascular, Boston Scientific, and Medtronic; and received research support from Biotronik. Dr Jaber has served on the advisory board for Medtronic; and received proctoring fees from Abbott Vascular. Dr Yeh has received grant or contract support from Abiomed, AstraZeneca, BD Bard, Boston Scientific, Cook Medical, Medtronic, and Philips; and consulting fees from Abbott, Boston Scientific, Edwards Lifesciences, Medtronic, and Shockwave Medical outside the submitted work. Dr Burke is a stockholder of MHI Ventures and Egg Medical. Dr Brilakis has received consulting or speaker honoraria from Abbott Vascular, the American Heart Association (associate editor, *Circulation*), Amgen, Asahi Intecc, Biotronik, Boston Scientific, the Cardiovascular Innovations Foundation (Board of Directors), ControlRad, CSI, Elsevier, GE Healthcare, IMDS, InfraRedx, Medicure, Medtronic, Opsens, Siemens, and Teleflex; has received research support from Boston Scientific, and GE Healthcare; is the owner of Hippocrates LLC; and is a shareholder of MHI Ventures, Cleerly Health, and Stallion Medical. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Emmanouil S. Brilakis, Minneapolis Heart Institute, 920 East 28th Street #300, Minneapolis, Minnesota 55407, USA. E-mail: esbrilakis@gmail.com. Twitter: @esbrilakis.

PERSPECTIVES

WHAT IS KNOWN? CTO PCI carries increased risk of complications. Accurate assessment of periprocedural risks is essential in risk-benefit assessment, patient counseling, and CTO PCI procedural planning.

WHAT IS NEW? The PROGRESS-CTO scores for MACE, in-hospital mortality, pericardiocentesis, and acute MI can assist with assessment of periprocedural risk in patients undergoing CTO PCI.

WHAT IS NEXT? External validation of the newly developed scores.

REFERENCES

1. Othman H, Seth M, Zein R, et al. Percutaneous coronary intervention for chronic total occlusion–the Michigan experience: insights from the BMC2 registry. *J Am Coll Cardiol Intv*. 2020;13:1357–1368.

2. Brilakis ES, Banerjee S, Karmpaliotis D, et al. Procedural outcomes of chronic total occlusion percutaneous coronary intervention: a report from the NCDR (National Cardiovascular Data Registry). *J Am Coll Cardiol Intv*. 2015;8:245–253.

3. Szijgyarto Z, Rampat R, Werner GS, et al. Derivation and validation of a chronic total coronary occlusion intervention procedural success score from the 20,000-patient EuroCTO registry: the EuroCTO (CASTLE) score. *J Am Coll Cardiol Intv*. 2019;12:335–342.

4. Morino Y, Abe M, Morimoto T, et al. 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. *J Am Coll Cardiol Intv*. 2011;4:213–221.

5. Alessandrino G, Chevalier B, Lefèvre T, et al. A clinical and angiographic scoring system to predict the probability of successful first-attempt percutaneous coronary intervention in patients with total chronic coronary occlusion. *J Am Coll Cardiol Intv*. 2015;8:1540–1548.

6. Christopoulos G, Kandzari DE, Yeh RW, et al. 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. *J Am Coll Cardiol Intv*. 2016;9:1–9.

7. Danek BA, Karatasakis A, Karmpaliotis D, et al. 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. *J Am Heart Assoc*. 2016;5:e004272.

8. Hirai T, Grantham JA, Sapontis J, et al. Development and validation of a prediction model for angiographic perforation during chronic total occlusion percutaneous coronary intervention: OPEN-CLEAN perforation score. *Catheter Cardiovasc Interv*. 2022;99:280–285.

9. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42:377–381.

10. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform*. 2019;95:103208.

11. Ybarra LF, Rinfret S, Brilakis ES, et al. Definitions and clinical trial design principles for coronary artery chronic total occlusion therapies: CTO-ARC Consensus recommendations. *Circulation*. 2021;143:479–500.

12. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *Eur Heart J*. 2012;33:2551–2567.

13. Galassi AR, Boukhris M, Azzarelli S, Castaing M, Marzà F, Tomasello SD. Percutaneous coronary revascularization for chronic total occlusions: a novel predictive score of technical failure using advanced technologies. *J Am Coll Cardiol Intv*. 2016;9:911–922.

14. Mohandes M, Moreno C, Fuertes M, et al. New scoring system for predicting percutaneous coronary intervention of chronic total occlusion success: Impact of operator's experience. *Cardiol J*. Published online September 28, 2021. https://doi.org/10.5603/CJ.a2021.0109

15. Ellis SG, Burke MN, Murad MB, et al. Predictors of successful hybrid-approach chronic total coronary artery occlusion stenting: an improved model with novel correlates. *J Am Coll Cardiol Intv*. 2017;10:1089–1098.

16. Maeremans J, Spratt JC, Knaapen P, et al. Towards a contemporary, comprehensive scoring system for determining technical outcomes of hybrid percutaneous chronic total occlusion treatment: the RECHARGE score. *Catheter Cardiovasc Interv*. 2018;91:192–202.

17. Khanna R, Pandey CM, Bedi S, Ashfaq F, Goel P. A weighted angiographic scoring model (W-CTO score) to predict success of antegrade wire crossing in chronic total occlusion: analysis from a single centre. *AsiaIntervention*. 2018;4:18–25.

18. Brilakis ES, Mashayekhi K, Tsuchikane E, et al. Guiding principles for chronic total occlusion

percutaneous coronary intervention. *Circulation*. 2019;140:420–433.

19. Azzalini L, Karmpaliotis D, Santiago R, et al. Contemporary issues in chronic total occlusion percutaneous coronary intervention. *J Am Coll Cardiol Intv*. 2022;15:1–21.

20. André R, Dumonteil N, Lhermusier T, et al. 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.

21. Sharma V, Wilson W, Smith W, et al. Comparison of characteristics and complications in men versus women undergoing chronic total occlusion percutaneous intervention. *Am J Cardiol*. 2017;119:535–541.

22. Cheney A, Kearney KE, Lombardi W. Sex-based differences in chronic total occlusion management. *Curr Atheroscler Rep*. 2018;20:60.

23. Karacsonyi J, Karmpaliotis D, Alaswad K, et al. Impact of calcium on chronic total occlusion percutaneous coronary interventions. *Am J Cardiol*. 2017;120:40–46.

24. Azzalini L, Poletti E, Ayoub M, et al. Coronary artery perforation during chronic total occlusion percutaneous coronary intervention: epidemiology, mechanisms, management, and outcomes. *EuroIntervention*. 2019;15:e804–e811.

25. Megaly M, Xenogiannis I, Abi Rafeh N, et al. Retrograde approach to chronic total occlusion percutaneous coronary intervention. *Circ Cardiovasc Interv*. 2020;13:e008900.

KEY WORDS acute myocardial infarction, chronic total occlusion, MACE, mortality, percutaneous coronary intervention, pericardiocentesis, risk prediction

APPENDIX For an expanded Methods section and a supplemental figure, please see the online version of this paper.