Clinical Research

Validating the Performance of 5 Risk Scores for Major Adverse Cardiac Events in Patients Who Achieved Complete Revascularization After Percutaneous Coronary Intervention

Dong Zhang, MD,[a],* Ruohua Yan, PhD,[a,b],* Guofeng Gao, MD,[a] Hao Wang, MD,[a] Rui Fu, MD,[a] Jia Li, MD,[a] Dong Yin, MD,[a] Chenggang Zhu, MD,[a] Lei Feng, MD,[a] Weihua Song, MD,[a] Bo Xu, MBBS,[a] Kefei Dou, MD,[a] and Yuejin Yang, MD[a]

[a] State Key Laboratory of Cardiovascular Disease, Department of Cardiology, Cardiovascular Institute, Fuwai Hospital and National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

[b] Center for Clinical Epidemiology and Evidence-based Medicine, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing, China

ABSTRACT

Background: Risk scores, like the **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score (SS), clinical SS, logistic SS (core model and extended model [LSS_extended]), **A**ge, **C**reatinine, and **E**jection **F**raction (ACEF) score, and modified ACEF score, are predictive for major adverse cardiac events (MACE; including all-cause mortality, myocardial infarction [MI], and revascularization) in patients who have undergone percutaneous coronary intervention (PCI). However, few studies have validated the performance of these scores in complete revascularization (CR) patients. We aimed to compare the performance of previous risk scores in patients who achieved CR after PCI.

Methods: All patients (N = 10,724) who underwent PCI at Fuwai Hospital in 2013 were screened, and those who achieved CR after PCI

RÉSUMÉ

Contexte : Les scores de risque comme le score SYNTAX (*Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery*) (SS), le SS clinique, le SS logistique (modèle de base et modèle étendu [LSS_étendu]), le score ACEF (*Age, Creatinine, and Ejection Fraction*) (ACEF) et le score ACEF modifié, permettent de prédire les événements cardiaques indésirables majeurs (ECIM, y compris la mortalité toutes causes confondues, l'infarctus du myocarde [IM] et la revascularisation) chez les patients ayant subi une intervention coronarienne percutanée (ICP). Toutefois, rares sont les études qui ont confirmé l'efficacité de ces scores chez les patients ayant obtenu une revascularisation complète (RC). Nous avons voulu comparer l'efficacité des scores de risque susmentionnés chez des patients ayant obtenu une RC après une ICP.

Complete revascularization (CR), which is defined as revascularization of all diseased coronary artery segments, has been reported to be associated with better long-term prognoses and clinical outcomes compared with the prognoses and outcomes of incomplete revascularization in patients who have undergone percutaneous coronary intervention (PCI).[1,2] Because CR is considered to be the optimal PCI strategy, interventionalists tend to revascularize all coronary arteries

whenever possible. It has been reported that approximately 40%-60% of patients achieve CR after PCI.[3-5] However, among patients who achieve CR after PCI, it is still unpredictable as to which subgroup of patients will have favourable prognoses and which subgroup is at high risk for adverse events in the long term.

Clinical prediction models, such as the **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score (SS), the derived scores of SS (residual SS [RSS], clinical SS [CSS], and logistic SS [LSS; core model (LSS_core) and extended model (LSS_extended)]), **A**ge, **C**reatinine, and **E**jection **F**raction (ACEF) score (AS), and modified AS (MAS), have been shown to predict adverse outcomes in patients who have undergone PCI.[5-10] However, few large-sample studies have been performed to validate the predictive capacities of these scores in CR patients.

Thus, the present study aimed to evaluate and compare the performance of these risk scores (SS, CSS, LSS_core, LSS_extended,

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were enrolled. Risk scores were calculated by experienced cardiologists blinded to the clinical outcomes. Discrimination of risk scores was assessed according to the area under the receiver operating characteristic curve (AUC).

Results: Fifty-one percent (5375/10,724) of patients who underwent PCI achieved CR. At a mean follow-up of 2.4 years, the mortality, MI, revascularization, and MACE rates were 1.2%, 1.0%, 6.3%, and 7.7%, respectively. SS was not predictive for mortality (AUC, 0.51; 95% confidence interval [CI], 0.44-0.59). All scores involving clinical variables, especially modified ACEF score (AUC, 0.73; 95% CI, 0.66-0.79), could predict mortality. LSS$_{extended}$ was the most accurate for MI (AUC, 0.68; 95% CI, 0.61-0.75). SS and LSS$_{extended}$ were predictive for revascularization, with marginally significant AUCs (SS, 0.54; LSS$_{extended}$, 0.55). No score was particularly accurate for predicting MACE, with AUCs ranging from 0.51 (ACEF score) to 0.58 (LSS$_{extended}$).

Conclusions: In CR patients, risk scores involving clinical variables might help to predict mortality; however, no risk scores showed helpful discrimination for MACE.

Méthodologie : Tous les patients (N = 10 724) ayant subi une ICP en 2013 à l'hôpital Fuwai ont été examinés et ceux qui ont obtenu une RC après une ICP ont été inclus dans l'étude. Les scores de risque ont été calculés par des cardiologues expérimentés qui n'étaient pas informés des issues cliniques de l'intervention. La discrimination des scores de risque a été évaluée par l'aire sous la courbe (ASC) ROC (*receiver operating characteristic*).

Résultats : Cinquante et un pour cent (5375/10 724) des patients ayant subi une ICP ont obtenu une RC. Après une période de suivi moyenne de 2,4 ans, les taux de mortalité, d'IM, de revascularisation et d'ECIM étaient de 1,2 %, 1,0 %, 6,3 % et 7,7 %, respectivement. Le SS ne permettait pas de prédire la mortalité (ASC, 0,51; intervalle de confiance [IC] à 95 %, de 0,44 à 0,59). Tous les scores tenant compte de variables cliniques, en particulier le score ACEF modifié (ASC, 0,73; IC à 95 %, de 0,66 à 0,79), étaient prédictifs de la mortalité. Le LSS$_{étendu}$ était le plus précis pour l'IM (ASC, 0,68; IC à 95 %, de 0,61 à 0,75). Le SS et le LSS$_{étendu}$ étaient prédictifs de la revascularisation, avec des valeurs de l'ASC marginalement significatives (SS, 0,54; LSS$_{étendu}$, 0,55). Aucun score n'a permis de prédire de façon particulièrement précise la survenue des ECIM, pour lesquels la valeur de l'ASC variait de 0,51 (score ACEF) à 0,58 (LSS$_{étendu}$).

Conclusions : Chez les patients RC, les scores de risque tenant compte de variables cliniques pourraient contribuer à prédire la mortalité; toutefois, aucun score de risque ne présentait une discrimination suffisante pour prédire la survenue des ECIM.

AS, and MAS) for predicting adverse cardiac events in patients who achieved CR after PCI.

Methods

Study population

Between January 2013 and December 2013, 10,724 consecutive patients underwent PCI at Fuwai Hospital in Beijing, China. Among these patients, only those who achieved CR after PCI were included in this study. CR was defined as RSS equal to 0.[5] The exclusion criteria were as follows: (1) history of coronary artery bypass grafting; and (2) hybrid coronary revascularization. Of the 10,724 patients, 5375 were eligible for this all-comer single-centre retrospective study.

The ethics committee of the Cardiovascular Institute and Fuwai Hospital approved this study.

Procedure and periprocedural medications

In all patients, the interventional strategy and instrumentation used were at the discretion of the interventional cardiologists. Coronary angioplasty was performed in the conventional manner, and coronary stents or other procedures/devices were used only when required.

Periprocedural antiplatelet and antithrombotic medications were administered at the discretion of the operator and according to current guidelines. For patients who did not receive clopidogrel and aspirin within 7 days, administration of 300 mg clopidogrel and 300 mg aspirin as loading doses within 24 hours before the procedure was mandatory. Lifelong aspirin (100 mg/d) was prescribed to all patients. Additionally, at least 12 months of clopidogrel (75 mg/d) was recommended to all patients.

Score calculations

Experienced interventional cardiologists who were blinded to the clinical outcomes performed score calculations in the core laboratory of Fuwai Hospital. If interobserver grading differed, consensus was reached after review. Baseline SS was calculated for each patient by scoring all coronary lesions using the SS algorithm, as described previously.[6,11] AS was calculated using the following formula: age (years)/ejection fraction (%) + 1 (if the serum creatinine level is > 2 mg/dL).[9] MAS was calculated using the following formula: age/ejection fraction + 1 point for every 10 mL/min reduction in creatinine clearance below 60 mL/min/1.73 m^2 (up to a maximum of 6 points).[7] CSS was calculated by multiplying the value of SS by MAS. LSS was calculated according to the method described in previous studies, and the scores for LSS$_{core}$ and LSS$_{extended}$ were recorded.[8,12] Among the 5375 patients, 133 had missing data for left ventricular ejection fraction and 1 had missing data for serum creatinine level. For these patients, single imputation was performed using the median of existing data. In total, 134 (2.49%) missing data items were imputed.

Data collection and definitions

Clinical data were obtained via a review of the medical records. All baseline and procedural cine angiograms were reviewed and analyzed by reviewers from an independent core laboratory. Coronary angiography findings, including lesion location, baseline **T**hrombolysis **i**n **M**yocardial **I**nfarction (TIMI) flow grade, thrombus-containing lesions, and stenosis diameter, were recorded. Additionally, procedural characteristics, including multivessel treatment, total stent length, and bifurcation treatment, were recorded. Blood samples were

routinely obtained from all patients before the procedure. Creatinine clearance was assessed using the Cockcroft-Gault equation.[13]

Follow-up data were obtained during outpatient clinic visits or via phone. The vital signs of each patient were determined by performing assessments during outpatient clinic visits or by evaluating patient-/family-reported data. If necessary, the vital status and cause of death were ascertained from the National Death Registry of China (Centers for Disease Control and Prevention's Death Registry System).

The term, "major adverse cardiac events" (MACE) indicated the composite of myocardial infarction (MI), revascularization, and all-cause mortality. The definition of periprocedural myocardial injury is presented in the *Methods* section of the Supplementary Material. All end points were defined according to Academic Research Consortium definitions.[14]

Statistical methods

Continuous data are presented as mean $\pm$ SD, and the data were compared using Student t test or the nonparametric test as appropriate. Categorical data are presented as counts and percentages, and the data were compared using the χ^2 test.

To assess the relationships between the risk scores and the incidence of mortality and MACE, we determined the tertiles of each score and evaluated the trends of event rates across tertiles using the Cochran-Armitage test.

The discrimination of risk scores was determined according to the area under the receiver operating characteristic curve (AUC),[15] with 0.5 indicating chance and 1 indicating perfect discrimination. AUCs were compared using a nonparametric approach, which has been described previously.[16] The calibration of risk scores was measured according to the calibration slope[17] (plotting the observed proportions vs the predicted probabilities), with 1 indicating perfect calibration. The utility of risk scores was described according to the decision curve,[18,19] with a higher net benefit across the range of thresholds indicating better clinical effects. The performance of each score compared with SS was evaluated according to the AUC improvement, continuous net reclassification improvement (NRI), and integrated discriminatory improvement (IDI).[20] To further account for the time to the event, the C-statistics of Cox regression models were calculated.[21] Patients with 3-vessel disease (3-VD) and/or left main disease (LM) were considered as high-risk patients, and for these patients, we performed a subgroup analysis to validate the discrimination and calibration of the risk scores. All P values were 2-tailed, and a P value < 0.05 was considered statistically significant. All statistical analyses were performed using SAS 9.4 software (SAS Institute, Cary, NC).

Results

Rates of adverse events

The proportion of patients who achieved CR after PCI was 50.1% (5375/10,724). The mean follow-up duration was 2.4 years. After the procedure, 40 patients were lost to follow-up at 1 year and 36 additional patients were lost to follow-up at 2 years. Thus, 5299 (98.6%) patients completed follow-up for 2 years. During the follow-up, the mortality, MI, and revascularization rates were 1.2%, 1.0%, and 6.3%, respectively, and the cumulative MACE rate was 7.7% (415/5375).

Among all CR patients, 25.4% (1363/5375) had 3-VD and/or LM. The event rates were higher in these high-risk patients, with mortality, MI, revascularization, and MACE rates of 1.2%, 1.3%, 9.1%, and 10.5%, respectively.

Baseline, lesion, and procedure characteristics

The baseline characteristics of the CR patients are presented in Table 1. The mean patient age was 57.3 years, and the proportion of male patients was 77.0% (4140/5375). Among all patients, the left ventricular ejection fraction was significantly lower, and histories of diabetes mellitus, MI, PCI, and cerebrovascular disease were significantly more frequent in the MACE group than in the non-MACE group. The other baseline characteristics were not significantly different between the MACE and non-MACE groups. Among patients in the 3-VD and/or LM subgroup, similar trends were noted; however, the differences were less significant.

Table 1 also shows the lesion and procedure characteristics. Among all patients, chronic total occlusion and type C lesions were significantly more frequent in the MACE group than in the non-MACE group. However, transradial PCI was significantly more frequently performed in the non-MACE group than in the MACE group. An intra-aortic balloon pump was more frequently used during PCI in the MACE group than in the non-MACE group. Among patients in the 3-VD and/or LM subgroup, similar trends were noted.

More details on the baseline, lesion, and procedure characteristics are presented in Supplemental Tables S1-S6.

Distributions of risk scores

The distributions of risk scores are presented in Figure 1 (for all CR patients) and Supplemental Figure S1 (for patients with 3-VD and/or LM). All risk scores showed abnormal distribution (all P values for normality < 0.01).

Supplemental Table S7 shows the median and interquartile range values of the risk scores according to event. Among all patients, SS, CSS, LSS_{core}, and $LSS_{extended}$ were significantly higher in the MACE group than in the non-MACE group (SS: 8 vs 7, $P = 0.01$; CSS: 7.22 vs 6.56, $P < 0.01$; LSS_{core}: 4 vs 3, $P < 0.01$; and $LSS_{extended}$: 9 vs 8, $P < 0.01$, respectively). There was no significant difference in AS and MAS between the groups. Among patients in the 3-VD and/or LM subgroup, similar trends were noted (Supplemental Table S8).

With regard to the incidence of MACE across the tertiles of risk scores (Supplemental Table S9), we found that the MACE rate increased significantly for SS and its derived scores. However, for AS and MAS, there were no significant differences.

Discrimination of risk scores

Figure 2 shows the receiver operating characteristic curves of the risk scores for mortality, MI, revascularization, and MACE according to logistic regression analyses. The accompanying odds ratios and AUCs are presented in Table 2. The performance of each score compared with SS is presented in Table 2 (AUC improvement), Table 3 (NRI), and Table 4 (IDI).

Table 1. Baseline, lesion, and procedure characteristics

Characteristic	All CR patients				Patients with 3-VD and/or LM			
	Total (n = 5375)	MACE (n = 415, 7.7%)	Non-MACE (n = 4960, 92.3%)	P*	Total (n = 1363)	MACE (n = 143, 10.5%)	Non-MACE (n = 1220, 89.5%)	P*
Age, years	57.3 ± 10.3	57.6 ± 10.4	57.3 ± 10.3	0.50	58.8 ± 10.3	58.8 ± 10.8	58.8 ± 10.2	1.00
Male sex	4140 (77.0)	328 (79.0)	3812 (76.9)	0.31	1050 (77.0)	115 (80.4)	935 (76.6)	0.31
BMI	25.9 ± 3.2	25.9 ± 3.2	25.9 ± 3.2	0.89	25.9 ± 3.4	26.2 ± 3.4	25.9 ± 3.4	0.32
EF, %	63.2 ± 6.9	62.1 ± 7.5	63.2 ± 6.9	0.003	62.6 ± 7.3	61.5 ± 7.7	62.7 ± 7.3	0.08
CCR, mL/min	99.9 ± 27.8	99.9 ± 28.7	99.9 ± 27.7	0.99	98.2 ± 28.9	99.0 ± 29.3	98.1 ± 28.9	0.73
Diabetes mellitus	1398 (26.0)	135 (32.5)	1263 (25.5)	0.002	446 (32.7)	57 (39.9)	389 (31.9)	0.05
Hypertension	3321 (61.8)	267 (64.3)	3054 (61.6)	0.27	882 (64.7)	101 (70.6)	781 (64.0)	0.12
Hyperlipidemia	3545 (66.0)	283 (68.2)	3262 (65.8)	0.32	894 (65.6)	104 (72.7)	790 (64.8)	0.06
Diagnosis at PCI				0.91				0.38
STEMI	763 (14.2)	64 (15.4)	699 (14.1)		189 (13.9)	24 (16.8)	165 (13.5)	
NSTEMI	232 (4.3)	17 (4.1)	215 (4.3)		67 (4.9)	9 (6.3)	58 (4.8)	
Unstable angina	2340 (43.5)	178 (42.9)	2162 (43.6)		542 (39.8)	61 (42.7)	481 (39.4)	
Stable angina	1619 (30.1)	127 (30.6)	1492 (30.1)		455 (33.4)	41 (28.7)	414 (33.9)	
Asymptomatic	421 (7.8)	29 (7.0)	392 (7.9)		110 (8.1)	8 (5.6)	102 (8.4)	
Previous MI	884 (16.5)	83 (20.0)	801 (16.2)	0.04	278 (20.4)	32 (22.4)	246 (20.2)	0.53
Previous PCI	1203 (22.4)	116 (28.0)	1087 (21.9)	0.005	342 (25.1)	39 (27.3)	303 (24.8)	0.52
Previous cerebrovascular disease	491 (9.1)	55 (13.3)	436 (8.8)	0.002	140 (10.3)	20 (14.0)	120 (9.8)	0.12
Current smoker	3057 (56.9)	252 (60.7)	2805 (56.6)	0.10	786 (57.9)	86 (60.1)	700 (57.4)	0.53
COPD	114 (2.1)	9 (2.2)	105 (2.1)	0.94	21 (1.5)	3 (2.1)	18 (1.5)	0.48
Peripheral vascular disease	121 (2.3)	10 (2.4)	111 (2.2)	0.82	36 (2.6)	1 (0.7)	35 (2.9)	0.17
Lesion type				< 0.001				0.08
A	494 (9.2)	25 (6.0)	469 (9.5)		50 (3.7)	1 (0.7)	49 (4.0)	
B1	957 (17.8)	64 (15.4)	893 (18.0)		146 (10.7)	18 (12.6)	128 (10.5)	
B2	969 (18.0)	58 (14.0)	911 (18.4)		188 (13.8)	14 (9.8)	174 (14.3)	
C	2955 (55.0)	268 (64.6)	2687 (54.2)		979 (71.8)	110 (76.9)	869 (71.2)	
CTO	935 (17.4)	110 (26.5)	825 (16.6)	< 0.001	345 (25.3)	59 (41.3)	286 (23.4)	< 0.001
Transradial approach	5131 (95.5)	386 (93.0)	4745 (95.7)	0.01	1291 (94.7)	130 (90.9)	1161 (95.2)	0.03
Total length of stents, mm	38.8 ± 26.3	41.3 ± 26.5	38.5 ± 26.3	0.002	54.5 ± 32.9	53.5 ± 28.9	54.6 ± 33.3	0.69
IABP	57 (1.1)	14 (3.4)	43 (0.9)	< 0.001	31 (2.3)	7 (4.9)	24 (2.0)	0.04

Data are mean ± SD or n (%) unless otherwise stated.

BMI, body mass index; CCR, creatinine clearance rate; COPD, chronic obstructive pulmonary disease; CR, complete revascularization; CTO, chronic total occlusion; EF, ejection fraction; IABP, intra-aortic balloon pump; LM, left main disease; MACE, major adverse cardiovascular events; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; 3-VD, 3-vessel disease.

*Comparisons between MACE and non-MACE were made using Student t tests for continuous variables and χ^2 tests or Fisher exact tests as appropriate for categorical variables.
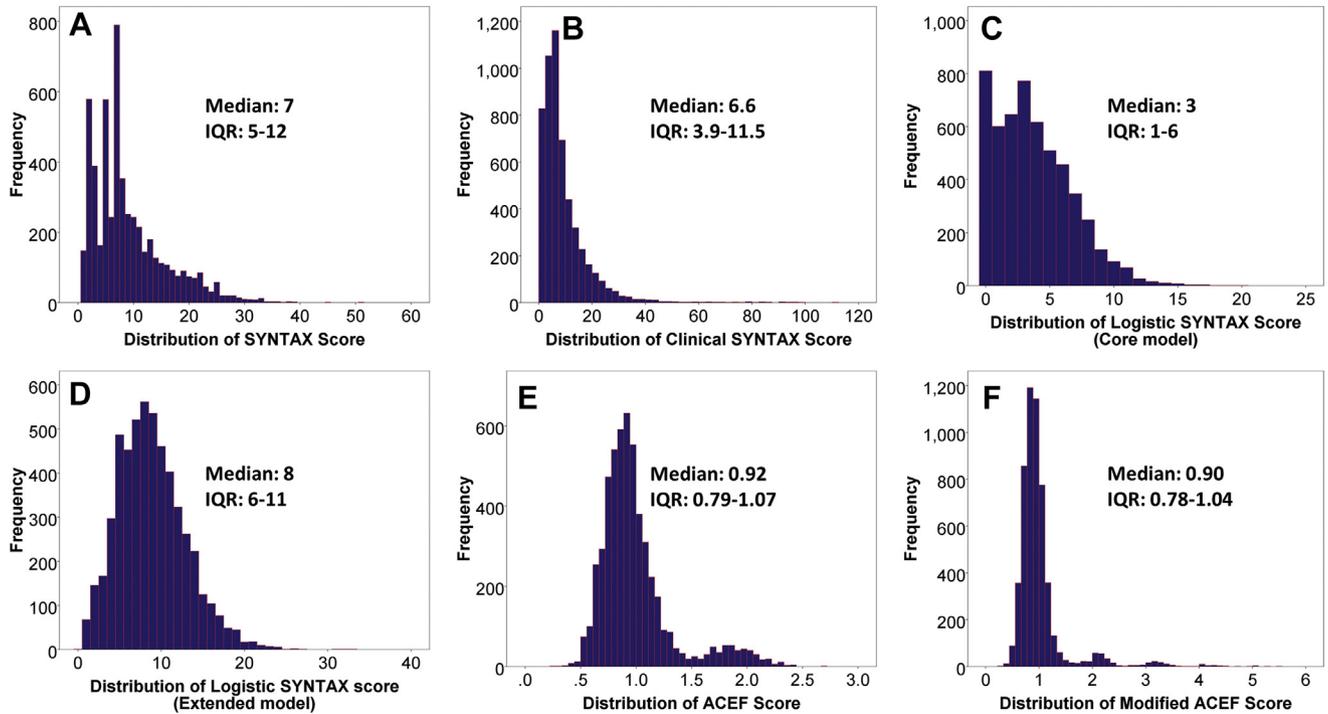
Figure 1. Distributions of risk scores for all CR patients. All of these risk scores were abnormal distribution (All *P* value for normality < 0.01). (**A**) Distribution of SYNTAX score. (**B**) Distribution of clinical SYNTAX score. (**C**) Distribution of logistic SYNTAX score (core model). (**D**) Distribution of logistic SYNTAX score (extended model). (**E**) Distribution of ACEF score. (**F**) Distribution of modified ACEF score. ACEF, **A**ge, **C**reatinine, and **E**jection **F**raction; IQR, interquartile range; SYNTAX, **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery.

Discrimination for mortality. SS was not predictive for mortality (AUC, 0.51; 95% confidence interval [CI], 0.44-0.59). All scores involving clinical variables (CSS, LSS_core, LSS_extended, AS, and MAS) could predict mortality significantly better than chance (all *P* < 0.05). The AUCs of these scores ranged from 0.60 (CSS) to 0.73 (MAS; Table 2).

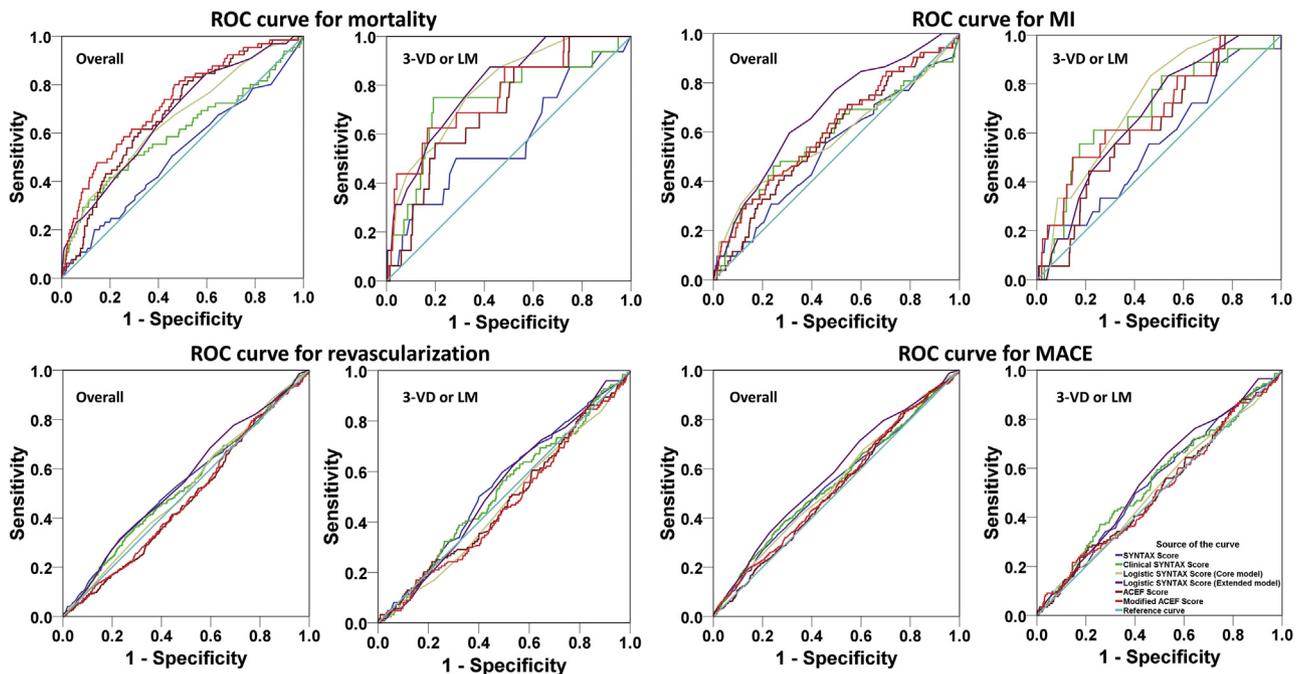Among the scores, MAS showed the highest AUC (0.73; 95% CI, 0.66-0.79). The odds ratio of MAS for mortality was

Figure 2. Receiver operating characteristic (ROC) curves of risk scores for mortality, myocardial infarction (MI), revascularization, and major adverse cardiac events (MACE). Area under the ROC curves are shown in Table 2. ACEF, **A**ge, **C**reatinine, and **E**jection **F**raction; LM, left main disease; SYNTAX, **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery; 3-VD, 3-vesseal disease.

Table 2. Discrimination of risk scores

	All CR patients			Patients with 3-VD and/or LM		
	OR (95% CI)	AUC (95% CI)*	Comparison with the AUC of SS (95% CI)	OR (95% CI)	AUC (95% CI)*	Comparison with the AUC of SS (95% CI)
Mortality						
SS	1.01 (0.98-1.05)	0.51 (0.44-0.59)	–	1.04 (0.99-1.11)	0.58 (0.42-0.73)	–
CSS	1.03 (1.02-1.05)[†]	0.60 (0.52-0.68)[†]	0.09 (0.06-0.12)[‡]	1.04 (1.02-1.06)[†]	0.74 (0.60-0.89)[†]	0.17 (0.05-0.29)[‡]
LSS_core	1.21 (1.13-1.30)[†]	0.66 (0.59-0.73)[†]	0.15 (0.07-0.22)[‡]	1.40 (1.22-1.59)[†]	0.79 (0.69-0.89)[†]	0.21 (0.06-0.37)[‡]
LSS_extended	1.17 (1.11-1.22)[†]	0.67 (0.61-0.74)[†]	0.16 (0.08-0.24)[‡]	1.26 (1.15-1.37)[†]	0.80 (0.70-0.90)[†]	0.22 (0.03-0.41)[‡]
AS	3.12 (1.81-5.38)[†]	0.68 (0.62-0.74)[†]	0.17 (0.09-0.25)[‡]	3.27 (1.16-9.17)[†]	0.70 (0.58-0.82)[†]	0.12 (−0.08 to 0.33)
MAS	2.19 (1.73-2.77)[†]	0.73 (0.66-0.79)[†]	0.21 (0.13-0.29)[‡]	2.72 (1.77-4.18)[†]	0.76 (0.64-0.89)[†]	0.19 (−0.04 to 0.41)
MI						
SS	1.02 (0.99-1.06)	0.53 (0.44-0.61)	–	1.04 (0.98-1.10)	0.56 (0.42-0.70)	–
CSS	1.02 (1.00-1.04)[†]	0.58 (0.49-0.67)	0.05 (0.02-0.09)[‡]	1.02 (1.00-1.05)	0.69 (0.56-0.82)[†]	0.13 (0.02-0.24)[‡]
LSS_core	1.12 (1.03-1.21)[†]	0.58 (0.49-0.67)	0.05 (−0.04 to 0.14)	1.23 (1.07-1.40)[†]	0.73 (0.64-0.82)[†]	0.17 (0.01-0.32)[‡]
LSS_extended	1.14 (1.08-1.21)[†]	0.68 (0.61-0.75)[†]	0.15 (0.07-0.24)[‡]	1.11 (1.01-1.23)[†]	0.68 (0.57-0.78)[†]	0.11 (−0.07 to 0.30)
AS	1.76 (0.87-3.53)	0.58 (0.50-0.66)[†]	0.05 (−0.05 to 0.16)	1.81 (0.59-5.58)	0.63 (0.51-0.74)[†]	0.07 (−0.15 to 0.29)
MAS	1.65 (1.19-2.30)[†]	0.61 (0.53-0.69)[†]	0.08 (−0.02 to 0.19)	2.02 (1.25-3.25)[†]	0.69 (0.56-0.81)[†]	0.13 (−0.10 to 0.35)
Revascularization						
SS	1.02 (1.01-1.04)[†]	0.54 (0.51-0.57)[†]	–	1.01 (0.99-1.04)	0.54 (0.49-0.59)	–
CSS	1.01 (0.99-1.02)	0.53 (0.49-0.56)	−0.01 (−0.02 to 0.00)[§]	1.00 (0.98-1.02)	0.48 (0.43-0.54)	−0.06 (−0.16 to 0.05)
LSS_core	1.02 (0.98-1.06)	0.52 (0.49-0.55)	−0.02 (−0.06 to 0.01)	0.96 (0.89-1.03)	0.53 (0.48-0.58)	−0.01 (−0.09 to 0.08)
LSS_extended	1.04 (1.01-1.07)[†]	0.55 (0.52-0.58)[†]	0.01 (−0.03 to 0.05)	1.02 (0.97-1.06)	0.53 (0.48-0.58)	−0.01 (−0.08 to 0.06)
AS	0.75 (0.53-1.08)	0.52 (0.49-0.56)	−0.01 (−0.06 to 0.03)	0.90 (0.53-1.55)	0.52 (0.47-0.57)	−0.02 (−0.10 to 0.06)
MAS	0.86 (0.67-1.11)	0.52 (0.49-0.55)	−0.02 (−0.06 to 0.03)	0.81 (0.54-1.21)	0.54 (0.48-0.59)	−0.00 (−0.08 to 0.07)
MACE						
SS	1.02 (1.01-1.04)[†]	0.54 (0.51-0.57)[†]	–	1.02 (1.00-1.04)	0.55 (0.50-0.59)	–
CSS	1.02 (1.01-1.02)[†]	0.54 (0.51-0.57)[†]	0.01 (−0.01 to 0.02)	1.01 (1.00-1.02)	0.55 (0.50-0.60)	0.00 (−0.03 to 0.03)
LSS_core	1.06 (1.03-1.09)[†]	0.54 (0.51-0.57)[†]	0.01 (−0.03 to 0.04)	1.03 (0.97-1.10)	0.52 (0.46-0.57)	−0.03 (−0.09 to 0.03)
LSS_extended	1.07 (1.04-1.09)[†]	0.58 (0.55-0.61)[†]	0.04 (0.01-0.08)[‡]	1.06 (1.01-1.10)[†]	0.57 (0.52-0.61)[†]	0.02 (−0.04 to 0.08)
AS	1.09 (0.81-1.46)	0.51 (0.49-0.54)	−0.02 (−0.06 to 0.02)	1.15 (0.71-1.85)	0.51 (0.46-0.56)	−0.03 (−0.10 to 0.04)
MAS	1.20 (1.01-1.43)[†]	0.53 (0.50-0.56)	−0.01 (−0.05 to 0.03)	1.16 (0.87-1.56)	0.51 (0.46-0.56)	−0.04 (−0.11 to 0.03)

AS, **A**ge, **C**reatinine, and **E**jection **F**raction (ACEF) score; AUC, area under the receiver operating characteristic curve; CSS, clinical **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score; CI, confidence interval; CR, complete revascularization; LM, left main disease; LSS_core, logistic **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score (core model); LSS_extended, logistic **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score (extended model); MACE, major adverse cardiovascular events; MAS, modified **A**ge, **C**reatinine, and **E**jection **F**raction (ACEF) score; MI, myocardial infraction; OR, odds ratio; SS, **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score; 3-VD, 3-vessel disease.

* Calculated using logistic regression models.

[†] $P < 0.05$.

[‡] Significantly improved from the AUC of SYNTAX score.

[§] Significantly decreased from the AUC of SYNTAX score.

Table 3. Net reclassification improvement of risk scores (compared with SYNTAX score)

	All CR patients			Patients with 3-VD and/or LM		
	NRI (95% CI)	Event correctly reclassified	Nonevent correctly reclassified	NRI (95% CI)	Event correctly reclassified	Nonevent correctly reclassified
Mortality						
CSS	0.48 (0.24-0.72)*	−13.8%	61.8%	0.66 (0.17-1.15)*	−12.5%	78.6%
LSS$_{core}$	0.47 (0.23-0.71)*	13.8%	33.3%	0.57 (0.08-1.06)*	12.5%	44.3%
LSS$_{extended}$	0.39 (0.15-0.63)*	4.6%	34.4%	0.83 (0.37-1.29)*	37.5%	45.4%
AS	0.54 (0.30-0.79)*	7.7%	46.8%	0.42 (−0.06 to 0.90)	25.0%	16.9%
MAS	0.54 (0.30-0.78)*	−17.0%	71.0%	0.79 (0.31-1.27)*	25.0%	54.0%
MI						
CSS	0.34 (0.06-0.61)*	3.8%	29.8%	0.09 (−0.48 to 0.55)	0	8.8%
LSS$_{core}$	0.17 (−0.10 to 0.44)	0	17.0%	0.36 (−0.11 to 0.82)	11.1%	24.5%
LSS$_{extended}$	0.52 (0.25-0.78)*	23.0%	28.4%	0.26 (−0.20 to 0.73)	11.1%	15.2%
AS	0.07 (−0.20 to 0.35)	0	7.4%	−0.08 (−0.55 to 0.38)	0	−8.3%
MAS	0.10 (−0.17 to 0.37)	−15.4%	25.0%	0.24 (−0.22 to 0.71)	0	24.2%
Revascularization						
CSS	−0.21 (−0.31 to −0.10)†	11.2%	−31.8%	−0.17 (−0.36 to 0.01)	3.2%	−20.4%
LSS$_{core}$	−0.09 (−0.20 to 0.02)	8.8%	−17.6%	0.01 (−0.17 to 0.19)	14.5%	−13.5%
LSS$_{extended}$	0.07 (−0.04 to 0.18)	3.6%	3.4%	−0.14 (−0.33 to 0.04)	−6.5%	−7.8%
AS	−0.07 (−0.18 to 0.04)	15.8%	−22.8%	−0.08 (−0.27 to 0.10)	9.7%	−18.0%
MAS	−0.12 (−0.23 to −0.01)†	15.3%	−27.2%	−0.07 (−0.25 to 0.11)	17.7%	−24.6%
MACE						
CSS	−0.03 (−0.13 to 0.07)	0.2%	−3.6%	−0.08 (−0.26 to 0.09)	−9.1%	0.7%
LSS$_{core}$	0.01 (−0.09 to 0.11)	−6.5%	7.0%	−0.13 (−0.31 to 0.04)	−4.9%	−8.4%
LSS$_{extended}$	0.23 (0.13-0.33)*	10.8%	11.8%	0.07 (−0.10 to 0.25)	−3.5%	10.8%
AS	−0.12 (−0.22 to −0.02)†	17.1%	−29.2%	−0.15 (−0.32 to 0.02)	2.1%	−17.0%
MAS	−0.05 (−0.15 to 0.05)	11.4%	−16.2%	−0.21 (−0.39 to −0.04)†	−4.9%	−16.6%

AS, **A**ge, **C**reatinine, and **E**jection **F**raction (ACEF) score; CI, confidence interval; CR, complete revascularization; CSS, clinical **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score; LM, left main disease; LSS$_{core}$, logistic **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score (core model); LSS$_{extended}$, logistic **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score (extended model); MACE, major adverse cardiovascular events; MAS, modified **A**ge, **C**reatinine, and **E**jection **F**raction (ACEF) score; MI, myocardial infraction; NRI, net reclassification improvement; SYNTAX, **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery; 3-VD, 3-vessel disease.

* Significantly improved from the net reclassification of SYNTAX score.

† Significantly decreased from the net reclassification of SYNTAX score.

2.19 (95% CI, 1.73-2.77; Table 2). In a comparison of SS and MAS, it was found that MAS significantly improved mortality predictability by correctly reclassifying 71% of patients who did not die at follow-up and incorrectly reclassifying 17% of patients who died. Thus, the NRI of MAS over SS was 54% (95% CI, 30%-78%; Table 3). Additionally, the IDI of MAS over SS was 0.75% (95% CI, 0.25%-1.25%), indicating that the average sensitivity and specificity with all possible cutoff values improved 0.75% from SS to MAS (Table 4).

Improvements in patient reclassification compared with angiographic SS in terms of mortality were seen in all scoring systems that involved clinical variables (Tables 3 and 4).

Discrimination for MI. The most accurate score for MI was LSS$_{extended}$ (AUC, 0.68; 95% CI, 0.61-0.75; Table 2). SS (AUC, 0.53; 95% CI, 0.44-0.61), CSS (AUC, 0.58; 95% CI, 0.49-0.67), and LSS$_{core}$ (AUC, 0.58; 95% CI, 0.49-0.67) could not effectively predict MI (Table 2). Discrimination for periprocedural myocardial injury is shown in Supplemental Table S10.

Discrimination for revascularization. SS and LSS$_{extended}$ were predictive for revascularization, although the AUCs were only 0.54 (95% CI, 0.51-0.57) and 0.55 (95% CI, 0.52-0.58),

respectively. The other scores could not predict the risk of revascularization better than chance (Table 2).

Discrimination for MACE. The discriminations of all of the risk scores for MACE were far from satisfactory. The AUCs of all the risk scores were lower than 0.6. SS, CSS, and LSS$_{core}$ showed marginally significant AUCs, and among the scores, LSS$_{extended}$ showed the highest AUC (0.58; 95% CI, 0.55-0.61). The discriminations of AS and MAS were not significantly better than chance (Table 2).

The C-statistics calculated using Cox regression analyses are presented in Supplemental Table S11, which showed similar results.

Discrimination for adverse events in patients with 3-VD and/or LM. Figure 2 shows the receiver operating characteristic curves of risk scores for adverse events in the 3-VD and/or LM subgroup. Similar to the findings among all CR patients, in this subgroup, we found that: (1) SS was not predictive for mortality (AUC, 0.58; 95% CI, 0.42-0.73); (2) scores involving clinical variables could predict mortality, with AUCs ranging from 0.70 (AS) to 0.80 (LSS$_{extended}$); (3) the most accurate score for MI was LSS$_{core}$ (AUC, 0.73; 95% CI, 0.64-0.82); and (4) all risk scores had poor discrimination for revascularization and MACE (all AUCs < 0.60; Table 2).

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Table 4. Integrated discrimination improvement of risk scores (compared with SYNTAX score)

	All CR patients			Patients with 3-VD and/or LM		
	IDI (95% CI)	Probability change for events	Probability change for nonevents	IDI (95% CI)	Probability change for events	Probability change for nonevents
Mortality						
CSS	0.57% (0.08%-1.06%)*	0.56%	−0.01%	1.56% (−0.41% to 3.52%)	1.54%	−0.02%
LSS$_{core}$	0.96% (0.30%-1.62%)*	0.95%	−0.01%	4.02% (−0.69% to 8.73%)	3.97%	−0.05%
LSS$_{extended}$	1.18% (0.39%-1.96%)*	1.16%	−0.01%	3.60% (−0.55% to 7.75%)	3.56%	−0.04%
AS	0.27% (0.08%-0.47%)*	0.27%	−0.00%	0.14% (−0.30% to 0.58%)	0.14%	−0.00%
MAS	0.75% (0.25%-1.25%)*	0.74%	−0.01%	1.53% (0.13%-2.93%)*	1.51%	−0.02%
MI						
CSS	0.01% (−0.03% to 0.06%)	0.01%	−0.00%	−0.01% (−0.22% to 0.19%)	−0.01%	0.00%
LSS$_{core}$	0.14% (0.01%-0.27%)*	0.14%	−0.00%	0.30% (−0.12% to 0.71%)	0.29%	−0.00%
LSS$_{extended}$	0.37% (0.13%-0.61%)*	0.37%	−0.00%	0.08% (−0.27% to 0.43%)	0.08%	−0.00%
AS	0.01% (−0.08% to 0.11%)	0.01%	−0.00%	−0.08% (−0.44% to 0.27%)	−0.08%	0.00%
MAS	0.10% (−0.05% to 0.26%)	0.10%	−0.00%	0.41% (−0.38% to 1.21%)	0.41%	−0.01%
Revascularization						
CSS	−0.12% (−0.20% to −0.03%)†	−0.11%	0.01%	−0.06% (−0.19% to 0.08%)	−0.05%	0.01%
LSS$_{core}$	−0.11% (−0.21% to −0.02%)†	−0.11%	0.00%	0.05% (−0.20% to 0.29%)	0.04%	−0.00%
LSS$_{extended}$	0.02% (−0.11% to 0.15%)	0.02%	−0.00%	−0.03% (−0.17% to 0.11%)	−0.03%	0.00%
AS	−0.09% (−0.21% to 0.04%)	−0.08%	0.01%	−0.05% (−0.19% to 0.09%)	−0.04%	0.00%
MAS	−0.11% (−0.22% to 0.01%)	−0.10%	0.01%	0.03% (−0.17% to 0.22%)	0.02%	−0.00%
MACE						
CSS	0.04% (−0.08% to 0.15%)	0.03%	−0.00%	0.05% (−0.19% to 0.30%)	0.05%	−0.01%
LSS$_{core}$	0.09% (−0.06% to 0.23%)	0.08%	−0.01%	−0.09% (−0.30% to 0.13%)	−0.08%	0.01%
LSS$_{extended}$	0.47% (0.22%-0.71%)*	0.43%	−0.04%	0.36% (−0.09% to 0.82%)	0.33%	−0.04%
AS	−0.15% (−0.27% to −0.04%)†	−0.14%	0.01%	−0.14% (−0.36% to 0.09%)	−0.12%	0.01%
MAS	−0.08% (−0.22% to 0.06%)	−0.08%	0.01%	−0.09% (−0.35% to 0.18%)	−0.08%	0.01%

AS, **A**ge, **C**reatinine, and **E**jection **F**raction (ACEF) score; CI, confidence interval; CR, complete revascularization; CSS, clinical **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score; IDI, integrated discrimination improvement; LM, left main disease; LSS$_{core}$, logistic **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score (core model); LSS$_{extended}$, logistic **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score (extended model); MACE, major adverse cardiovascular events; MAS, modified **A**ge, **C**reatinine, and **E**jection **F**raction (ACEF) score; MI, myocardial infraction; SYNTAX, **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery; 3-VD, 3-vessel disease.

* Significantly improved from the integrated discrimination of SYNTAX score.

† Significantly decreased from the integrated discrimination of SYNTAX score.

Calibration of risk scores

The calibration plots of the risk scores for different outcomes are presented in Figure 3 (MACE) and Supplemental Figure S2 (mortality, MI, and revascularization). LSS$_{extended}$ showed the best agreement between the observed and predicted event rates (grouped according to deciles of score; calibration slope for MACE: 1.00 [95% CI, 0.48-1.51]; mortality: 0.87 [95% CI, 0.66-1.08]; MI: 1.01 [95% CI, 0.77-1.25]; revascularization: 1.15 [95% CI, −0.12 to 2.41]). All risk scores showed good calibration for each outcome, expected MAS for mortality (calibration slope, 1.57; 95% CI, 1.17-1.98) and CSS for MI (calibration slope, 2.31; 95% CI, 1.26-3.36).

Utility of risk scores

The decision curves of the risk scores for MACE are presented in Figure 4. The decision curves of the risk scores for mortality, MI, and revascularization are presented in Supplemental Figure S3. LSS$_{extended}$ had the greatest net benefit for MACE, MI, and revascularization, whereas MAS had the greatest net benefit for mortality.

Discussion

The major findings of the present study are as follows: (1) for mortality prediction, scores involving clinical variables, especially MAS, were superior to the baseline SS in CR patients; and (2) with regard to the predictive capacity for MACE, the performance of all the risk scores did not indicate helpful discrimination in CR patients. To our knowledge, the present study is the first and largest all-comer study to specifically evaluate and compare the performance of 5 risk scores among a cohort of consecutive patients who have achieved CR after PCI.

Necessity of risk prediction in CR patients

Revascularization of all diseased coronary artery segments during PCI is noted in a considerable proportion (40%-60%) of patients. In the present study, more than half of the patients who underwent PCI achieved CR. A recent meta-analysis reported that the incidence of MACE was significantly lower in patients with CR after PCI than in patients with incomplete revascularization.[22] Although CR patients are anticipated to have a better prognosis, CR does not guarantee an excellent clinical outcome. Various clinical factors can affect the prognosis. The identification of the subgroups of CR patients at high risk for adverse events would help cardiologists and interventionalists perform more individualized risk estimation.

Established risk scores

Five established prediction models were compared in the present study. SS was initially intended to characterize the
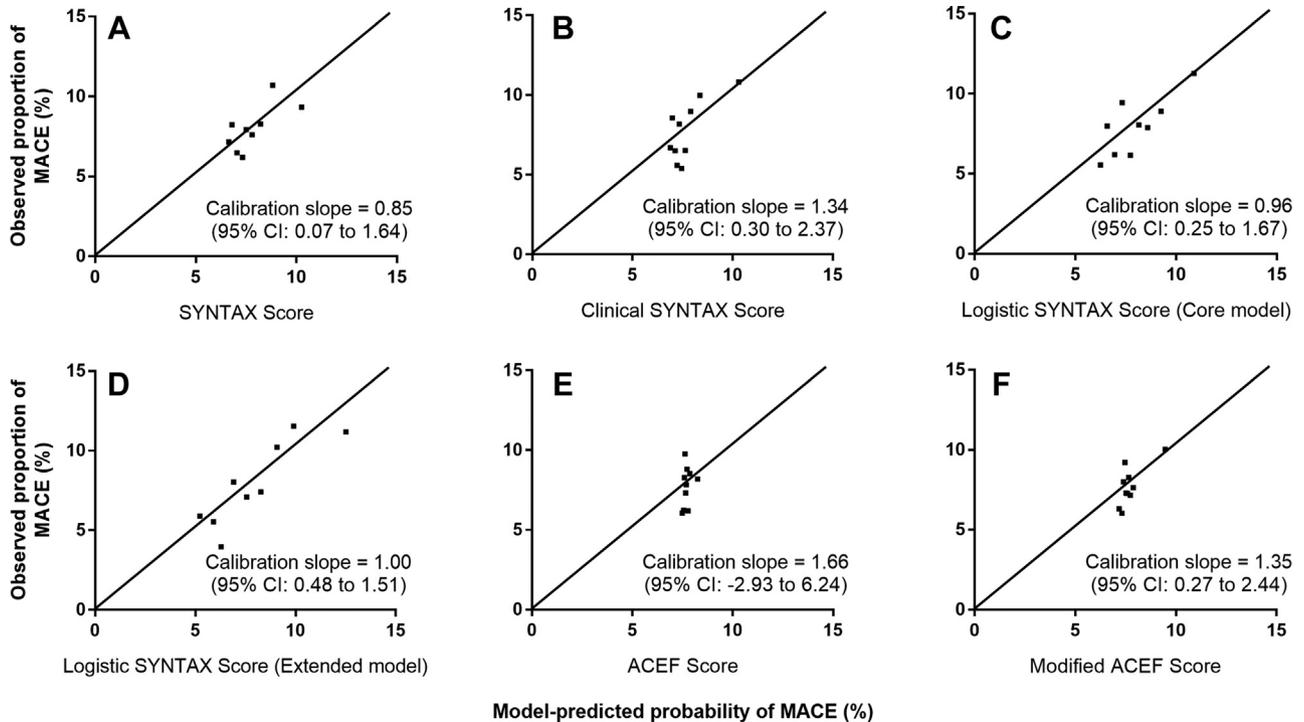
Figure 3. Calibration plots of risk scores for major adverse cardiac events (MACE). Logistic **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score extended model showed the best agreement between the observed and predicted event rates grouped according to deciles of score (calibration slope for MACE: 1.00, 95% confidence interval [CI], 0.48-1.51). All risk scores were good calibrated (all CIs of calibration slopes covered 1) for MACE. (**A**) Calibration plot of SYNTAX score. (**B**) Calibration plot of clinical SYNTAX score. (**C**) Calibration plot of logistic SYNTAX score (core model). (**D**) Calibration plot of logistic SYNTAX score (extended model). (**E**) Calibration plot of ACEF score. (**F**) Calibration plot of modified ACEF score. ACEF, **A**ge, **C**reatinine, and **E**jection **F**raction.

number, location, type, and complexity of coronary atherosclerosis lesions. Additionally, SS is recommended by current guidelines for the selection of the revascularization strategy.[23,24] A higher SS indicates a more complex disease and worse prognosis. The derived scores of SS (eg, RSS, CSS, and LSS) have the ability to predict MACE and mortality in patients who have undergone PCI. However, SS, CSS, and LSS are calculated according to baseline cine angiograms and lesion characteristics before PCI. In CR patients who have revascularized all diseased coronary artery segments, it is unclear whether SS and its derived scores can still be the indicators of adverse events. Additionally, in these patients, the performance of AS or MAS (both scores involve only 3 clinical variables) is unknown.

In a previous study the authors attempted to examine whether SS and CSS could predict clinical outcomes in patients with CR and reported that these 2 scores were related to prognosis.[25] The areas under the curve for SS and CSS with regard to 3-year MACE were 0.595 and 0.649, respectively. The performance of SS and CSS in this previous study appear to be better than the performance in our study. However, in this previous study, the sample size was not large enough and approximately half of the patients received sirolimus-eluting stents, which are not widely used nowadays. Few studies, especially large sample studies, have been performed to validate the predictive discrimination and calibration of SS, CSS, and LSS in CR patients. Additionally, to our knowledge, the

predictive abilities of AS and MAS have not been evaluated among CR patients in an all-comer study.

Performance of prediction models

It is generally considered that an AUC of < 0.60 reflects poor discrimination, an AUC of 0.60-0.75 reflects possibly helpful discrimination, and an AUC of > 0.75 reflects clearly
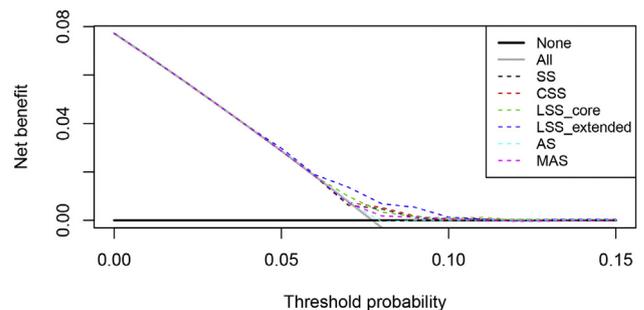

Figure 4. Decision curves of risk scores for major adverse cardiac events (MACE). The net benefit of logistic **Syn**ergy Between Percutaneous Coronary Intervention With **Tax**us and Cardiac Surgery (SYNTAX) score were the greatest for MACE. AS, **A**ge, **C**reatinine, and **E**jection **F**raction (ACEF) score; CSS, clinical SYNTAX score; LSS_core, logistic SYNTAX score core model; LSS_extended, logistic SYNTAX score extended model; MAS, modified ACEF score; SS, SYNTAX score.

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useful discrimination.[26] From this perspective, SS showed poor discrimination for all adverse events. The scores that involved clinical variables (CSS, LSS, AS, and MAS) showed possibly helpful discrimination for mortality. Among these scores, the most predictive score for mortality was MAS, which also showed possibly helpful discrimination for MI. With regard to revascularization and MACE, all of the risk scores showed poor discrimination.

The predictive value of SS for mortality and MACE was limited. One potential reason is that CR patients showed revascularization of all coronary arteries, and thus, the predictive ability of baseline angiographic characteristics might have been compromised. Therefore, the strictly anatomic SS could not accurately predict the risk of mortality. This result might suggest that the baseline anatomy, if fixed completely, will have a minimal effect on subsequent outcomes.

The scoring systems involving clinical variables had possibly helpful discrimination for the prediction of mortality, especially in patients with 3-VD and/or LM, indicating that, after achieving CR, clinical characteristics, such as age, cardiac function, and renal function might be the main factors to influence prognosis.

No score showed helpful discrimination for MACE. A potential explanation is that none of the scores had been developed specifically for CR patients. All coronary lesions were relieved by PCI in CR patients. Many factors, such as PCI procedural characteristics, complications after PCI, and adherence to medication after PCI, can affect clinical outcomes in multiple ways among CR patients.[27-29] The 5 risk scores, which were calculated according to the baseline characteristics before PCI, might not be able to accurately assess the risk of MACE. Considering that a considerable portion (40%-60%) of patients achieved CR after PCI,[3-5] a risk prediction model specifically for CR patients should be established.

Limitations

Despite being, to our knowledge, the first and largest study to validate the performance of preexisting risk scores in CR patients, the present study has some limitations that should be acknowledged. First, this study is limited by its retrospective single-centre design. Selection bias and unknown confounding factors cannot be excluded. The study was performed at a large single centre (Fuwai Hospital) that has a large PCI volume every year and has interventionalists who have undergone standardized PCI training. Patients who undergo PCI performed by high-volume and experienced operators might have better prognoses. This might partly explain the relatively low event rate in the present study. However, considering that this study was performed in a large and consecutive cohort of patients, we believe that the results could reflect the real-world practice. Second, part of the events was self-reported and not adjudicated, and this approach might underestimate or overestimate the total event rates. However, previous studies have shown that self-reporting is highly reliable for cardiovascular events.[30,31] Moreover, vital status was ascertained from the National Death Registry of China, if needed. Therefore, the incidence of adverse cardiac events in the present study is considered dependable.

Conclusions

The current study performed in a large cohort of consecutive patients who achieved CR after PCI showed that risk scores involving clinical variables, especially MAS, might help in the prediction of mortality. However, no risk score showed helpful discrimination for MACE in CR patients.

Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2019.02.017.