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A comparison of risk prediction models for patients with acute coronary syndromes

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Introduction

In the current guidelines for acute coronary syndrome (ACS), the GRACE risk score is recommended for risk stratification. The GRACE risk score 2.0 provides the risk of death and myocardial infarction (MI) after ACS, but it does not provide a bleeding risk prediction. The PRECISE-DAPT and PARIS scores were developed from patient populations treated with percutaneous coronary intervention (PCI) regardless of their clinical presentations. They predict out-of-hospital bleeding risk. The PARIS score also provides a thrombotic risk prediction. As a tool for mortality prediction, the logistic clinical SYNTAX score was redeveloped from the GLOBAL LEADERS trial[1,2]. Recently, the PRAISE score, based on a machine-learning algorithm, was developed for the combined prediction of death, MI, and major bleeding one year after discharge in ACS patients[3]. These risk prediction models have been introduced into clinical practice, but their performances have not been compared **(Supplementary Table 1)**.

Methods

We applied five scores to ACS patients treated with PCI in the GLOBAL LEADERS trial for the assessment of all-cause death, MI defined by the third universal definition, and Bleeding Academic Research Consortium (BARC) type 3 or 5 major bleeding at one year after discharge[2]. The GLOBAL LEADERS trial investigated aspirin-free antiplatelet treatment after PCI (experimental arm: 1-month dual antiplatelet therapy [DAPT] followed by 11-month ticagrelor monotherapy vs control arm: 12-month DAPT) in an all-comers population. Out of 15,968 patients, 7,457 presented with ACS and were treated with PCI. Thirty-one patients died before discharge. The database of 7,426 patients who were discharged has been used for the validation of death prediction. Nineteen patients were lost to follow-up for MI and bleeding and only vital status in these patients was available after discharge. Thus, the data of 7,407 patients were used for the validation of MI and bleeding prediction. Details of score calculation are provided

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in **Supplementary Appendix 1**. The discriminative abilities were assessed using Harrell's C statistic, and integrated discrimination improvement (IDI). The calibration was evaluated using the Hosmer-Lemeshow goodness-of-fit statistical test. Regarding the PRAISE score, agreement between observed and predicted rates was assessed by calibration plots, and Brier scores were reported as overall measures of performance.

Results

One year after discharge, all-cause death, MI, and BARC type 3 or 5 major bleeding occurred in 103 patients (1.4%), 140 patients (1.9%), and 111 patients (1.5%), respectively. The numbers of missing variables for score calculation are presented in **Supplementary Table 2**. C-statistics, IDIs and the results of the Hosmer-Lemeshow test are summarised in **Table 1**, **Supplementary Figure 1** (overall population), **Supplementary Table 3** and **Supplementary Figure 2** (the experimental and control arms). In all models predicting death, calibrations based on the Hosmer-Lemeshow tests were poor. The calibration plots and Brier scores for the PRAISE score are shown in **Supplementary Figure 3** and **Supplementary Figure 4**.

Discussion

All-cause mortality may be viewed as the ultimate endpoint; however, MI and major bleeding have significant bearing on subsequent mortality[4]. Two separate risk scores for bleeding events and thrombosis events provide not only risk stratification but also trade-off between ischaemic and bleeding risks, which supports the individual optimal antiplatelet and anticoagulant therapy[5].

The predictivities in the development cohorts can be higher than those observed in the external validation cohort, which may depend on the eras of development and external cohorts. Advances in medicine could have an influence on the predictivity. Of note, observed versus predicted rates of the PRAISE score in the control arm were well calibrated according to calibration plots but, in the experimental arm, the PRAISE score overestimated the rates of death and bleeding **(Supplementary Figure 4)**. Therefore, external validation using contemporary data should be performed.

The results stemming from the GLOBAL LEADERS trial demonstrated that the PRAISE score could provide combined predicted event rates of death, MI, and bleeding with useful or helpful discrimination. Calibration based on Hosmer-Lemeshow tests was poor for the prediction of death. Thus, improved risk scores are still warranted. The predictive values of the PRAISE score were at least non-inferior to those of conventional statistical models when the models were externally validated **(Table 1)**, which suggests that using machine learning approaches might have some promise in risk prediction.

Limitation

Outcomes predicted by the scores are different in the timing (i.e., at 1 year vs 2 years, etc.) and criteria for events (i.e., BARC vs Thrombolysis In Myocardial Infarction [TIMI] bleeding criteria,

Table 1. Contemporary risk scores and their validation in the GLOBAL LEADERS trial.

Death (n=7,426)	PRAISE	GRACE 2.0	LCSS (new model)	PRAISE vs GRACE 2.0	PRAISE vs LCSS	GRACE 2.0 vs LCSS
C-statistic	0.76 (0.72-0.81)	0.74 (0.69-0.79)	0.82 (0.78-0.86)	*p*=0.295	*p*=0.001	*p*<0.001
IDI	–	–	–	0.007 (–0.009 to 0.022) *p*=0.412	–0.020 (–0.045 to 0.004) *p*=0.103	–0.027 (–0.052 to –0.001) *p*=0.039
Hosmer-Lemeshow	Chi-square=28.4, *p*<0.001	Chi-square=34.4, *p*<0.001	Chi-square=47.5, *p*<0.001	–	–	–
MI (n=7,407)	**PRAISE**	**GRACE 2.0**	**PARIS**	**PRAISE vs GRACE 2.0**	**PRAISE vs PARIS**	**GRACE 2.0 vs PARIS**
C-statistic	0.63 (0.58-0.68)	0.56 (0.51-0.61)	0.67 (0.63-0.71)	*p*=0.030	*p*=0.059	*p*<0.001
IDI	–	–	–	0.004 (0.001 to 0.007) *p*=0.004	–0.007 (–0.011 to –0.002) *p*=0.003	–0.011 (–0.015 to –0.007) *p*<0.001
Hosmer-Lemeshow	Chi-square=8.6, *p*=0.381	Chi-square=7.6, *p*=0.471	Chi-square=2.5, *p*=0.647	–	–	–
Major bleeding (n=7,407)	**PRAISE**	**PRECISE-DAPT**	**PARIS**	**PRAISE vs PRECISE-DAPT**	**PRAISE vs PARIS**	**PRECISE-DAPT vs PARIS**
C-statistic	0.64 (0.59-0.69)	0.66 (0.61-0.71)	0.64 (0.59-0.69)	*p*=0.301	*p*=0.909	*p*=0.483
IDI	–	–	–	0.000 (–0.005 to 0.007) *p*=0.765	0.002 (–0.007 to 0.011) *p*=0.654	0.001 (–0.003 to 0.005) *p*=0.567
Hosmer-Lemeshow	Chi-square=12.3, *p*=0.139	Chi-square=8.4, *p*=0.394	Chi-square=4.1, *p*=0.542	–	–	–

In terms of integrated discrimination improvement (IDI) for A vs B, positive values mean A is better, compared to B. LCSS: logistic clinical SYNTAX score; MI: myocardial infarction

etc.); therefore, calibration plots and Brier scores were evaluated only for the PRAISE score. The logistic clinical SYNTAX score was developed from the GLOBAL LEADERS trial to predict death occurring post procedure up to two years (internal validation). MI and bleeding were site-reported and were not centrally adjudicated due to limited financial resources.

Conclusion

The PRAISE score provides the predicted rates of death, MI, and major bleeding one year after discharge in ACS patients with useful or helpful discrimination, which will support the individual optimal antiplatelet and anticoagulant therapy.

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Conflict of interest statement

H. Hara reports a grant for studying overseas from the Japanese Circulation Society, a grant-in-aid for JSPS Fellows and a grant from the Fukuda Foundation for Medical Technology. P.W. Serruys reports personal fees from Sino Medical Sciences Technology, Philips/Volcano, Xeltis, HeartFlow, Meril Life, and SMT outside the submitted work. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix 1. Methods.

Supplementary Table 1. Comparison between contemporary risk scores.

Supplementary Table 2. Number of missing variables for score calculation.

Supplementary Table 3. Contemporary risk scores and their validation in the GLOBAL LEADERS trial according to antiplatelet treatment.

Supplementary Figure 1. Calibration comparing the observed and expected probabilities.

Supplementary Figure 2. Calibration comparing the observed and expected probabilities according to antiplatelet treatment.

Supplementary Figure 3. Calibration plots for the PRAISE score.

Supplementary Figure 4. Calibration plots for the PRAISE score according to antiplatelet treatment.

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Supplementary data

Supplementary Appendix 1. Methods

Variables were collected by electronic case report form (eCRF) prospectively in the GLOBAL LEADERS trial. Percentages (numbers) of missing variables are shown in **Supplementary Table 1**. The PRAISE score accepts "missing values" as "unknown" for the score calculation. Therefore, "missing values" were treated as "unknown" in the calculation of the PRAISE score. For other scores, multiple imputation (20 times) of missing values was carried out to make efficient use of the available data. Score calculation was performed according to the following web calculators or formulas.

Web calculators:

PRAISE: https://praise.hpc4ai.it/

PRECISE-DAPT: http://www.precisedaptscore.com/predapt/

Formula
GRACE 2.0:

1A. 1-year death/MI model (page 2-8 July 12, 2012

Final model, n=32,037 patients, 3655 deaths or MI's (2422 deaths, 1562 MI's, 329 MI then death)

	Beta_hat*	Hazard Ratio	95%CI	Chi-square value * *
Age per 10 years	.14677			853
Non-linear age (x12_3)	.02090			
Systolic BP per -20 mm Hg	.01797			200
Non-linear SBP (x22_3)	.01020			
Pulse per 30 BPM	.04230			126
Non-linear pulse term 1 (x32_4)	.37817			
Non-linear pulse term 2 (x33_4)	-1.25782			
Creatinine per 1mg	-.15965			338
Non-linear crt term 1	5.02142			
Non-linear crt term 2	-12.33887			
Killip class II vs I	.53625	1.71	1.57-1.86	288
Killip class III vs I	.68594	1.99	1.77-2.23	
Killip class IV vs I	1.15850	3.19	2.61-3.89	
Cardiac arrest at admission	.67071	1.96	1.66-2.30	55
Positive initial enzymes	.22710	1.26	1.17-1.35	42
ST deviation	.32831	1.39	1.30-1.49	92
$S_{0(365)}$	.9865696068			
C index	.7458			

*Beta_hat's are the model estimates on the model estimation scale, which is a log scale; generally exp (Beta_hat) are hazard ratios, but this is more complicated for age, etc with several terms.

* *The chi-square values represent the change in-2 log likelihood for the final model with and without the given factor.

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Plots for model probability of 1-yr Death or MI by non-linear factors follow.

Model-predicted probability of 1-year Death or MI for a given patient.

Basic formula:
Probability of 1-year DMI=$1 - S_{0(365)}^{\exp(X\hat{\beta})}$.

$S_{0(365)}$ = baseline survival to 365 days (similar to linear regression intercept, where all terms = 0).
$S_{0(365)}$ = 0. 9865696068.

$X\hat{\beta}$= inner product of covariate values for a given patient (X), times model estimates on ln(HR) scale ($\hat{\beta}$).

Estimates on ln(HR) scale (Bhat) are on pg. 2.

Non-linear terms (for age, etc) are defined below:

```
a1=4.8165;
b1=6.6571;
c1=8.3095;
  if age_10>=a1 then f11=(age_10-a1)**3; if age_10<a1 then f11=0;
  if age_10>=b1 then f12=((age_10-b1)**3)*(c1-a1)/(c1-b1); if age_10<b1 then f12=0;
  if age_10>=c1 then f13=((age_10-c1)**3)*(b1-a1)/(c1-b1); if age_10<c1 then f13=0;
x12_3=f11 - f12 + f13;

a2=-9.02;
b2=-6.97;
c2=-5.32;
  if sbp_20>=a2 then f21=(sbp_20-a2)**3; if sbp_20<a2 then f21=0;
  if sbp_20>=b2 then f22=((sbp_20-b2)**3)*(c2-a2)/(c2-b2); if sbp_20<b2 then f22=0;
  if sbp_20>=c2 then f23=((sbp_20-c2)**3)*(b2-a2)/(c2-b2); if sbp_20<c2 then f23=0;
x22_3=f21 - f22 + f23;

  a3=1.71;
  b3=2.31;
  c3=2.77;
  d3=3.95;
  if pulse_30>=a3 then f31=(pulse_30-a3)**3; if pulse_30<a3 then f31=0;
  if pulse_30>=c3 then f32=((pulse_30-c3)**3)*(d3-a3)/(d3-c3); if pulse_30<c3 then f32=0;
  if pulse_30>=d3 then f33=((pulse_30-d3)**3)*(c3-a3)/(d3-c3); if pulse_30<d3 then f33=0;
x32_4=f31 - f32 + f33;

  if pulse_30>=b3 then f34=(pulse_30-b3)**3; if pulse_30<b3 then f34=0;
  if pulse_30>=c3 then f35=((pulse_30-c3)**3)*(d3-b3)/(d3-c3); if pulse_30<c3 then f35=0;
  if pulse_30>=d3 then f36=((pulse_30-d3)**3)*(c3-b3)/(d3-c3); if pulse_30<d3 then f36=0;
x33_4=f34 - f35 + f36;

  a4=.685;
  b4=.925;
```

```
  c4=1.145;
  d4=2.065;
  if creat_mg>=a4 then f41=(creat_mg-a4)**3; if creat_mg<a4 then f41=0;
  if creat_mg>=c4 then f42=((creat_mg-c4)**3)*(d4-a4)/(d4-c4); if creat_mg<c4 then f42=0;
  if creat_mg>=d4 then f43=((creat_mg-d4)**3)*(c4-a4)/(d4-c4); if creat_mg<d4 then f43=0;
x42_4=f41 - f42 + f43;

  if creat_mg>=b4 then f44=(creat_mg-b4)**3; if creat_mg<b4 then f44=0;
  if creat_mg>=c4 then f45=((creat_mg-c4)**3)*(d4-b4)/(d4-c4); if creat_mg<c4 then f45=0;
  if creat_mg>=d4 then f46=((creat_mg-d4)**3)*(c4-b4)/(d4-c4); if creat_mg<d4 then f46=0;
x43_4=f44 - f45 + f46;
```

As a check of above, one should get:

1-yr prob Death/ MI	age	pulse	systolic BP	creat	Killip class	Cardiac arrest	Pos enz	ST dev
.34	90	92	139	1.06	I	no	yes	yes
.07	40	82	107	1.00	I	no	no	yes

1B. 1 year model for death alone

Final model, n=32,037 patients, 2422 deaths; Kaplan-Meier 1 yr estimate: 9.3%

	Beta_hat	Hazard ratio	95% CI	chi-square value
Age per 10 years	.41157			1069
Non-linear age (x12_3)	.01290			
Systolic BP per -20 mm Hg	.08222			293
Non-linear SBP (x22_3)	.01020			
Pulse per 30 BPM	.13138			131
Non-linear pulse term 1 (x32_4)	.40176			
Non-linear pulse term 2 (x33_4)	-1.37249			
Creatinine per 1 mg	-.51259			305
Non-linear crt term 1 (x42_4)	7.52634			
Non-linear crt term 2 (x43_4)	-18.23023			
Killip class II vs I	.63827	1.89	1.72-2.09	305
Killip class III vs I	.85325	2.35	2.06-2.68	
Killip class IV vs I	1.29372	3.65	2.94-4.52	
Cardiac arrest at admission	.87185	2.39	2.00-2.87	74
Positive initial enzymes	.37660	1.46	1.33-1.59	72
ST deviation	.44303	1.56	1.43-1.70	109
$S_{0(365)}$	.9983577131			
C index	0.8294			

Non-linear terms (x12_3, etc) defined as in 1A above.

As a check of above, one should get:

1-yr prob Death	age	pulse	systolic BP	creat	Killip class	Cardiac arrest	Pos enz	ST dev
.28	90	92	139	1.06	I	no	yes	yes
.02	40	82	107	1.00	I	no	no	yes

PARIS:

Risk score for major bleeding	
Parameter	Scores
Age	
<50	0
50–59	1
60–69	2
70–79	3
≥80	4
Body mass index	
<25	2
25-34.9	0
≥35	2
Current smoking	
Yes	2
No	0
Anaemia	
Present	3
Absent	0
Creatinine clearance <60 ml/min	
Present	2
Absent	0
Triple therapy on discharge	
Yes	2
No	0

Risk score for thrombotic events	
Parameter	Scores
Diabetes mellitus	
None	0
Non-insulin-dependent	1
Insulin-dependent	3
Acute coronary syndrome	
No	0
Yes, troponin-negative	1
Yes, troponin-positive	2
Current smoking	
Yes	1
No	0
Creatinine clearance <60 ml/min	
Present	2
Absent	0
Prior PCI	
Yes	2
No	0
Prior CABG	
Yes	2
No	0

LCSS (new model):

LN hazard (death)=0.0410*(SYNTAX score) – 0.5314*(SYNTAX-like)+0.0394*(age) -

0.0076*(creatinine clearance) – 0.0991*(LVEF)+0.0007*(LVEF*LVEF) –

0.0883*(BMI)+0.0018*(BMI*BMI)+0.4174*(PVD)+0.1579*(DM)+0.7829*(COPD)+0.6070*(p

rior stroke)+0.2440*(15-Hb)+0.0771*(WBC)+0.3729*(current smoking) – 3.0766

risk of 2-year death=1-exp (-exp [LN hazard {death}])

(15-Hb) indicates 15-haemoglobin for positive value, 0 for negative value.

Supplementary Table 1. Comparison between contemporary risk scores.

Scores	Number of variables	Publication	Population	Outcomes in the original scores	Development cohort	Death	MI	Major bleeding
PRAISE	25	2021	ACS patients	Out-of-hospital death, MI, BARC 3 or 5 bleeding at 1 year	19,826 patients, multicentre registry	0.91 (0.90-0.92): training; 0.82 (0.78-0.85): internal validation	0.88 (0.86-0.89): training; 0.74 (0.70-0.78): internal validation	0.87 (0.85-0.88): training; 0.70 (0.66-0.75): internal validation
GRACE 2.0	8	2014	ACS patients	Death, death/MI at 1 year	32,037 patients, multicentre registry	0.83	0.75 (for death or MI)	-
PRECISE-DAPT	5	2017	PCI patients	Out-of-hospital TIMI major and/or minor bleeding at 1 year	14,963 patients, randomised clinical trials	-	-	0.73 (0.61-0.85)
PARIS	10	2016	PCI patients	Out-of-hospital MI/ST, BARC 3 or 5 bleeding at 2 years	4,190 patients, multicentre registry	-	0.70	0.72
LCSS (new model)	13	2021	PCI patients	Death at 2 years	15,883 patients, randomised clinical trial (GLOBAL LEADERS)	0.78 (0.76–0.80)	-	-

Continued	Validation cohort	Death	MI	Major bleeding	Outcomes in the GLOBAL LEADERS	Validation in the GLOBAL LEADERS: Death (n=7,426)	MI (n=7,407)	Major bleeding (n=7,407)
PRAISE	3,444 patients, a randomised trial and multicentre registry	0.92 (0.90-0.93)	0.81 (0.76-0.85)	0.86 (0.82-0.89)	Out-of-hospital death, MI, BARC 3 or 5 bleeding at 1 year	0.76 (0.72–0.81)	0.63 (0.58–0.68)	0.64 (0.59–0.69)
GRACE 2.0	2,959 patients, multicentre registry	0.82	0.8 (for death or MI)	-		0.74 (0.69–0.79)	0.56 (0.51–0.61)	-
PRECISE-DAPT	8,595 patients, randomised clinical trial	-	-	0.70 (0.65-0.74)		-	-	0.66 (0.61–0.71)
	6,172 patients, single-centre registry			0.66 (0.61-0.71)				
PARIS	8,130 patients, multicentre registry	-	0.65	0.64		-	0.67 (0.63–0.71)	0.64 (0.59–0.69)
LCSS	10,010 patients, single-centre registry	0.72 (0.67–0.77)	-	-		0.82 (0.78–0.86): internal validation	-	-

Discriminative abilities are presented as C-indices.
ACS: acute coronary syndrome; LCSS: logistic clinical SYNTAX score; MI: myocardial infarction; PCI: percutaneous coronary intervention; ST: stent thrombosis

Supplementary Table 2. Number of missing variables for score calculation.

	Death (n=7,426)	MI/Major bleeding (n=7,407)
PRAISE *	0.0 (0)	0.0 (0)
Age	0.0 (0)	0.0 (0)
Sex	0.0 (0)	0.0 (0)
Hypertension	0.5 (38)	0.5 (38)
Hyperlipidaemia	4.5 (336)	4.5 (336)
Diabetes mellitus	0.1 (5)	0.1 (5)
eGFR	0.7 (54)	0.7 (54)
PVD	1.0 (75)	1.0 (75)
Prior stroke	0.1 (11)	0.1 (11)
Prior MI	0.2 (13)	0.2 (13)
Prior CABG	0.0 (1)	0.0 (1)
Prior bleeding	0.2 (14)	0.2 (14)
Malignancy	100.0 (7,426)	100.0 (7,407)
LVEF	4.5 (334)	4.5 (332)
Haemoglobin	3.3 (247)	3.3 (246)
NSTEMI	0.0 (0)	0.0 (0)
STEMI	0.0 (0)	0.0 (0)
Multivessel disease	75.5 (5,610)	75.5 (5,592)
PCI with DES	4.9 (366)	4.9 (366)
Vascular access	1.1 (83)	1.1 (83)
Complete revascularisation	100.0 (7,426)	100.0 (7,407)
Statin at discharge	0.3 (25)	0.3 (24)
ACEI/ARB at discharge	0.5 (38)	0.5 (37)
Beta-blocker at discharge	0.5 (34)	0.4 (33)
PPI at discharge	0.5 (40)	0.5 (39)
OAC at discharge **	50.7 (3,768)	50.7 (3,756)

	Death (n=7,426)	MI (n=7,407)
GRACE 2.0	11.9 (881)	11.9 (879)
Age	0.0 (0)	0.0 (0)
Creatinine	0.7 (54)	0.7 (54)
Heart rate/pulse	0.0 (0)	0.0 (0)
Systolic BP	0.0 (0)	0.0 (0)
ST segment deviation	0.0 (0)	0.0 (0)
Abnormal cardiac enzymes	11.7 (872)	11.7 (870)
Killip class	0.0 (0)	0.0 (0)
Cardiac arrest at admission	0.0 (0)	0.0 (0)

	Major bleeding (n=7,407)
PRECISE-DAPT	4.3 (320)
Age	0.0 (0)
Creatinine clearance	0.7 (55)
Prior bleeding	0.2 (14)
Haemoglobin	3.3 (246)
White blood cell	6.6 (492)

	MI/Major bleeding (n=7,407)
PARIS	57.5 (4,262)
Age	0.0 (0)
BMI	0.0 (2)
Diabetes mellitus+insulin	0.4 (26)
Current smoking	0.0 (0)
Creatinine clearance	0.7 (55)
Prior PCI	0.1 (4)
Prior CABG	0.0 (1)
Anaemia	3.3 (246)
ACS+troponin	14.6 (1,081)
Triple therapy at discharge **	50.7 (3,756)

	Death (n=7,426)
LCSS (new model)	77.6 (5,766)
Age	0.0 (0)
BMI	0.0 (2)
Diabetes mellitus	0.1 (5)
Current smoking	0.0 (0)
Creatinine clearance	0.7 (55)
COPD	0.5 (38)
PVD	1.0 (75)
Prior stroke	0.1 (11)
LVEF	4.5 (334)
Haemoglobin	3.3 (247)
White blood cell	6.6 (493)
SYNTAX score ***	74.5 (5,532)
Disease type (3VD or LMCAD) ***	74.5 (5,532)

Data are presented as percentage (number).

* PRAISE score accepts “missing values” as “unknown” for the score calculation.
** Patients were enrolled between 1 July 2013 and 9 November 2015, and anticoagulation at discharge was collected from 18 Dec 2014 (8,237 patients out of 15,968 patients) in the GLOBAL LEADERS trial.
*** The SYNTAX score was collected in the first 4,000 patients in the overall population in the GLOBAL LEADERS trial.
ACEI: angiotensin-converting enzyme inhibitor; ACS: acute coronary syndrome; ARB: angiotensin receptor blocker; BMI: body mass index; BP: blood pressure; CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; DES: drug-eluting stent; eGFR: estimated glomerular filtration rate; LMCAD: left main coronary artery disease; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NSTEMI: non-ST-segment elevation myocardial infarction; OAC: oral anticoagulant; PCI: percutaneous coronary intervention; PPI: proton pump inhibitor; PVD: peripheral vascular disease; STEMI: ST-segment elevation myocardial infarction; 3VD: three-vessel disease

Supplementary Table 3. Contemporary risk scores and their validation in the GLOBAL LEADERS trial according to antiplatelet treatment.

(A)

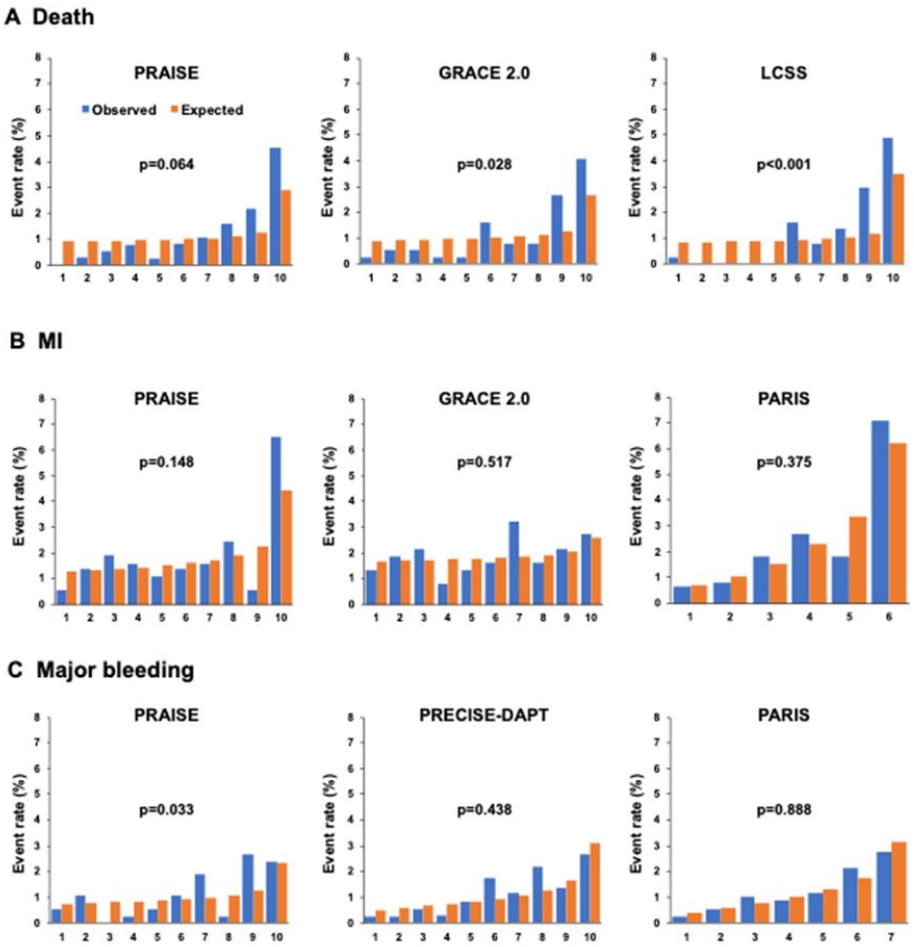
Death (n=3,715)	PRAISE	GRACE 2.0	LCSS (new model)	PRAISE vs GRACE 2.0	PRAISE vs LCSS	GRACE 2.0 vs LCSS
C-statistics	0.76 (0.69–0.83)	0.73 (0.65–0.81)	0.81 (0.75–0.87)	*p*=0.448	*p*=0.043	*p*=0.010
IDI	-	-	-	-0.006 (-0.023 to 0.010); *p*=0.446	-0.037 (-0.077 to 0.004); *p*=0.076	-0.030 (-0.069 to 0.008); *p*=0.125
Hosmer-Lemeshow	Chi-square=14.8, *p*=0.064	Chi-square=17.2, *p*=0.028	Chi-square=29.2, *p*<0.001	-	-	-
MI (n=3,705)	PRAISE	GRACE 2.0	PARIS	PRAISE vs GRACE 2.0	PRAISE vs PARIS	GRACE 2.0 vs PARIS
C-statistics	0.63 (0.56–0.71)	0.56 (0.49–0.63)	0.67 (0.61–0.74)	*p*=0.071	*p*=0.181	*p*=0.005
IDI	-	-	-	0.007 (0.001 to 0.012); *p*=0.016	-0.003 (-0.009 to 0.003); *p*=0.334	-0.010 (-0.015 to -0.005); *p*<0.001
Hosmer-Lemeshow	Chi-square=12.1, *p*=0.148	Chi-square=7.2, *p*=0.517	Chi-square=4.2, *p*=0.375	-	-	-
Major bleeding (n=3,705)	PRAISE	PRECISE-DAPT	PARIS	PRAISE vs PRECISE-DAPT	PRAISE vs PARIS	PRECISE-DAPT vs PARIS
C-statistics	0.67 (0.58–0.75)	0.68 (0.61–0.76)	0.66 (0.58–0.74)	*p*=0.520	*p*=0.881	*p*=0.521
IDI	-	-	-	-0.002 (-0.003 to 0.000); *p*=0.100	-0.004 (-0.011 to 0.002); *p*=0.188	-0.003 (-0.008 to 0.003); *p*=0.337
Hosmer-Lemeshow	Chi-square=16.7, *p*=0.033	Chi-square=8.0, *p*=0.438	Chi-square=1.7, *p*=0.888	-	-	-

(B)

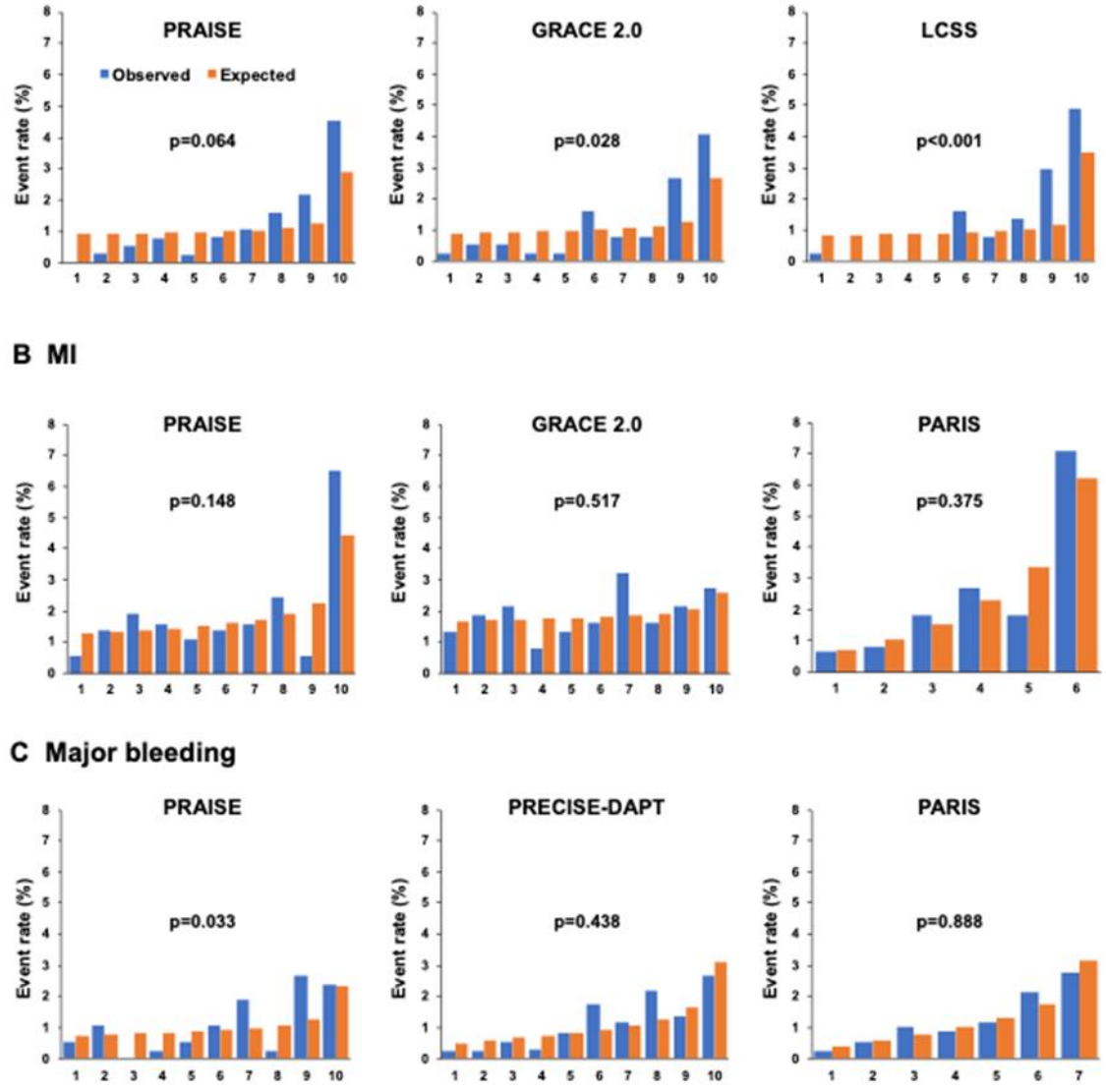
Death (n=3,711)	PRAISE	GRACE 2.0	LCSS (new model)	PRAISE vs GRACE 2.0	PRAISE vs LCSS	GRACE 2.0 vs LCSS
C-statistics	0.77 (0.70–0.83)	0.75 (0.69–0.81)	0.83 (0.78–0.88)	*p*=0.499	*p*=0.014	*p*=0.004
IDI	-	-	-	0.027 (-0.005 to 0.059); *p*=0.096	0.007 (-0.026 to 0.041); *p*=0.665	-0.020 (-0.058 to 0.018); *p*=0.309
Hosmer-Lemeshow	Chi-square=17.9, *p*=0.022	Chi-square=25.5, *p*=0.001	Chi-square=28.7, *p*<0.001	-	-	-
MI (n=3,702)	PRAISE	GRACE 2.0	PARIS	PRAISE vs GRACE 2.0	PRAISE vs PARIS	GRACE 2.0 vs PARIS
C-statistics	0.62 (0.55–0.69)	0.56 (0.49–0.64)	0.67 (0.60–0.73)	*p*=0.200	*p*=0.186	*p*=0.021
IDI	-	-	-	0.001 (-0.002 to 0.004); *p*=0.469	-0.010 (-0.017 to -0.003); *p*=0.004	-0.011 (-0.019 to -0.004); *p*=0.002
Hosmer-Lemeshow	Chi-square=4.0, *p*=0.861	Chi-square=6.9, *p*=0.546	Chi-square=0.9, *p*=0.922	-	-	-
Major bleeding (n=3,702)	PRAISE	PRECISE-DAPT	PARIS	PRAISE vs PRECISE-DAPT	PRAISE vs PARIS	PRECISE-DAPT vs PARIS
C-statistics	0.62 (0.56–0.69)	0.64 (0.58–0.71)	0.63 (0.57–0.70)	*p*=0.429	*p*=0.836	*p*=0.683
IDI	-	-	-	0.003 (-0.008 to 0.013); *p*=0.621	0.007 (-0.009 to 0.023); *p*=0.401	0.004 (-0.003 to 0.011); *p*=0.219
Hosmer-Lemeshow	Chi-square=9.0, *p*=0.342	Chi-square=3.1, *p*=0.927	Chi-square=3.6, *p*=0.611	-	-	-

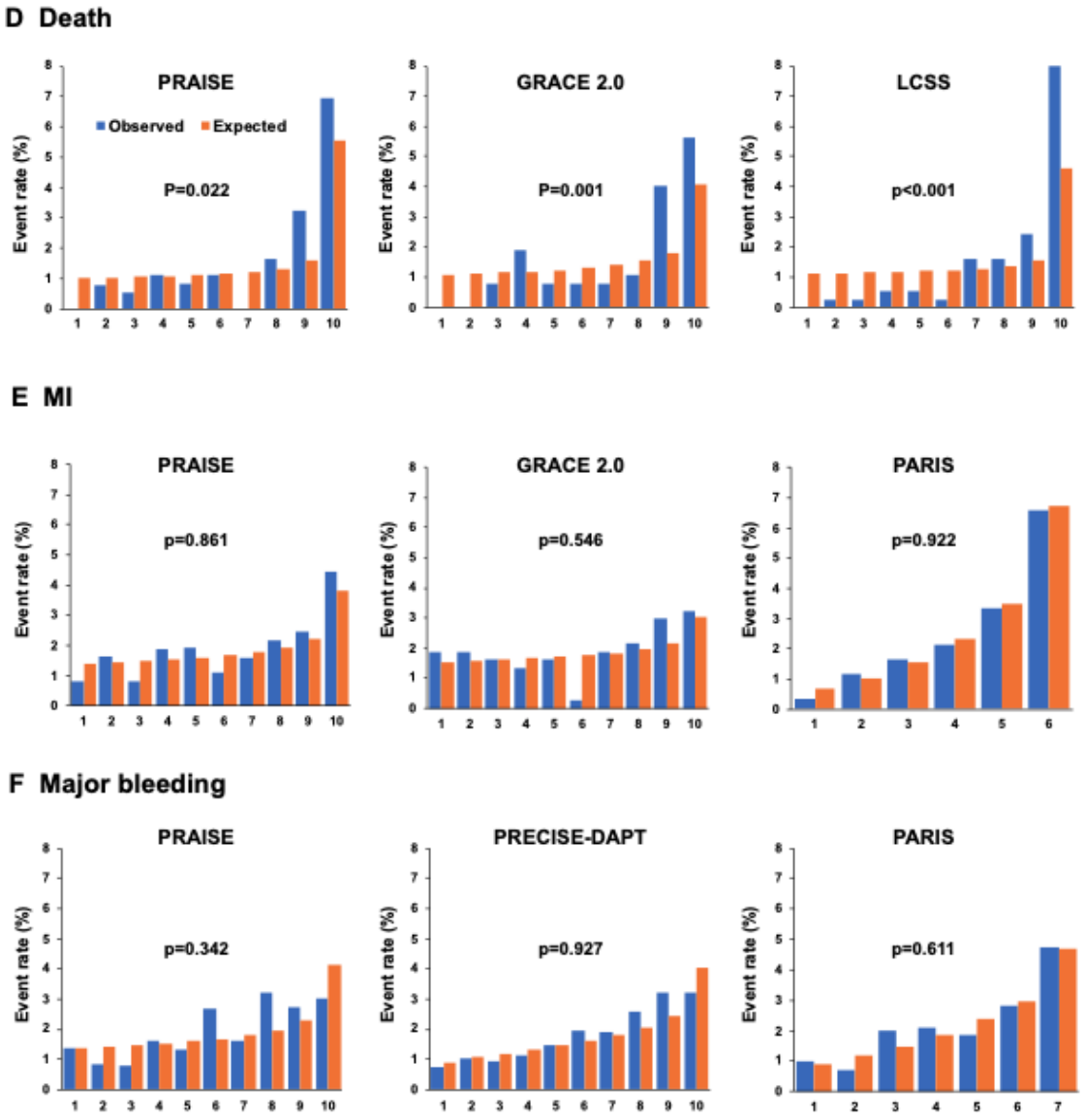
(A) Experimental arm: 1-month dual antiplatelet therapy (DAPT) followed by 11-month ticagrelor monotherapy. (B) Control arm: 12-month DAPT.

LCSS: logistic clinical SYNTAX score; MI: myocardial infarction



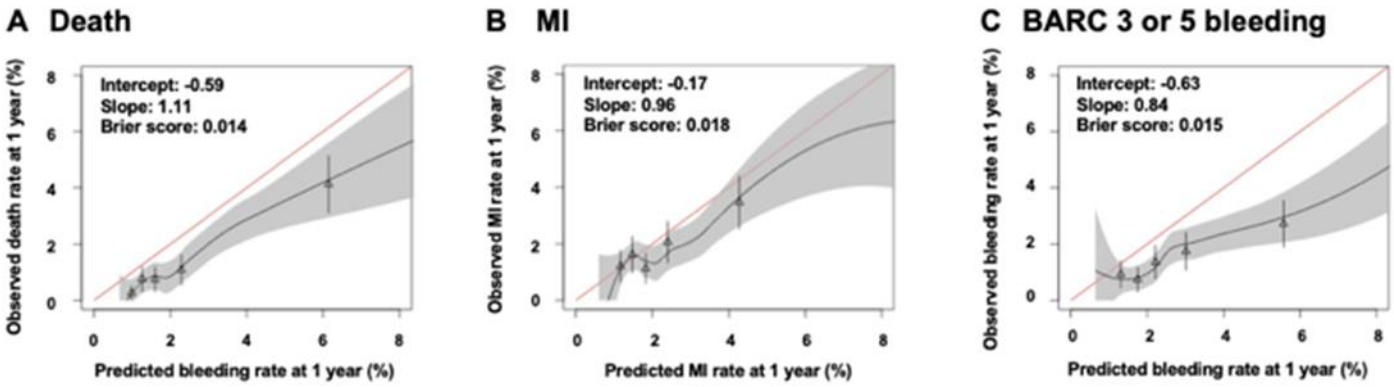
Supplementary Figure 1. Calibration comparing the observed and expected probabilities. Calibration for (A) death, (B) myocardial infarction (MI), and (C) major bleeding, according to the Hosmer-Lemeshow goodness-of-fit statistical test.


A Death
PRAISE
Observed
Expected
p=0.064
GRACE 2.0
p=0.028
LCSS
p<0.001
B MI
PRAISE
p=0.148
GRACE 2.0
p=0.517
PARIS
p=0.375
C Major bleeding
PRAISE
p=0.033
PRECISE-DAPT
p=0.438
PARIS
p=0.888
Event rate (%)



Supplementary Figure 2. Calibration comparing the observed and expected probabilities according to antiplatelet treatment.

Calibration for (A) death, (B) MI, and (C) major bleeding in the experimental arm and for (D) death, (E) MI, and (F) major bleeding in the control arm, according to the Hosmer-Lemeshow goodness-of-fit statistical test.



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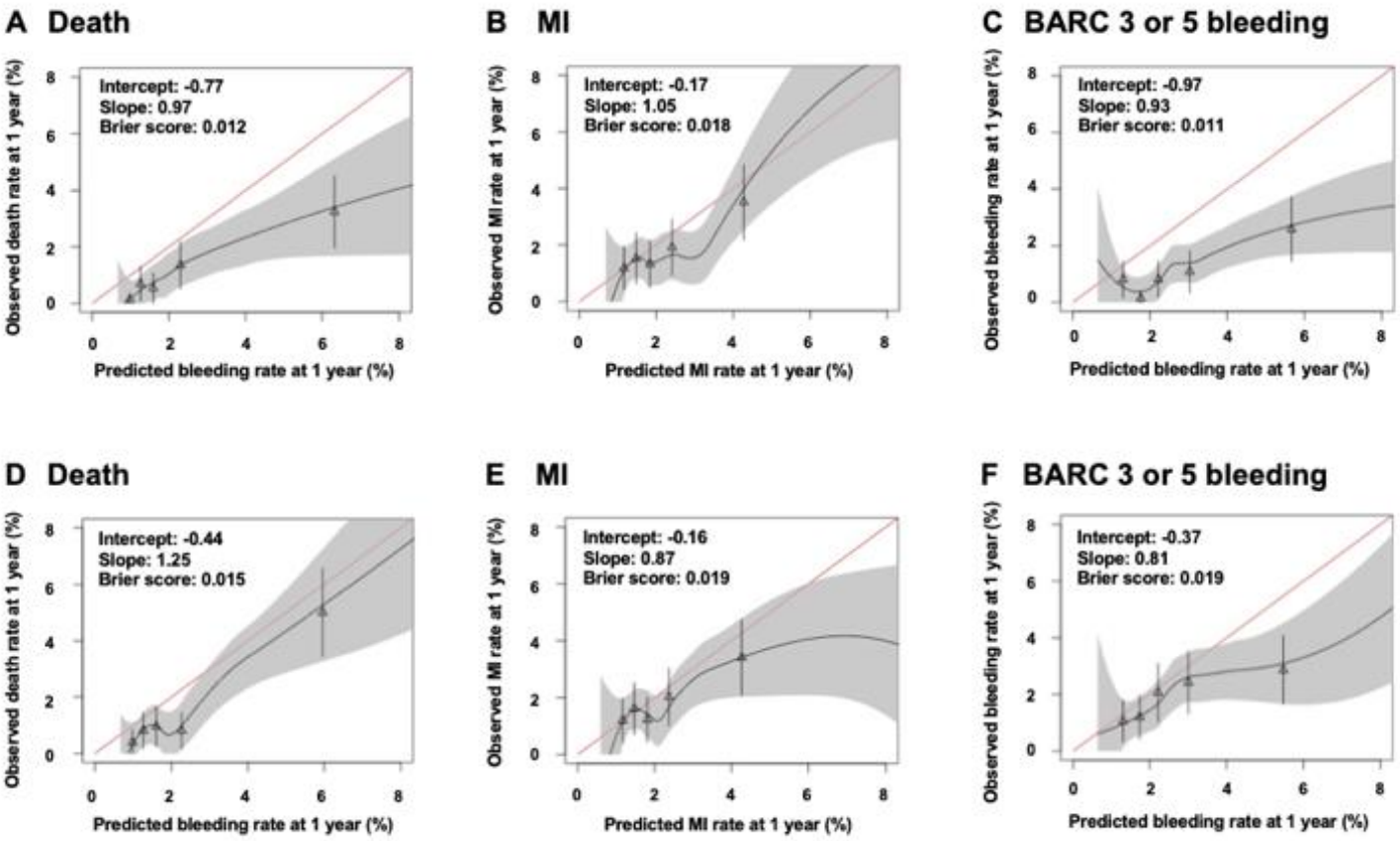
Supplementary Figure 3. Calibration plots for the PRAISE score.

Calibration plots for (A) death, (B) MI, and (C) BARC 3 or 5 bleeding. Triangles represent 5 groups of patients with mean predicted probability and mean observed all-cause mortality rate with 95% confidence interval.



Supplementary Figure 4. Calibration plots for the PRAISE score according to antiplatelet treatment.

Calibration plots for (A) death, (B) MI, and (C) BARC 3 or 5 bleeding in the experimental arm, and for (D) death, (E) MI, and (F) BARC 3 or 5 bleeding in the control arm. Triangles represent 5 groups of patients with mean predicted probability and mean observed all-cause mortality rate with 95% confidence interval.