Circulation

ORIGINAL RESEARCH ARTICLE

Derivation and Validation of the PRECISE-HBR Score to Predict Bleeding After Percutaneous Coronary Intervention

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BACKGROUND: Accurate bleeding risk stratification after percutaneous coronary intervention is important for treatment individualization. However, there is still an unmet need for a more precise and standardized identification of patients at high bleeding risk. We derived and validated a novel bleeding risk score by augmenting the Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy (PRECISE-DAPT) score with the Academic Research Consortium for High Bleeding Risk (ARC-HBR) criteria.

METHODS: The derivation cohort comprised 29 188 patients undergoing percutaneous coronary intervention, of whom 1136 (3.9%) had Bleeding Academic Research Consortium (BARC) 3 or 5 bleeding at 1 year, from 4 contemporary real-world registries and the XIENCE V USA trial. The PRECISE-DAPT score was refitted with a Fine-Gray model in the derivation cohort and extended with the ARC-HBR criteria. The primary outcome was BARC 3 or 5 bleeding within 1 year. Independent predictors of BARC 3 or 5 bleeding were selected at multivariable analysis ($P<0.01$). The discrimination of the score was internally assessed with apparent validation and cross-validation. The score was externally validated in 4578 patients from the MASTER DAPT trial (Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Prolonged DAPT Regimen) and 5970 patients from the STOPDAPT-2 (Short and Optimal Duration of Dual Antiplatelet Therapy-2) total cohort.

RESULTS: The PRECISE-HBR score (age, estimated glomerular filtration rate, hemoglobin, white blood cell count, previous bleeding, oral anticoagulation, and ARC-HBR criteria) showed an area under the curve (AUC) for 1-year BARC 3 or 5 bleeding of 0.73 (95% CI, 0.71–0.74) at apparent validation, 0.72 (95% CI, 0.70–0.73) at cross-validation, 0.74 (95% CI, 0.68–0.80) in MASTER DAPT, and 0.73 (95% CI, 0.66–0.79) in STOPDAPT-2, with superior discrimination compared with PRECISE-DAPT (cross-validation: Δ AUC, 0.01; $P=0.02$; MASTER DAPT: Δ AUC, 0.05; $P=0.004$; STOPDAPT-2: Δ AUC, 0.02; $P=0.20$) and other risk scores. In the derivation cohort, a cutoff of 23 points identified 11 414 patients (39.1%) with a 1-year BARC 3 or 5 bleeding risk ≥4%. An alternative version of the score, including acute myocardial infarction on admission instead of white blood cell count, showed similar predictive ability.

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This manuscript was sent to Dawn Abbott, Guest Editor, for review by expert referees, editorial decision, and final disposition.
This work was presented as an abstract at the Transcatheter Cardiovascular Therapeutics conference, Washington, DC, October 27–30, 2024.
Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/CIRCULATIONAHA.124.072009.
For Sources of Funding and Disclosures, see page 353.

Circulation is available at www.ahajournals.org/journal/circ

CONCLUSIONS: The PRECISE-HBR score is a contemporary, simple 7-item risk score to predict bleeding after percutaneous coronary intervention, offering a moderate improvement in discrimination over multiple existing scores. Further evaluation is required to assess its impact on clinical practice.

Key Words: anticoagulants ■ dual anti-platelet therapy ■ hemorrhage ■ percutaneous coronary intervention ■ risk ■ stents

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Clinical Perspective

What Is New?

- In this study, a simple risk score for predicting bleeding after percutaneous coronary intervention is derived, cross-validated, and externally validated using data from large multinational patient cohorts.
- The PRECISE-HBR score provides a moderate improvement over current guideline-recommended risk tools (eg, Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy [PRECISE-DAPT] score and Academic Research Consortium for High Bleeding Risk [ARC-HBR] criteria) for bleeding prediction after percutaneous coronary intervention.

What Are the Clinical Implications?

- The PRECISE-HBR score addresses the inconsistency between the PRECISE-DAPT and ARC-HBR scores in identifying patients with percutaneous coronary intervention at high bleeding risk, enabling standardized risk stratification in clinical practice and trials.
- Routine evaluation of relevant and readily available bleeding predictors with the PRECISE-HBR score could assist clinicians in counseling patients and anticipate and prevent bleeding after percutaneous coronary intervention.

Nonstandard Abbreviations and Acronyms

ACUITY	Acute Catheterization and Urgent Intervention Triage Strategy
ARC-HBR	Academic Research Consortium for High Bleeding Risk
AUC	area under the curve
BARC	Bleeding Academic Research Consortium
DAPT	dual antiplatelet therapy
MASTER DAPT	Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Prolonged DAPT Regimen
PCI	percutaneous coronary intervention
PRECISE-DAPT	Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy
STOPDAPT-2	Short and Optimal Duration of Dual Antiplatelet Therapy-2
TIMI	Thrombosis in Myocardial Infarction

The prediction and prevention of bleeding hold an essential role in managing patients undergoing percutaneous coronary intervention (PCI).[1,2] The Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy (PRECISE-DAPT) score is a 5-item tool that can assist clinicians in predicting bleeding risk and adjusting the duration of dual antiplatelet therapy (DAPT) after PCI.[3] This score was generated with data from 8 randomized trials, excluding subjects on oral anticoagulation or featured by other high bleeding risk conditions (eg, severe renal or liver disease, thrombocytopenia, and bleeding diathesis).[3] These aspects limit the performance and applicability of the score in clinical practice. In addition, the PRECISE-DAPT score was developed to predict bleeding according to the TIMI (Thrombosis in Myocardial Infarction) classification, which is no longer the standard for grading bleeding severity.[3]

The Academic Research Consortium for High Bleeding Risk (ARC-HBR) has recently defined high bleeding risk as a Bleeding Academic Research Consortium (BARC) 3 or 5 bleeding risk of ≥4% at 1 year and proposed 20 consensus criteria for a standardized definition of bleeding risk after PCI.[2] This framework comprises meaningful risk conditions that were not considered in the PRECISE-DAPT score and has been included across guidelines as an alternative to bleeding risk scores.[4,5] The ARC-HBR weighed high bleeding risk criteria into major and minor exclusively on the basis of consensus opinions.[2] Recent studies identified the need to reweigh these criteria and the limits of dichotomizing continuous variables such as age.[6,7]

Given their inherent potential and limitations, the PRECISE-DAPT score and the ARC-HBR criteria appear complementary, rather than alternative, in informing bleeding risk assessment after PCI. We augmented

the PRECISE-DAPT score with the ARC-HBR criteria to derive the novel PRECISE-HBR score.

METHODS

Study Design

We conducted a multinational study using 7 independent cohorts of patients undergoing PCI from geographically diverse centers across the globe. The study data set comprised patients from 4 real-world registries, 1 single-arm observational trial, and 2 randomized controlled trials. All included studies complied with the Declaration of Helsinki and were approved by institutional ethics committees. All patients provided written informed consent for participation in individual studies. The senior author (M.V.) had full access to all the data in the study and takes responsibility for its integrity and data analysis. Further information is provided in the Supplemental Methods and Table S1. Data from this study will be made available from the corresponding author and the study steering committee on reasonable request.

Study Population

Patient-level data from 4 contemporary real-world registries and 1 multicenter trial including patients undergoing PCI were pooled (Supplemental Methods; Table S1). The Bern PCI registry (NCT02241291) prospectively enrolled 17 339 consecutive patients undergoing PCI for acute or chronic coronary syndrome at Bern University Hospital (February 2009 through September 2018); the CardioCHUVI registry (Registry of Acute Coronary Syndrome From University Hospital of Vigo; NCT03664388) included 4021 consecutive patients with acute coronary syndrome admitted at the University Hospital Alvaro Cunqueiro of Vigo (January 2010 through January 2018); the FORCE-ACS registry (Future Optimal Research and Care Evaluation in Patients With Acute Coronary Syndrome; NCT03823547) prospectively included 3047 consecutive patients with acute coronary syndrome admitted in 9 Dutch centers[8] (January 2015 through June 2018); and the Clinical Governance of Patients With Acute Coronary Syndrome in Italy study (NCT04255537) included 1523 consecutive patients with acute coronary syndrome from 9 Italian centers (September 2015 through December 2017). The PRECISE-DAPT score[3] and the ARC-HBR criteria[2] were assessed in each study as originally reported. All registries implemented central event adjudication by independent clinical event committees using the BARC and TIMI classifications. The XIENCE V USA trial (NCT00676520) is a prospective, multicenter, single-arm study of 8040 all-comer patients undergoing PCI for acute or chronic coronary syndrome in the United States.[9] In the XIENCE V USA, TIMI bleedings were adjudicated by the study clinical event committee; BARC bleedings were adjudicated with an adjudication algorithm (Supplemental Methods).

Two independent cohorts of 4578 and 5970 patients with centrally adjudicated bleeding events from the MASTER DAPT trial (Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Prolonged DAPT Regimen)[1] and the STOPDAPT-2 (Short and Optimal Duration of Dual Antiplatelet Therapy-2) total cohort[10] were used for external validation after the exclusion of 1 and 27 patient(s), respectively, because of incomplete information. The MASTER DAPT trial is a global, multicenter, randomized trial that compared an abbreviated antiplatelet therapy with standard therapy after PCI in patients with high bleeding risk.[1] The STOPDAPT-2 total cohort is a pooled population of 2 multicenter, companion randomized trials in Japan comparing 1-month DAPT with standard DAPT after PCI.[10] In MASTER DAPT and STOPDAPT-2, bleeding events were centrally adjudicated according to the BARC and TIMI classifications.

Study Outcomes

The primary outcome of the study was BARC type 3 or 5 bleeding within 1 year after PCI. The secondary outcome was TIMI major or minor bleeding within 1 year after PCI.

Stratification Effect of Combining the PRECISE-DAPT and ARC-HBR Scores

Before the development phase, we explored the ability of the PRECISE-DAPT and ARC-HBR scores to yield incremental information for bleeding risk stratification when appraised in combination. Using the Bern PCI registry, we evaluated the distribution of the PRECISE-DAPT score by the ARC-HBR score and the 1-year incidence of bleeding stratifying patients by the combination of the PRECISE-DAPT score (high: score ≥25; nonhigh: score <25)[3] and the ARC-HBR definition (ARC-HBR: score ≥1; non–ARC-HBR: score <1).[6]

Statistical Analysis

Derivation of the PRECISE-HBR Score

We developed the PRECISE-HBR score on the basis of a core model consisting of the 5 predictors of the PRECISE-DAPT score.[3] Hereto, we fitted a Fine-Gray (proportional subdistribution hazards) model in the derivation cohort to account for censoring and competing death events.[11–13] Potential nonlinear effects of continuous predictors and calendar time were assessed by fitting restricted cubic splines with 5 knots at the 5%, 27.5%, 50%, 72.5%, and 95% percentiles. We extended the refitted PRECISE-DAPT score with the ARC-HBR criteria.[2] To avoid redundancy, the ARC-HBR criteria containing information on age, hemoglobin, renal function, and previous bleeding, which are factored into the PRECISE-DAPT score, were excluded. Independent predictors of BARC 3 or 5 bleeding were selected at multivariable analysis ($P<0.01$) and included in the final model with weights proportional to the model coefficients. Linear predictor values of the final model were linearly transformed (eg, scaled and rounded) to a score with integer values between 0 and 70. We used a Fine-Gray model to convert the PRECISE-HBR score to the risk of BARC 3 or 5 bleeding within 1 year after PCI. Thus, risk predictions are based on the regression coefficient and the baseline subdistribution hazard of a Fine-Gray model with the PRECISE-HBR score as the single predictor. Further information on the score variables is reported in the Supplemental Methods and Tables S2 and S3.

Internal and External Validation

We assessed the performance of the score in the derivation cohort at apparent validation and leave-1-cohort-out cross-validation.[14,15] For cross-validation, each of the 5 contributing

studies was iteratively excluded from the development set; the model was then trained using the selected predictors in the remaining studies and validated in the omitted study.[14] The score was externally validated in the MASTER DAPT[1] and STOPDAPT-2 trials.[10] Because bleeding events in the first month after PCI were not collected in MASTER DAPT, score calibration was evaluated on the basis of observed bleeding events between 1 and 12 months in this trial.[1]

Discrimination was quantified with the area under the receiver-operating characteristic curve (AUC) at 1 year. Hereto, we evaluated the inverse probability of censoring the weighted estimate of the time-dependent receiver-operating characteristic curve at 1 year, with bleeding events as cases and either death or no events as controls.[12,16] Calibration was assessed by comparing the predicted versus observed cumulative incidences of 1-year bleeding in 10 equally sized groups stratified according to predicted bleeding risk using calibration plots.[14] Risk stratification ability was assessed by comparing cumulative incidence curves in clinically relevant bleeding risk strata with the Gray test in cross-validation data. Hereto, based on the 1-year risk of BARC 3 or 5 bleeding, we used two cutoffs to identify patients at high bleeding risk (≥4%), consistent with the ARC-HBR definition,[2] and very high bleeding risk (≥6%). In secondary analyses, we evaluated score discrimination after excluding access site–related bleeding and in subgroups of interest. We compared the discrimination of the PRECISE-HBR score with previous scores[2,3,6,17–21] by statistically comparing AUCs.[22] We used bootstrapping to obtain variances and CIs of AUC estimates and of estimates of differences in AUC between risk scores. Cross-validated AUC estimates were pooled into a summary AUC with random-effects meta-analysis.[12,23] The net reclassification index was also computed to compare the PRECISE-HBR score with the PRECISE-DAPT and ARC-HBR scores[24]; thresholds for comparison were set for each cohort so that the proportion of predicted high-risk patients was equal to that obtained with the ARC-HBR score. Analyses were performed following the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis statement (Table S4),[25] with R packages Survival (version 3.5-5) for Fine-Gray modeling and timeROC (version 0.4) for assessing discriminative ability of competing risk models (R Foundation, Vienna, Austria).[26–28]

RESULTS

Study Population

The derivation cohort of 29 188 patients was obtained from a population of 33 970 participants after the exclusion of 4782 patients with incomplete data (Table S1). Baseline characteristics and 1-year incidence of bleeding are shown in Table 1 and Table S5. Mean age was 66.2 years; 73.7% were men; and 59.8% presented with acute coronary syndrome. At discharge, DAPT was prescribed in 94.7% of patients, oral anticoagulation in 9.3% of patients, and the combination of DAPT plus oral anticoagulation in 7.5% of patients. At 1 year, BARC 3 or 5 bleeding occurred in 1136 patients (3.9%), with a median time to first event of 40 days (interquartile range, 2–163 days).

Risk Stratification With PRECISE-DAPT and ARC-HBR Scores

In a preliminary analysis examining the stratification effect of combining the PRECISE-DAPT and ARC-HBR scores in the Bern PCI registry (n=14 785), high values of PRECISE-DAPT score generally corresponded with high values of the ARC-HBR score (Figure S1). Bleeding rates at 1 year were the highest in the 3546 patients (24.0%) with PRECISE-DAPT score ≥25 and ARC-HBR score ≥1, intermediate in the 2879 patients (19.5%) with discordant scores, and lowest in the 8360 patients (56.5%) with a PRECISE-DAPT score <25 and an ARC-HBR score <1 (Figure S2).

Development of the PRECISE-HBR Score

The PRECISE-HBR score consisted of 7 items: age, hemoglobin, estimated glomerular filtration rate, white blood cell count, previous spontaneous bleeding, long-term oral anticoagulation, and the presence of at least one of the remaining ARC-HBR elements (except previous stroke; Table 2; Figure S3). Nonlinear associations, modeled first with restricted cubic splines, were simplified to closely resemble linear associations in combination with caps and floors (Figure S4). Among the ARC-HBR criteria, oral anticoagulation was considered a distinct domain because of its high prevalence in the derivation cohort (n=2703). The other ARC-HBR elements (thrombocytopenia, bleeding diathesis, active malignancy, liver cirrhosis with portal hypertension, recent major surgery or trauma, and chronic use of nonsteroidal anti-inflammatory drugs or corticosteroids) were clustered into a composite risk item because of the low prevalence (2122 patients overall; Supplemental Methods). The ARC-HBR criteria featured by previous stroke were excluded because of the negative and nonsignificant association with bleeding (regression coefficient, −0.13; P=0.31). An alternative model was developed by omitting white blood cell count and including acute myocardial infarction on admission because of its independent association with 1-year BARC 3 or 5 bleeding after the former covariate was removed from the model (χ^2=29.4; P<0.001; Table S6).

The score distribution and predicted 1-year bleeding rate in the derivation cohort are shown in Figure 1; data stratified by the presence of acute myocardial infarction are shown in Figure S5. According to the 1-year incidence of BARC 3 or 5 bleeding (eg, <4%, 4%–5.9%, and ≥6%), 17 774 patients (60.9%) were classified as at nonhigh risk, 5121 patients (17.5%) as at high risk, and 6293 patients (21.6%) as at very high risk for bleeding. Cumulative incidence curves were consistently separated by score categories (nonhigh risk: score ≤22; high risk: score 23–26; very high risk: score ≥27) with significant differences (P<0.001; Figure 2). Stratification effect remained consistent in patients on oral

Table 1. Baseline Characteristics of the Derivation Cohort Stratified by Individual Studies

	Overall population (n=29 188)	Bern PCI registry (n=14 785)	CardioCHUVI (n=4017)	FORCE-ACS (n=2045)	Clinical Governance of Patients With ACS (n=1120)	XIENCE V USA (n=7221)
Age, y	(n=29 188) 66.2 (11.9)	(n=14 785) 67.6 (11.9)	(n=4017) 64.1 (13.2)	(n=2045) 65.2 (11.6)	(n=1120) 65.8 (12.5)	(n=7221) 64.7 (10.8)
Female sex, n/N (%)	7684/29 188 (26.3)	3769/14 785 (25.5%)	871/4017 (21.7)	547/2045 (26.7)	292/1120 (23.1)	2205/7221 (30.5)
Male sex, n/N (%)	21 504/29 188 (73.7)	11 016/14 785 (74.5)	3146/4017 (78.3)	1498/2045 (73.3)	828/1120 (73.9)	5016/7221 (69.5)
Body mass index, kg/m²	(n=28 413) 28.3 (5.23)	(n=14 314) 27.4 (4.7)	(n=4017) 28.3 (4.4)	(n=1969) 27.5 (4.4)	(n=1019) 26.7 (4.5)	(n=7221) 30.4 (6.27)
Current smoker, n/N (%)	8102/28 675 (28.3)	38 747/14 596 (26.5)	1551/4017 (38.6)	682/2033 (33.5)	462/1120 (41.3)	1533/6909 (22.2)
Hypertension, n/N (%)	15 856/28 895 (54.9)	10 374/14 693 (70.6)	2465/4017 (61.4)	1067/2029 (52.6)	710/1120 (63.4)	1240/7036 (17.6)
Diabetes, n/N (%)	7856/29 079 (27.0)	3538/14 740 (24.0)	970/4017 (24.1)	549/2038 (26.9)	241/1120 (21.5)	2558/7164 (35.7)
Previous PCI, n/N (%)	7754/28 966 (26.8)	3675/14 730 (24.9)	672/4017 (16.7)	411/2044 (20.1)	240/1120 (21.4)	2756/7055 (39.1)
Previous CABG, n/N (%)	3075/28 981 (10.6)	1578/14 744 (10.7)	139/4017 (3.5)	120/2045 (5.9)	57/1120 (5.1)	1181/7055 (16.7)
Previous stroke, n/N (%)	1333/29 188 (4.6)	786/14 785 (5.3)	166/4017 (4.1)	46/2045 (2.2)	19/1120 (1.7)	316/7221 (4.4)
Previous spontaneous bleeding, n/N (%)	1041/29 188 (3.6)	656/14 785 (4.4)	253/4017 (6.3)	44/2045 (2.2)	11/1120 (1.0)	77/7221 (1.1)
Active malignancy, n/N (%)	467/29 188 (1.6)	348/14 785 (2.4)	25/4017 (0.6)	59/2045 (2.9)	35/1120 (3.1)	0/7221 (0.0)
Liver disease, n/N (%)	159/21 967 (0.7)	44/14 785 (0.3)	111/4017 (2.8)	4/2045 (0.2)	0/1120 (0.0)	NA
Liver cirrhosis with PH, n/N (%)	44/29 188 (0.2)	22/14 785 (0.1)	18/4017 (0.4)	4/2045 (0.2)	0/1120 (0.0)	0/7221 (0.0)
Bleeding diathesis, n/N (%)	38/29 188 (0.1)	12/14 785 (0.1)	5/4017 (0.1)	1/2045 (0.05)	1/1120 (0.1%)	19/7221 (0.3)
Chronic use of NSAIDs or steroids, n/N (%)	1143/29 188 (3.9)	656/14 785 (4.4)	352/4017 (8.8)	66/2045 (3.2)	11/1120 (1.0)	58/7221 (0.8)
Recent major surgery or trauma, n/N (%)	194/29 188 (0.7)	182/14 785 (1.2)	8/4017 (0.2)	4/2045 (0.2)	0/1120 (0.0)	0/7221 (0.0)
Clinical presentation, n/N (%)						
CCS	11 607/28 873 (40.2)	6993/14 785 (47.3)	0/4017 (0)	0/2045 (0)	0/1120 (0)	4614/6906 (66.8)
ACS	17 266/28 873 (59.8)	7792/14 785 (52.7)	4017/4017 (100)	2045/2045 (100)	1120/1120 (100)	2292/6906 (33.2)
Unstable angina	2690/17 266 (15.5)	706/7792 (9.1)	333/4017 (8.3)	126/2045 (6.2)	24/1120 (2.1)	1501/2292 (65.4)
NSTEMI	7352/17 266 (42.6)	3771/7792 (48.4)	1723/4017 (42.9)	819/2045 (40.0)	427/1120 (38.1)	612/2292 (26.7)
STEMI	7224/17 266 (41.9)	3315/7792 (42.5)	1961/4017 (48.8)	1100/2045 (53.8)	669/1120 (59.8)	179/2292 (7.9)
eGFR, mL·min^{-1}·1.73 m^{-2}	(n=29 188) 78.3 (26.3)	(n=14 785) 80.7 (27.1)	(n=4017) 80.2 (28.6)	(n=2045) 77.7 (22.8)	(n=1120) 79.5 (28.2)	(n=7221) 72.3 (22.8)
Hemoglobin levels, g/L	(n=29 188) 13.8 (1.8)	(n=14 785) 13.7 (1.8)	(n=4017) 14.3 (1.8)	(n=2045) 14.0 (1.6)	(n=1120) 13.9 (1.7)	(n=7221) 13.7 (1.7)
Leucocytes, 10^3 cells/μL	(n=29 188) 9.0 (4.2)	(n=14 785) 9.0 (4.3)	(n=4017) 10.1 (4.2)	(n=2045) 10.3 (6.0)	(n=1120) 10.8 (4.0)	(n=7221) 7.7 (2.6)
Platelet count <100×10^9/L	236/29 188 (0.8)	151/14 785 (1.0)	9/4017 (0.2)	13/2045 (0.6)	13/1120 (1.2)	50/7221 (0.7)
Medications at discharge, n/N (%)						
Aspirin	27 975/28 849 (97.0)	13 979/14 476 (96.6)	4011/4017 (99.9)	1830/2045 (89.5)	1054/1120 (94.1)	7101/7191 (98.7)
Clopidogrel	19 264/28 831 (66.8)	8137/14 476 (56.2)	3319/3993 (83.1)	564/2045 (27.6)	264/1120 (23.6)	6980/7197 (97.0)
Ticagrelor	6425/21 634 (29.7)	3815/14 476 (26.4)	430/3993 (10.8)	1412/2045 (69.0)	768/1120 (68.6)	0/7221 (0.0)
Prasugrel	2704/24 352 (11.1)	2253/14 476 (15.6)	244/3993 (6.1)	14/2045 (0.7)	29/1120 (2.6)	164/7197 (2.3)
DAPT	27 643/29 188 (94.7)	13 753/14 785 (93.0%)	3993/4017 (99.4)	1816/2045 (88.8)	1005/1120 (89.7)	7076/7221 (98.0)
DAPT plus OAC	2200/29 188 (7.5)	1487/14 785 (10.1)	174/4017 (4.3)	92/2045 (4.5)	45/1120 (4.0)	402/7221 (5.6)
Long-term OAC	2703/29 188 (9.3)	1741/14 785 (11.8)	198/4017 (4.9)	269/2045 (13.2)	61/1120 (5.4)	434/7221 (6.0)
Proton pump inhibitors	11 020/18 050 (61.1)	4342/10 868 (40.0)	4017/4017 (100)	1616/2045 (79.0)	1045/1120 (93.3)	NA

Data expressed as number (percent) or mean (SD).

ACS indicates acute coronary syndrome; ARC-HBR, Academic Research Consortium for High Bleeding Risk; CABG, coronary artery bypass grafting; CardioCHUVI, Registry of Acute Coronary Syndrome From University Hospital of Vigo; CCS, chronic coronary syndrome; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; FORCE-ACS, Future Optimal Research and Care Evaluation in Patients With Acute Coronary Syndrome; NA, not available; NSAID, nonsteroidal anti-inflammatory drug; NSTEMI, non–ST-segment–elevation myocardial infarction; OAC, oral anticoagulation; PCI, percutaneous coronary intervention; PH, portal hypertension; and STEMI, ST-segment–elevation myocardial infarction.

Renal failure: eGFR <60 mL·min^{-1}·1.73 m^{-2} using the Modification of Diet in Renal Diseases equation. ARC-HBR: at least 1 major or at least 2 minor criteria. Non–ARC-HBR: no major or minor criteria or only 1 minor criterion.

Table 2. Multivariable Association of the PRECISE-HBR Score Items With 1-Year BARC 3 or 5 Bleeding

	Subdistribution hazard ratio (95% CI)	*P* value
Age (for each increase of 10 y)	1.28 (1.19–1.37)	<0.001
Hemoglobin (for each increase of 1 g/dL)	0.78 (0.76–0.81)	<0.001
Estimated glomerular filtration rate (for each increase of 10 mL·min^{-1}·1.73 m^{-2})	0.95 (0.92–0.98)	<0.001
White blood cell count (for each increase of 10^3 cells/μL)	1.08 (1.06–1.10)	<0.001
Previous bleeding	1.96 (1.59–2.42)	<0.001
Long-term oral anticoagulation	1.58 (1.35–1.85)	<0.001
Additional ARC-HBR elements ≥1	1.34 (1.11–1.62)	0.002

ARC-HBR indicates Academic Research Consortium for High Bleeding Risk; and BARC, Bleeding Academic Research Consortium.

Age, hemoglobin, and estimated glomerular filtration rate were considered continuous predictors. Age was truncated above 80 years and below 30 years. Hemoglobin was truncated above 15 g/dL and below 5 g/dL. Estimated glomerular filtration rate was truncated above 100 mL·min^{-1}·1.73 m^{-2}. White blood cell count was truncated above 15×10^3 cells/μL. Additional ARC-HBR elements included thrombocytopenia (platelet count <100×10^9/L), chronic bleeding diathesis, liver cirrhosis with portal hypertension, active malignancy, recent major surgery or trauma, and chronic use of nonsteroidal anti-inflammatory drugs or corticosteroids.

anticoagulation and in patients presenting with acute or chronic coronary syndrome (Figure S6).

The distribution of risk categories by score item was assessed visually (Figure S7). In general, patients at high and very high bleeding risk more frequently populated strata featured by advanced age, anemia, low estimated glomerular filtration rate, high white blood cell count, anticoagulation, previous bleeding, and ≥1 ARC-HBR elements. Yet, these strata also accommodated, in lower proportions, patients at nonhigh risk of bleeding.

Internal Validation

At apparent validation, the PRECISE-HBR score showed an AUC of 0.73 (95% CI, 0.71–0.74) for 1-year BARC 3 or 5 bleeding (Table 3). Discrimination was consistent across subgroups, regardless of sex, clinical presentation, or antithrombotic therapy (Table S7). In a sensitivity analysis excluding access site bleeding, the score had an identical AUC (0.73 [95% CI, 0.71–0.74]). Discrimination was similar when TIMI major or minor bleeding was assessed (AUC, 0.71 [95% CI, 0.69–0.73]). In a random-effects meta-analysis of cross-validation AUCs, the score showed an AUC for 1-year BARC 3 or 5 bleeding of 0.72 (95% CI, 0.70–0.73; Table 3; Table S8), yielding consistent results after the exclusion of access site bleeding (AUC, 0.72 [95% CI, 0.70–0.73]). The PRECISE-HBR score achieved improved discrimination for 1-year BARC 3 or 5 bleeding compared with the PRECISE-DAPT, ARC-HBR, and other risk scores (Table 3). The performance of the alternative score version was similar to that of the original model (Table 3).

The PRECISE-HBR and its alternative version showed accurate calibration for BARC 3 or 5 bleeding in cross-validation data (Figures S8 and S9); score calibration remained similar in patients with oral anticoagulation and for TIMI-defined bleeding (Figures S10 through S12). The PRECISE-DAPT showed poor calibration in the derivation cohort because of consistent risk underestimation (Figure S13). The net reclassification index of the PRECISE-HBR was 0.020 and 0.025 compared with the PRECISE-DAPT and ARC-HBR scores, respectively (Table S9).

External Validation

At external validation in the MASTER DAPT cohort, the PRECISE-HBR score had an AUC of 0.74 (95% CI, 0.68–0.80) for 1- to 12-month BARC 3 or 5 bleeding. In the STOPDAPT-2 cohort, the AUC for 1-year BARC 3 or 5 bleeding was 0.73 (95% CI, 0.66–0.79). The novel score was superior to the PRECISE-DAPT score, ARC-HBR score, ARC-HBR definition, and HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, and drugs/alcohol concomitantly), ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy), ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation), and ORBIT (Outcomes Registry for Better Informed Treatment of Atrial Fibrillation) scores in MASTER DAPT and the ARC-HBR score, ARC-HBR definition, and ACUITY score in STOPDAPT-2 for the prediction of BARC 3 or 5 bleeding (Table 3). Discrimination in the external validation cohorts remained consistent in patients receiving proton pump inhibitors and abbreviated or standard DAPT (Table S10). In calibration analysis, the novel score overestimated the risk of BARC 3 or 5 bleeding between 1 and 12 months after PCI in the MASTER DAPT cohort (Figure S14) and within 1 year after PCI in the STOPDAPT-2 cohort (Figure S15). The net reclassification index of the PRECISE-HBR versus the PRECISE-DAPT and ARC-HBR scores was 0.29 and 0.70 in the MASTER DAPT and 0.035 and 0.085 in the STOPDAPT-2, respectively (Table S9). The performance of the alternative version of the score in the MASTER DAPT and STOPDAPT-2 data sets was similar to that of the original model.

DISCUSSION

We developed, cross-validated, and externally validated a novel bleeding risk score in patients undergoing PCI. We combined 2 contemporary and guideline-recommended[4,5,29,30] risk algorithms, the PRECISE-DAPT score and the ARC-HBR criteria, into the PRECISE-HBR score to provide a comprehensive bleeding risk scheme for the full spectrum of PCI recipients. The new

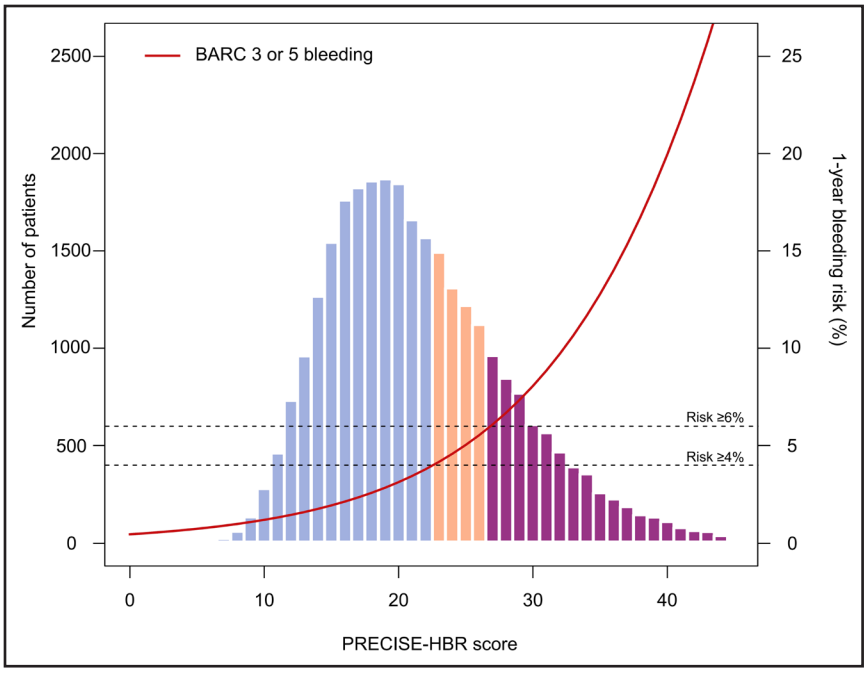

Figure 1. Distribution of the PRECISE-HBR score and predicted 1-year rate of BARC 3 or 5 bleeding in the derivation cohort.
The risk curve refers to Bleeding Academic Research Consortium (BARC) 3 or 5 bleeding at 1 year. Dotted lines refer to the thresholds for high and very high bleeding risk. Histogram refers to the score distribution in the derivation cohort: blue bars, patient at nonhigh bleeding risk (1-year BARC 3 or 5 bleeding rate, <4% [score ≤22]); orange bars, patients at high bleeding risk (1-year rate, ≥4% and <6% [score, 23–26]); and purple bars, patients at very high bleeding risk (1-year rate, ≥6% [score ≥27]).

score, based on 7 domains (age, hemoglobin, estimated glomerular filtration rate, white blood cell count, previous bleeding, oral anticoagulation, and ARC-HBR elements), showed a moderate discrimination in independent cohorts of patients undergoing PCI; It consistently predicted bleeding in clinically important subgroups, retained consistent estimation of spontaneous (eg, not procedurally related) events, and retained discriminative capability toward more severe bleeding (eg, TIMI major or minor). An alternative version of the score with acute myocardial infarction on admission was derived and validated that could be useful if white blood cell count is not available or altered by concomitant systemic conditions. The original and alternative PRECISE-HBR scores provided a moderate improvement in discrimination compared with the PRECISE-DAPT and other bleeding risk scores at cross-validation and external validation, although the numerical improvement in AUC was not always statistically significant. Calibration was accurate in the cross-validation cohort of real-world studies, but the score overestimated bleeding risk in the external validation cohorts from the MASTER DAPT and STOPDAPT-2 randomized trials. Reclassification analyses indicated that the novel score offers incremental value over existing tools.

The management of antithrombotic therapy after PCI remains complex.[4,5,29] DAPT confers ischemic protection after stent implantation, although with an inherent increase in the risk of bleeding.[1,31–34] These considerations are amplified when coexisting conditions require long-term anticoagulation (eg, atrial fibrillation and heart valve prosthesis).[35] International guidelines recommend the selection of antithrombotic treatment based on the individual bleeding risk.[4,5,29,30] Hence, accurate prediction of bleeding is essential, and many algorithms have been proposed with this intent. Some risk scores have been developed for modeling bleeding risk after acute coronary syndrome,[18,36–38] in selected patients at high bleeding risk,[39] or in patients who have tolerated 1-year DAPT[40]; therefore, they do not cover the entire spectrum of patients undergoing PCI. The utility of bleeding scores developed for atrial fibrillation[19–21] remains unclear when coronary revascularization occurs. The PRECISE-DAPT score is widely adopted and endorsed by guidelines[4,5,29,30] but has limitations.[41] It was created using randomized trials with mandated use of DAPT and excluded subjects on oral anticoagulation or with other high bleeding risk conditions.[3] This limits its applicability in anticoagulated patients and raises concerns for possible risk underestimation in real-world patients, which was confirmed here by the poor calibration observed in the derivation cohort. The PRECISE-DAPT was also modeled for the prediction of TIMI bleeding and featured the identification of patients at high bleeding risk based on the score distribution in the derivation data set.[3] More recently, the ARC-HBR consortium offered a framework for the identification of patients at high bleeding risk with a cutoff of ≥4% risk of BARC 3 or 5 bleeding at 1 year.[2] This framework is pragmatic but limited by the consensus definition; thus, the risk associated with the ARC-HBR major or minor criteria is not defined.[2] Current guidelines[4,5,30] recommend the PRECISE-DAPT score or the ARC-HBR criteria to define bleeding risk. However, the nonhigh bleeding risk category of the PRECISE-DAPT conceals a significant proportion of patients at high bleeding risk according to the ARC-HBR criteria and vice versa; these patients are possibly misclassified and improperly treated in daily practice.[1–3] The PRECISE-HBR score was developed to address the inconsistency

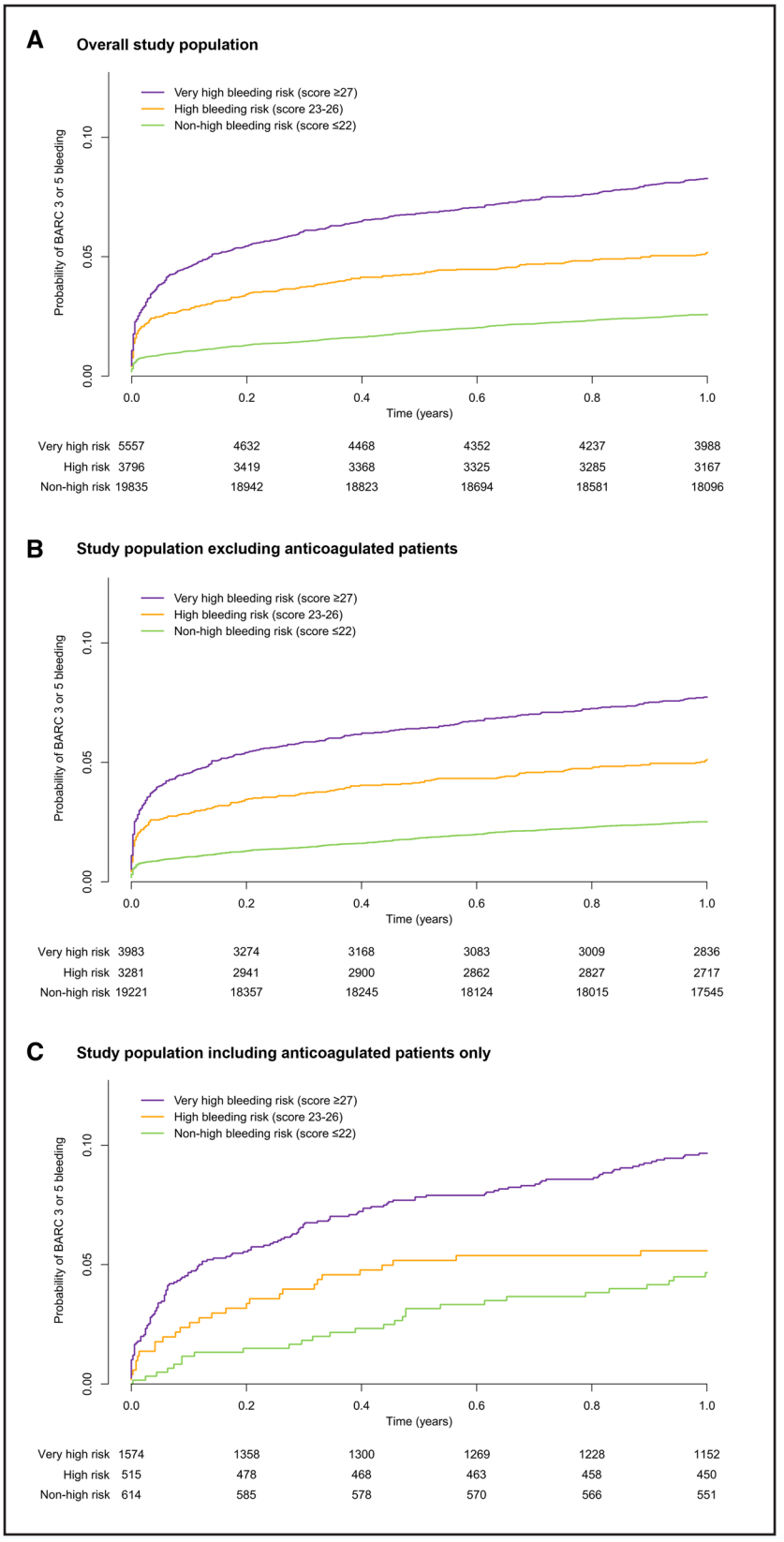

Figure 2. Cumulative incidence curves of BARC 3 or 5 bleeding in the cross-validation cohort stratified by bleeding risk according to the PRECISE-HBR score.
Cumulative incidence of Bleeding Academic Research Consortium (BARC) 3 or 5 bleeding occurring within 1 year is presented. **A**, Overall cross-validation analysis included 29 188 patients undergoing PCI from 4 real-world registries and the XIENCE V USA trial. **B**, Cross-validation analysis excluding anticoagulated patients. **C**, Cross-validation analysis including anticoagulated patients only. Anticoagulated patients are those with anticipated use of long-term oral anticoagulation. Patients were stratified as at nonhigh bleeding risk (1-year BARC 3 or 5 bleeding rate, <4% [score ≤22]), at high bleeding risk (1-year rate, ≥4% and <6% [score, 23–26]), or at very high bleeding risk (1-year rate, ≥6% [score ≥27]).

between these 2 stratification systems through an update of the PRECISE-DAPT score with the ARC-HBR criteria,[2] the use of the more modern BARC instead of TIMI scales, and the adoption of a standard threshold for the identification of high-risk patients instead of a study-specific cutoff.[3] In addition, we propose a standardized definition for very high bleeding risk (≥6% risk of 1-year BARC 3 or 5 bleeding

Table 3. Discrimination of the PRECISE-HBR Score and Comparison With Other Risk Scores for 1-Year BARC 3 or 5 Bleeding and TIMI Major or Minor Bleeding

	BARC 3 or 5 bleeding					TIMI major or minor bleeding				
	AUC (95% CI)	ΔAUC (95% CI)*	*P* value*	ΔAUC (95% CI)†	*P* value†	AUC (95% CI)	ΔAUC (95% CI)*	*P* value*	ΔAUC (95% CI)†	*P* value†
Apparent validation										
PRECISE-HBR	0.73 (0.71 to 0.74)	…	…	…	…	0.71 (0.69 to 0.73)	…	…	…	…
PRECISE-HBR alternative	0.72 (0.71 to 0.74)	…	…	…	…	0.71 (0.69 to 0.72)	…	…	…	…
Cross-validation										
PRECISE-HBR	0.72 (0.70 to 0.73)	Ref*	Ref*	…	…	0.71 (0.68 to 0.73)	Ref*	Ref*	…	…
PRECISE-HBR alternative	0.72 (0.70 to 0.74)	…	…	Ref†	Ref†	0.71 (0.68 to 0.74)	…	…	Ref†	Ref†
PRECISE-DAPT	0.71 (0.68 to 0.73)	0.01 (0.00 to 0.03)	0.02	0.01 (0.00 to 0.03)	0.09	0.70 (0.67 to 0.73)	0.01 (0.00 to 0.03)	0.02	0.01 (0.00 to 0.03)	0.13
ARC-HBR (score)	0.69 (0.67 to 0.72)	0.03 (0.02 to 0.04)	<0.001	0.02 (0.01 to 0.03)	0.002	0.69 (0.66 to 0.72)	0.02 (0.01 to 0.03)	<0.001	0.02 (0.01 to 0.03)	0.005
ARC-HBR (original definition)	0.65 (0.63 to 0.68)	0.07 (0.06 to 0.08)	<0.001	0.07 (0.06 to 0.08)	<0.001	0.65 (0.61 to 0.68)	0.07 (0.05 to 0.08)	<0.001	0.06 (0.05 to 0.08)	<0.001
PARIS	0.67 (0.64 to 0.70)	0.05 (0.03 to 0.07)	<0.001	0.05 (0.03 to 0.07)	<0.001	0.66 (0.63 to 0.69)	0.04 (0.02 to 0.06)	<0.001	0.05 (0.02 to 0.07)	<0.001
ACUITY	0.69 (0.68 to 0.71)	0.03 (0.01 to 0.05)	0.009	0.03 (0.00 to 0.05)	0.02	0.69 (0.67 to 0.71)	0.02 (0.00 to 0.04)	0.07	0.02 (-0.01 to 0.05)	0.12
HAS-BLED	0.65 (0.60 to 0.70)	0.07 (0.04 to 0.11)	<0.001	0.07 (0.04 to 0.11)	<0.001	0.64 (0.58 to 0.70)	0.07 (0.03 to 0.11)	<0.001	0.07 (0.03 to 0.11)	<0.001
ATRIA	0.67 (0.64 to 0.71)	0.05 (0.02 to 0.07)	<0.001	0.05 (0.03 to 0.07)	<0.001	0.66 (0.62 to 0.71)	0.05 (0.02 to 0.08)	<0.001	0.05 (0.02 to 0.08)	0.001
ORBIT	0.68 (0.65 to 0.71)	0.04 (0.02 to 0.06)	<0.001	0.04 (0.02 to 0.06)	0.001	0.67 (0.63 to 0.72)	0.04 (0.02 to 0.06)	<0.001	0.04 (0.01 to 0.06)	0.003
MASTER DAPT validation cohort‡										
PRECISE-HBR	0.74 (0.68 to 0.80)	Ref*	Ref*	…	…	0.67 (0.61 to 0.72)	Ref*	Ref*	…	…
PRECISE-HBR alternative	0.75 (0.69 to 0.80)	…	…	Ref†	Ref†	0.67 (0.61 to 0.73)	…	…	Ref†	Ref†
PRECISE-DAPT	0.69 (0.63 to 0.75)	0.05 (0.02 to 0.09)	0.004	0.06 (0.02 to 0.10)	0.003	0.63 (0.57 to 0.68)	0.05 (0.00 to 0.09)	0.05	0.05 (0.00 to 0.09)	0.04
ARC-HBR (score)	0.70 (0.63 to 0.76)	0.04 (0.00 to 0.09)	0.04	0.05 (0.02 to 0.08)	0.001	0.63 (0.57 to 0.70)	0.04 (0.00 to 0.07)	0.07	0.04 (0.00 to 0.07)	0.04
ARC-HBR (original definition)	0.57 (0.53 to 0.61)	0.17 (0.12 to 0.22)	<0.001	0.18 (0.14 to 0.21)	<0.001	0.55 (0.51 to 0.59)	0.12 (0.07 to 0.17)	<0.001	0.12 (0.07 to 0.17)	<0.001
PARIS	0.73 (0.67 to 0.79)	0.01 (–0.04 to 0.06)	0.64	0.02 (–0.03 to 0.07)	0.44	0.65 (0.59 to 0.71)	0.02 (–0.03 to 0.07)	0.48	0.02 (–0.03 to 0.07)	0.47
ACUITY	0.65 (0.59 to 0.70)	0.10 (0.04 to 0.15)	<0.001	0.10 (0.05 to 0.15)	<0.001	0.61 (0.56 to 0.66)	0.06 (0.00 to 0.11)	0.045	0.06 (0.00 to 0.11)	0.035
HAS-BLED	0.61 (0.55 to 0.68)	0.13 (0.06 to 0.19)	<0.001	0.13 (0.08 to 0.19)	<0.001	0.60 (0.55 to 0.66)	0.07 (0.01 to 0.13)	0.017	0.07 (0.02 to 0.12)	0.007
ATRIA	0.67 (0.62 to 0.73)	0.07 (0.02 to 0.11)	0.004	0.07 (0.03 to 0.12)	0.001	0.62 (0.57 to 0.68)	0.05 (0.00 to 0.10)	0.050	0.05 (0.01 to 0.10)	0.026
ORBIT	0.67 (0.61 to 0.73)	0.07 (0.03 to 0.11)	0.001	0.07 (0.04 to 0.11)	<0.001	0.61 (0.56 to 0.67)	0.06 (0.02 to 0.10)	0.007	0.06 (0.02 to 0.10)	0.005
STOPDAPT-2 validation cohort										
PRECISE-HBR	0.73 (0.66 to 0.79)	Ref*	Ref*	…	…	0.72 (0.66 to 0.78)	Ref*	Ref*	…	…
PRECISE-HBR alternative	0.71 (0.64 to 0.78)	…	…	Ref†	Ref†	0.69 (0.63 to 0.76)	…	…	Ref†	Ref†

(*Continued*)

Table 3. Continued

	BARC 3 or 5 bleeding					TIMI major or minor bleeding				
	AUC (95% CI)	ΔAUC (95% CI)*	*P* value*	ΔAUC (95% CI)†	*P* value†	AUC (95% CI)	ΔAUC (95% CI)*	*P* value*	ΔAUC (95% CI)†	*P* value†
PRECISE-DAPT	0.71 (0.64 to 0.77)	0.02 (−0.01 to 0.06)	0.20	0.00 (−0.03 to 0.04)	0.87	0.70 (0.63 to 0.76)	0.02 (−0.02 to 0.06)	0.28	0.00 (−0.04 to 0.03)	0.87
ARC-HBR (score)	0.66 (0.59 to 0.73)	0.07 (0.03 to 0.11)	0.001	0.05 (0.01 to 0.09)	0.02	0.65 (0.58 to 0.72)	0.07 (0.02 to 0.12)	0.004	0.05 (0.00 to 0.09)	0.03
ARC-HBR (original definition)	0.62 (0.55 to 0.68)	0.11 (0.06 to 0.16)	<0.001	0.09 (0.04 to 0.14)	0.001	0.60 (0.53 to 0.67)	0.12 (0.05 to 0.18)	<0.001	0.09 (0.04 to 0.15)	0.001
PARIS	0.69 (0.62 to 0.76)	0.04 (−0.01 to 0.08)	0.12	0.02 (−0.04 to 0.07)	0.53	0.69 (0.61 to 0.76)	0.03 (−0.03 to 0.10)	0.32	0.01 (−0.04 to 0.06)	0.75
ACUITY	0.68 (0.61 to 0.74)	0.05 (0.01 to 0.09)	0.013	0.03 (−0.01 to 0.07)	0.15	0.67 (0.60 to 0.75)	0.04 (−0.01 to 0.10)	0.11	0.02 (−0.02 to 0.06)	0.38
HAS-BLED	0.68 (0.62 to 0.75)	0.05 (0.00 to 0.09)	0.055	0.03 (−0.02 to 0.07)	0.22	0.68 (0.62 to 0.74)	0.04 (0.00 to 0.08)	0.071	0.01 (−0.03 to 0.06)	0.48
ATRIA	0.71 (0.65 to 0.78)	0.01 (−0.03 to 0.06)	0.52	0.00 (−0.05 to 0.04)	0.80	0.70 (0.63 to 0.77)	0.02 (−0.03 to 0.06)	0.43	−0.01 (−0.05 to 0.04)	0.79
ORBIT	0.70 (0.63 to 0.76)	0.03 (−0.01 to 0.07)	0.12	0.01 (−0.02 to 0.05)	0.53	0.68 (0.61 to 0.75)	0.04 (0.00 to 0.08)	0.055	0.02 (−0.02 to 0.06)	0.42

ACUITY indicates Acute Catheterization and Urgent Intervention Triage Strategy; ARC-HBR, Academic Research Consortium for High Bleeding Risk; ATRIA, Anticoagulation and Risk Factors in Atrial Fibrillation; AUC, area under the curve; BARC, Bleeding Academic Research Consortium; HAS-BLED, hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly; MASTER DAPT, Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Prolonged DAPT Regimen; ORBIT, Outcomes Registry for Better Informed Treatment of Atrial Fibrillation; PARIS, Patterns of Non-Adherence to Anti-Platelet Regimen in Stented Patients; PCI, percutaneous coronary intervention; PRECISE-DAPT, Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy; Ref, reference; STOPDAPT-2, Short and Optimal Duration of Dual Antiplatelet Therapy-2; and TIMI, Thrombosis in Myocardial Infarction.

Δ AUC expresses the absolute difference in AUC between scores. The alternative version of the PRECISE-HBR score included acute myocardial infarction on admission instead of white blood cell count.

The PRECISE-HBR score (*) or its alternative version (†) were used as reference to test the AUC.

‡In the MASTER DAPT trial, postrandomization bleeding events (eg, occurring between 1 and 12 months after PCI) were used for external validation.

[PRECISE-HBR score ≥27]), a patient category for which dedicated treatments are recommended[4,5] but remained poorly defined.

This study confirmed the value, yet reweighed the association with bleeding, of the 5 PRECISE-DAPT items[3] and showed that bleeding discrimination can be improved by adding the ARC-HBR criteria.[2] Cross-validation in unselected PCI cohorts provided evidence of generalizability to real-world settings. At external validation, effective discrimination was observed in a lower-risk East Asian cohort[10] and in a selected high-risk population.[1] The discrimination ability of the novel score enriched with the ARC-HBR elements was superior to that of the PRECISE-DAPT score in the MASTER DAPT cohort, in which the prevalence of such risk elements was high. In the STOPDAPT-2 trial, a numerical but nonsignificant improvement in AUC was observed, which may be partly attributable to the lower prevalence of the ARC-HBR elements in this cohort, limiting the incremental discrimination ability of the novel score over its original version.

The inclusion of oral anticoagulation in the PRECISE-HBR score is at variance with the PRECISE-DAPT score and extends the applicability of the novel score to this clinically relevant patient category. We observed that a nonnegligible proportion of patients undergoing PCI and receiving oral anticoagulation (16.6% of cases in the derivation cohort) remained below the high bleeding risk threshold set by the ARC-HBR. This shows that the appraisal of bleeding risk based on a single risk factor, although practical, may misclassify individual risks. The PRECISE-HBR score outperformed the ARC-HBR framework,[2] underscoring the limitations of dichotomizing continuous clinical and laboratory data into binary criteria. The inclusion of biomarkers in the novel score contributed to the enhanced discrimination observed compared with clinical risk factor–based scores.[2,19–21] The new score incorporates all comorbidities proposed by the ARC-HBR except stroke. Myocardial infarction at admission, which was not included in the ARC-HBR framework, confirmed its independent association with bleeding, as observed in

previous studies,[42,43] although after omission of white blood cell count.

Limitations

The discrimination ability of the novel score in our study was moderate, and future studies should evaluate whether an alternative modeling strategy or incorporation of additional variables can enhance score performance. The improvement in the AUC with the PRECISE-HBR score was also moderate compared with the PRECISE-DAPT score, which underscores the complexity of bleeding prediction. However, a few-points difference in the AUC between 2 risk scores may imply clinically meaningful differences in their performance.[44] In the MASTER DAPT and STOPDAPT-2 cohorts, the discrimination of the PRECISE-HBR score was reassuring, although bleeding risk was overestimated. This may reflect the lack of data on bleeding in the first month in MASTER DAPT[1] and different risk profiles related to ethnic diversity between the validation and derivation cohorts.[10] Poor calibration in randomized trials may also reflect the selection of relatively lower-risk patients compared with real-world observational studies of the derivation cohort and other trial-specific factors that may make data from clinical trials less generalizable.[1,10] Further external validation studies are desirable to provide evidence of the generalizability of our findings.

Conclusions

The PRECISE-HBR score offers a comprehensive bleeding risk stratification scheme for the entire spectrum of PCI patients, including those treated with oral anticoagulation, and yields a moderate improvement in discrimination compared with available risk scores. Further evaluation and validation are required to assess its impact on clinical practice.

ARTICLE INFORMATION

Received August 25, 2024; accepted October 14, 2024.

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Sources of Funding

This study was funded by institutional support from Cardiocentro Ticino Institute, Ente Ospedaliero Cantonale, and the Department of Cardiology, Bern University Hospital.

Disclosures

Dr Valgimigli reports grants and personal fees from Terumo and personal fees from AstraZeneca, Alvimedica/CID, Abbott Vascular, Daiichi Sankyo, Bayer, CoreFLOW, IDORSIA PHARMACEUTICALS LTD, Universität Basel, Department Klinische Forschung, Bristol Myers Squib SA, Medscape, Biotronik, and Novartis, outside the submitted work. Dr Gragnano reports personal fees from SANOFI for advisory board outside the submitted work. Dr Heg is affiliated with the Department of Clinical Research (DCR), University of Bern, which has a staff policy of not accepting honoraria or consultancy fees. DCR Bern is involved in the design, conduct, or analysis of clinical studies funded by not-for-profit and for-profit organizations. Pharmaceutical and medical device companies provide direct funding to some of these studies. Dr Räber reports grants or contracts from Abbott, Biotronik, BostonScientific, Heartfolow, Sanofi, and Regeneron; consulting fees from Canon; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Abbott, Amgen, Sanofi, and Occlutech; and participation on a data safety monitoring board or advisory board for Abbott, Amgen, NovoNordisk, Medtronic, and Sanofi outside the submitted work. Dr ten Berg reports support by an institutional research grant from AstraZeneca for the present article. Dr Bär reports grants or contracts from Medis Medical Imaging Systems, Abbott, Bangerter-Rhyner Stiftung, and Swiss National Science Foundation, outside the submitted work. Dr Kimura reports research grants from Abbott and Boston Scientific, outside the submitted work. Dr Leonardi reports grants from AstraZeneca and consulting fees from AstraZeneca, Daiichi Sankyo, Bayer, Pfizer/BMS, ICON, Chiesi, and Novo Nordisk, outside the submitted work. Dr Bhatt reports the following relationships outside the submitted work: Advisory Board: Angiowave, Bayer, Boehringer Ingelheim, CellProthera, Cereno Scientific, Elsevier Practice Update Cardiology, High Enroll, Janssen, Level Ex, McKinsey, Medscape Cardiology, Merck, MyoKardia, NirvaMed, Novo Nordisk, PhaseBio, PLx Pharma, and Stasys; board of directors: American Heart Association, New York City, Angiowave (stock options), Bristol Myers Squibb (stock), DRS. LINQ (stock options), and High Enroll (stock); consultant: Broadview Ventures, GlaxoSmithKline, Hims, SFJ, and Youngene; data monitoring committee: Acesion Pharma, Assistance Publique-Hôpitaux de Paris, Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Boston Scientific (chair, PEITHO trial), Cleveland Clinic, Contego Medical (chair, PERFORMANCE 2), Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo; for the ABILITY-DM trial, funded by Concept Medical; for ALLAY-HF, funded by Alleviant Medical), Novartis, Population Health Research Institute, and Rutgers University (for the National Institutes of Health–funded MINT Trial); honoraria: American College of Cardiology (senior associate editor, Clinical Trials and News, ACC.org; chair, ACC accreditation oversight committee), Arnold and Porter law firm (work related to Sanofi/Bristol-Myers Squibb clopidogrel litigation), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim; AEGIS-II executive committee funded by CSL Behring), Belvoir Publications (editor in chief, *Harvard Heart Letter*), Canadian Medical and Surgical Knowledge Translation Research Group (clinical trial steering committees), CSL Behring (American Heart Association lecture), Cowen and Company, Duke Clinical Research Institute (clinical trial steering committees, including for the PRONOUNCE trial, funded by Ferring Pharmaceuticals), HMP Global (editor in chief, *Journal of Invasive Cardiology*), *Journal of the American College of Cardiology* (guest editor; associate editor), K2P (co-chair, interdisciplinary curriculum), Level Ex, Medtelligence/ReachMD (CME steering committees), MJH Life Sciences, Oakstone CME (course director, Comprehensive Review of Interventional Cardiology), Piper Sandler, Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and US national co-leader, funded by Bayer), WebMD (CME steering committees), Wiley (steering committee); other: *Clinical Cardiology* (deputy editor); patent: Sotagliflozin (named on a patent for sotagliflozin assigned to Brigham and Women's Hospital, which assigned to Lexicon; neither Dr Bhatt nor Brigham and Women's

Hospital receives any income from this patent); research funding: Abbott, Acesion Pharma, Afimmune, Aker Biomarine, Alnylam, Amarin, Amgen, AstraZeneca, Bayer, Beren, Boehringer Ingelheim, Boston Scientific, Bristol-Myers Squibb, Cardax, CellProthera, Cereno Scientific, Chiesi, CinCor, Cleerly, CSL Behring, Eisai, Ethicon, Faraday Pharmaceuticals, Ferring Pharmaceuticals, Forest Laboratories, Fractyl, Garmin, HLS Therapeutics, Idorsia, Ironwood, Ischemix, Janssen, Javelin, Lexicon, Lilly, Medtronic, Merck, Moderna, MyoKardia, NirvaMed, Novartis, Novo Nordisk, Otsuka, Owkin, Pfizer, PhaseBio, PLx Pharma, Recardio, Regeneron, Reid Hoffman Foundation, Roche, Sanofi, Stasys, Synaptic, The Medicines Company, Youngene, and 89Bio; royalties: Elsevier (editor, *Braunwald's Heart Disease*); site co-investigator: Abbott, Biotronik, Boston Scientific, CSI, Endotronix, St. Jude Medical (now Abbott), Philips, SpectraWAVE, Svelte, and Vascular Solutions; trustee: American College of Cardiology; and unfunded research: FlowCo. Dr Urban reports consulting fees from Biosensors and MedAlliance; support for attending meetings and/or travel from MedAlliance; and stock or stock options for MedAlliance and CERC, outside the submitted work. Dr Windecker reports research, travel, or educational grants to the institution from Abbott, Abiomed, Amgen, Astra Zeneca, Bayer, Biotronik, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Cardinal Health, CardioValve, Corflow Therapeutics, CSL Behring, Daiichi Sankyo, Edwards Lifesciences, Guerbet, InfraRedx, Janssen-Cilag, Johnson & Johnson, Medicure, Medtronic, Merck Sharp & Dohm, Miracor Medical, Novartis, Novo Nordisk, Organon, OrPha Suisse, Pfizer, Polares, Regeneron, Sanofi-Aventis, Servier, Sinomed, Terumo, Vifor, and V-Wave. He serves as Advisory Board member and/or member of the steering/executive group of trials funded by Abbott, Abiomed, Amgen, AstraZeneca, Bayer, Boston Scientific, Biotronik, Bristol Myers Squibb, Edwards Lifesciences, Janssen, MedAlliance, Medtronic, Novartis, Polares, Recardio, Sinomed, Terumo, V-Wave, and Xeltis, with payments to the institution but no personal payments. He is also member of the steering/executive committee group of several investigator-initiated trials that receive funding by industry without impact on his personal remuneration. The other authors report no conflicts.

Supplemental Material

Supplemental Methods

Tables S1–S10

Figures S1–S15

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