Evaluation of CRUSADE and ACUITY-HORIZONS Scores for Predicting Long-term Out-of-Hospital Bleeding after Percutaneous Coronary Interventions

Xue-Yan Zhao[1], Jian-Xin Li[1], Xiao-Fang Tang[1], Ying Xian[2], Jing-Jing Xu[1], Ying Song[1], Lin Jiang[1], Lian-Jun Xu[1], Jue Chen[1], Yin Zhang[1], Lei Song[1], Li-Jian Gao[1], Zhan Gao[1], Jun Zhang[1], Yuan Wu[1], Shu-Bin Qiao[1], Yue-Jin Yang[1], Run-Lin Gao[1], Bo Xu[1], Jin-Qing Yuan[1]

[1]Department of Cardiology, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100037, China
[2]Department of Neurology, Duke Clinical Research Institute, Durham, NC 27705, USA

Abstract

Background: There is scanty evidence concerning the ability of Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines (CRUSADE) and Acute Catheterization and Urgent Intervention Triage Strategy and Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (ACUITY-HORIZONS) scores to predict out-of-hospital bleeding risk after percutaneous coronary interventions (PCIs) with drug-eluting stents (DES) in patients receiving dual antiplatelet therapy. We aimed to assess and compare the long-term prognostic value of these scores regarding out-of-hospital bleeding risk in such patients.

Methods: We performed a prospective observational study of 10,724 patients undergoing PCI between January and December 2013 in Fuwai Hospital, China. All patients were followed up for 2 years and evaluated through the Fuwai Hospital Follow-up Center. Major bleeding was defined as Types 2, 3, and 5 according to Bleeding Academic Research Consortium Definition criteria.

Results: During a 2-year follow-up, 245 of 9782 patients (2.5%) had major bleeding (MB). CRUSADE (21.00 [12.00, 29.75] vs. 18.00 [11.00, 26.00], $P < 0.001$) and ACUITY-HORIZONS (9.00 [3.00, 14.00] vs. 6.00 [3.00, 12.00], $P < 0.001$) risk scores were both significantly higher in the MB than non-MB groups. Both scores showed a moderate predictive value for MB in the whole study cohort (area under the receiver-operating characteristics curve [AUROC], 0.565; 95% confidence interval [CI], 0.529–0.601, $P = 0.001$; AUROC, 0.566; 95% CI, 0.529–0.603, $P < 0.001$, respectively) and in the acute coronary syndrome (ACS) subgroup (AUROC: 0.579, 95% CI: 0.531–0.627, $P = 0.001$; AUROC, 0.591; 95% CI, 0.544–0.638, $P < 0.001$, respectively). However, neither score was a significant predictor in the non-ACS subgroup ($P > 0.05$). The value of CRUSADE and ACUITY-HORIZONS scores did not differ significantly ($P > 0.05$) in the whole cohort, ACS subgroup, or non-ACS subgroup.

Conclusions: CRUSADE and ACUITY-HORIZONS scores showed statistically significant but relatively limited long-term prognostic value for out-of-hospital MB after PCI with DES in a cohort of Chinese patients. The value of CRUSADE and ACUITY-HORIZONS scores did not differ significantly ($P > 0.05$) in the whole cohort, ACS subgroup, or non-ACS subgroup.

Key words: Bleeding Score; Dual Antiplatelet Therapy; Major Bleeding; Percutaneous Coronary Intervention; Prognosis

INTRODUCTION

Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 receptor inhibitor is recommended for patients undergoing percutaneous coronary intervention (PCI) to reduce the risk of ischemic cardiovascular events, but this benefit may be at the expense of increasing risk of bleeding,[1,2] in turn increasing the risk of adverse cardiovascular events and death.[3,4] Therefore, it is very important to identify patients at high risk of bleeding and

minimize the occurrence of bleeding events to improve clinical outcomes.

Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines (CRUSADE) score[5] and Acute Catheterization and Urgent Intervention Triage Strategy and Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (ACUITY-HORIZONS) score[6] are both currently commonly used tools for predicting in-hospital bleeding risk in patients with acute coronary syndrome (ACS). However, to the best of our knowledge, only one study[7] has assessed the ability of CRUSADE and ACUITY-HORIZONS scores to predict long-term bleeding risk after PCI. Thus, there is no published research about these scores' ability to predict long-term out-of-hospital bleeding in patients receiving DAPT after PCI and no such data for Asian patients. The purpose of this study was to evaluate and compare the long-term prognostic value of CRUSADE and ACUITY-HORIZONS scores for out-of-hospital bleeding risk after PCI with drug-eluting stents (DES) in a large cohort of Chinese patients.

METHODS

Ethical approval

Ethical approvals were obtained from the Fuwai Hospital Research Ethics Committees (No. 2013-449). The Institutional Review Board approved the study protocol and all patients provided written informed consent.

Study design

This was a prospective, single-center, observational study of 10,724 consecutive patients attending Fuwai Hospital (National Center for Cardiovascular Diseases, Beijing, China) between January 2013 and December 2013.

All patients underwent electrocardiogram, echocardiography, X-ray examination, and blood tests within 24 h of admission in the morning, including routine blood screening, hepatic and renal function, troponin, creatine kinase, and serum lipid concentrations. Additionally, all patients underwent coronary angiography and successful DES of at least one native coronary artery. Clinically relevant baseline data were recorded in detail, including age, sex, body mass index, and medical history.

Exclusion criteria were as follows: DAPT not prescribed on discharge and the in-hospital events of major bleed (MB), stent thrombosis, myocardial infarction, and death. After applying these exclusions, 9782 patients remained for the final analysis. Aspirin was prescribed at a dose of 100 mg daily indefinitely and clopidogrel 75 mg daily or ticagrelor 90 mg twice daily was advised for at least 1 year after the PCI.

End points and definitions

MB was defined as Types 2, 3, or 5 according to Bleeding Academic Research Consortium (BARC) criteria.[8] ACUITY-HORIZONS score[6] consists of seven factors, namely, age, sex, anemia, use of bivalirudin, type of ACS,

serum creatinine concentration, and white blood cell count.[6] CRUSADE score[5] consists of eight factors, namely, sex, diabetes, peripheral artery disease, evidence of heart failures, hematocrit, creatinine clearance rate (Ccr), systolic blood pressure, and heart rate.[5] Ccr was calculated using the Cockcroft-Gault formula.

Follow-up

All patients were evaluated by telephone, letter, messages, or by clinic visit at 30 days, 6 months, 12 months, and 24 months through the Fuwai Hospital Follow-up Center. They were advised to return for coronary angiography if indicated clinically by symptoms or documentation of myocardial ischemia. All adverse events were identified and assessed centrally by two independent cardiologists and disagreements were resolved by consensus.

Statistical analysis

Continuous variables with normal distribution or nonnormal distribution are expressed as mean ± standard deviation (SD) or median (P25, P75), and categorical variables are expressed as n (%). Mean values of continuous variables with normal distribution were compared by Student's t-test, median values of continuous variables with nonnormal distribution were compared using nonparametric test (Mann–Whitney U-test), and Pearson's Chi-square or Fisher's exact test were used to compare categorical variables. When CRUSADE scoring was originally reported, there were five strata for risk of bleeding (very low ≤20, low 21–30, moderate 31–40, high 41–50, and very high risk >50); whereas, there were four risk strata for ACUITY-HORIZONS scores (low <10, moderate 10–14, high 15–19, and very high risk ≥20). In the present study, three risk strata were defined for CRUSADE and ACUITY-HORIZONS scores by combining very high risk and high risk to high risk strata; low risk and very low risk categories to low risk strata.[7] Thus, there were three risk strata for CRUSADE scores (low risk ≤30, moderate risk 31–40, and high risk >40) and three risk strata for ACUITY-HORIZONS scores (low risk <10, moderate risk 10–14, and high risk >14). The predictive values of CRUSADE and ACUITY-HORIZONS scores were assessed with area under the receiver-operating characteristics curves (AUROC) and these AUROCs were compared using the Z-test, net reclassification improvement (NRI), and integrated discrimination improvement (IDI). The significance level was set at 0.05 for all two-sided tests. Statistical analysis was performed with SAS 9.2 (SAS Institute, Cary, NC, USA).

RESULTS

Patient characteristics

After exclusion of 942 patients who did not receive DAPT on discharge, underwent only balloon dilatation, received bare metal stents, experienced specified in-hospital events (MB, stent thrombosis, myocardial infarction, and death), or were lost to follow-up, 9782 of 10,724 patients remained for the final analysis [Figure 1]. Their average age was 58.2 ± 10.2, 22.9% were women, and 60.0%

had ACS. Only 13 patients (0.13%) received ticagrelor, the remaining patients received clopidogrel (99.87%). Only 17 patients received triple therapy with aspirin, a P2Y12 receptor inhibitor, and an oral anticoagulant drug.
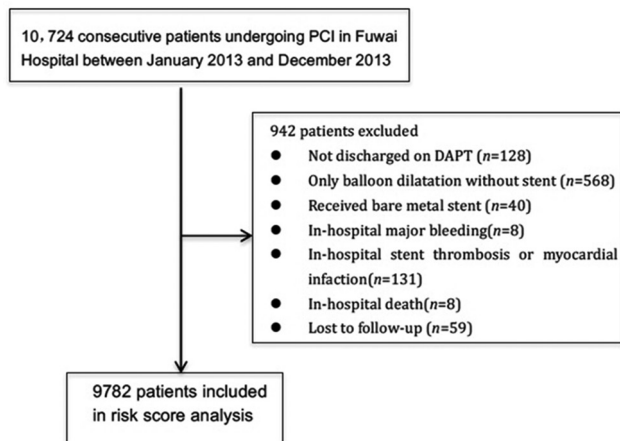

Figure 1: Flow chart showing patient selection for study. PCI: Percutaneous coronary intervention; DAPT: Dual antiplatelet therapy.

No patients received bivalirudin or prasugrel treatment. A high proportion of patients underwent a trans-radial approach (TRA) PCI in this study (91.2%). As shown in Table 1, 245 patients experienced MB events (2.5%) during a 2-year follow-up. These patients were older, had a higher proportion of women, more frequently had histories of cerebral strokes or vascular disease, and more frequently had admission systolic blood pressures of less than 90 mmHg than those without MB.

CRUSADE and ACUITY-HORIZONS scores according to the occurrence of major bleeding

CRUSADE (21.00 [12.00, 29.75] vs. 18.00 [11.00, 26.00], $P < 0.001$) and ACUITY-HORIZONS (9.00 [3.00, 14.00] vs. 6.00 [3.00, 12.00], $P < 0.001$) risk scores were both significantly higher in the MB than non-MB groups [Table 1].

Bleeding risk stratification by CRUSADE and ACUITY-HORIZONS scores

Bleeding risk stratification by CRUSADE

According to CRUSADE risk strata (low risk [$\leq$30],

Table 1: Baseline clinical characteristics in patients undergoing percutaneous coronary interventions according to major bleeding status

Characteristics	MB (*n* = 245)	No MB (*n* = 9537)	Statistics	*P*
Age (years)	61.2 ± 10.2	58.2 ± 10.2	−4.67*	<0.001
Female	70 (28.57)	2166 (22.71)	4.65†	0.031
BMI (kg/m²)	25.62 ± 3.12	25.95 ± 3.18	1.60*	0.110
CRUSADE score	21.00 (12.00, 29.75)	18.00 (11.00, 26.00)	−3.45‡	<0.001
ACUITY-HORIZONS score	9.00 (3.00, 14.00)	6.00 (3.00, 12.00)	−3.55‡	<0.001
Clinical presentation				
Stable CHD	101 (41.22)	3814 (39.99)	0.68†	0.713
Troponin-negative ACS	106 (43.27)	4052 (42.49)		
Troponin-positive ACS	38 (15.51)	1671 (17.52)		
Hypertension	171 (69.80)	6103 (63.99)	3.50†	0.061
Diabetes mellitus				
Nondiabetes mellitus	179 (73.06)	6683 (70.07)	1.50†	0.473
Noninsulin treated	46 (18.78)	1866 (19.57)		
Insulin treated	20 (8.16)	988 (10.36)		
Current smoking	143 (58.37)	5448 (57.12)	0.15†	0.698
Dyslipidemia	170 (69.39)	6409 (67.20)	0.52†	0.471
Previous MI	39 (15.92)	1801 (18.88)	1.38†	0.241
Previous PCI	50 (20.41)	2264 (23.74)	1.47†	0.226
Previous CABG	11 (4.49)	377 (3.95)	0.18†	0.671
Previous stroke	42 (17.14)	1000 (10.49)	11.12†	0.001
Previous vascular disease	46 (18.78)	1176 (12.33)	9.08†	0.003
Anemia	10 (4.08)	325 (3.41)	0.33†	0.567
Ccr <60 ml/min	31 (12.86)	1052 (11.47)	0.45†	0.502
Heart rate >100 beats/min	1 (0.41)	93 (0.98)	0.81†	0.369
Systolic BP <90 mmHg	2 (0.82)	20 (0.21)	3.92†	0.048
ST deviation	48 (19.59)	2058 (21.58)	0.56†	0.455
Heart failure history	6 (2.49)	179 (1.92)	0.41†	0.524
Abnormal myocardial enzyme	48 (19.59)	2053 (21.53)	0.53†	0.467
Creatinine (mg/dl)	0.86 ± 0.19	0.85 ± 0.18	−0.28*	0.783

Values are presented as mean ± SD, *n* (%), or median (P25, P75). **t* values; †χ² values; ‡Z values. SD: Standard deviation; ACS: Acute coronary syndrome; BMI: Body mass index; CRUSADE: Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines; ACUITY-HORIZONS: Acute Catheterization and Urgent Intervention Triage Strategy and Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction; CABG: Coronary artery bypass graft; Ccr: Creatinine clearance rate; CHD: Coronary heart disease; MB: Major bleeding; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; BP: Blood pressure.

intermediate risk [31–40], and high risk [>40]), the risk of bleeding was 1.58 times greater in the intermediate- than the low-risk group (hazard ratio [HR], 1.58; 95% confidence interval [CI], 1.12–2.23; $P = 0.010$). However, the risk did not differ significantly between high- and low-risk groups (HR, 1.33; 95% CI, 0.77–2.28; $P = 0.307$) [Table 2].

Bleeding risk stratification by ACUITY-HORIZONS

According to ACUITY-HORIZONS risk strata (low risk [<10], intermediate risk [10–14], and high risk [>14]), the risk of bleeding was 1.66 times in the high- than the low-risk group (HR, 1.21; 95% CI, 1.12–2.28; $P = 0.002$). However, the risk did not differ significantly between intermediate- and low-risk groups (HR, 1.07; 95% CI, 0.78–1.48; $P = 0.662$) [Table 2].

Ability of CRUSADE and ACUITY-HORIZONS scores to predict bleeding events

CRUSADE scores appeared to have predictive value concerning MB in the whole cohort (AUROC, 0.565; 95% CI, 0.529–0.601; $P = 0.001$) and in the ACS subgroup (AUROC, 0.579; 95% CI, 0.531–0.627; $P = 0.001$). However, they did not have significant predictive value in the non-ACS subgroup (AUROC, 0.545; 95% CI, 0.492–0.599; $P = 0.123$) [Table 3].

ACUITY-HORIZONS score appeared to have predictive value concerning MB in the whole cohort (AUROC, 0.566; 95% CI, 0.529–0.603; $P < 0.001$) and in the ACS subgroup (AUROC, 0.591; 95% CI, 0.544–0.638; $P < 0.001$). However, they did not have significant predictive value in the non-ACS subgroup (AUROC, 0.535; 95% CI, 0.478–0.592; $P = 0.234$) [Table 3].

Comparison of predictive value for bleeding events by CRUSADE and ACUITY-HORIZONS scores

CRUSADE (AUROC, 0.565) and ACUITY-HORIZONS scores (AUROC, 0.566) did not differ significantly in the whole cohort ($Z = 0.038$, $P = 0.970$; NRI, $P = 0.960$; IDI, $P = 0.187$); in the ACS subgroup (CRUSADE score: AUROC, 0.579; ACUITY-HORIZONS score: AUROC, 0.591) ($Z = 0.350$, $P = 0.726$; NRI, $P = 0.845$; IDI, $P = 0.309$), or in the non-ACS subgroup (CRUSADE score: AUROC, 0.545; ACUITY-HORIZONS score: AUROC, 0.535) ($Z = 0.251$, $P = 0.802$; NRI, $P = 0.357$; IDI, $P = 0.222$) [Figure 2].

DISCUSSION

CRUSADE[5,9] and ACUITY-HORIZONS scores[6] are widely used to assess the risk of in-hospital bleeding in patients with ACS. However, the predictive value of these scores for bleeding in patients who are being treated with PCI and DAPT has not been clarified. In our study, we therefore evaluated the ability of CRUSADE and ACUITY-HORIZONS scores to predict the risk of long-term out-of-hospital bleeding in patients with DAPT after PCI in a large Chinese patient cohort. We also conducted head-to-head comparisons between CRUSADE[4] and ACUITY-HORIZONS[5] scores in the same cohort. The main findings of the study are as follows.

The incidence of 2-year out-of-hospital MB (BARC Types 2, 3, and 5) was 2.5% in these Chinese patients with DAPT after PCI. Previous studies have reported markedly different rates of bleeding after PCI, these discrepancies mainly being attributable to differences in definitions of bleeding,

Table 2: Stratification of risk of major bleeding by CRUSADE and ACUITY-HORIZONS scores

Scores	Major bleeding, % (n/N)	HR	95% CI	P
CRUSADE score				
Low (≤30)	2.33 (187/8015)	Reference	–	
Intermediate (31–40)	3.66 (39/1067)	1.58	1.12–2.23	0.010
High (>40)	3.05 (14/459)	1.33	0.77–2.28	0.307
ACUITY-HORIZONS score				
Low (<10)	2.26 (143/6319)	Reference	–	
Intermediate (10–14)	2.43 (50/2057)	1.07	0.78–1.48	0.662
High (>14)	3.70 (52/1405)	1.66	1.21–2.28	0.002

–: Not applicable; CRUSADE: Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines; ACUITY-HORIZONS: Acute Catheterization and Urgent Intervention Triage Strategy and Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction; HR: Hazard ratio; CI: Confidence interval.

Table 3: Receiver-operating characteristic curves of major bleeding according to CRUSADE and ACUITY-HORIZONS scores in whole cohort and non-ACS and ACS subgroups

Scores	Whole cohort		Non-ACS patients		ACS patients	
	AUC (95% CI)	P	AUC (95% CI)	P	AUC (95% CI)	P
CRUSADE score	0.565 (0.529–0.601)	0.001	0.545 (0.492–0.599)	0.123	0.579 (0.531–0.627)	0.001
ACUITY-HORIZONS score	0.566 (0.529–0.603)	0.000	0.535 (0.478–0.592)	0.234	0.591 (0.544–0.638)	0.000

CRUSADE: Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines; ACUITY-HORIZONS: Acute Catheterization and Urgent Intervention Triage Strategy and Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction; ACS: Acute coronary syndrome; AUC: Area under the curve; CI: Confidence interval.
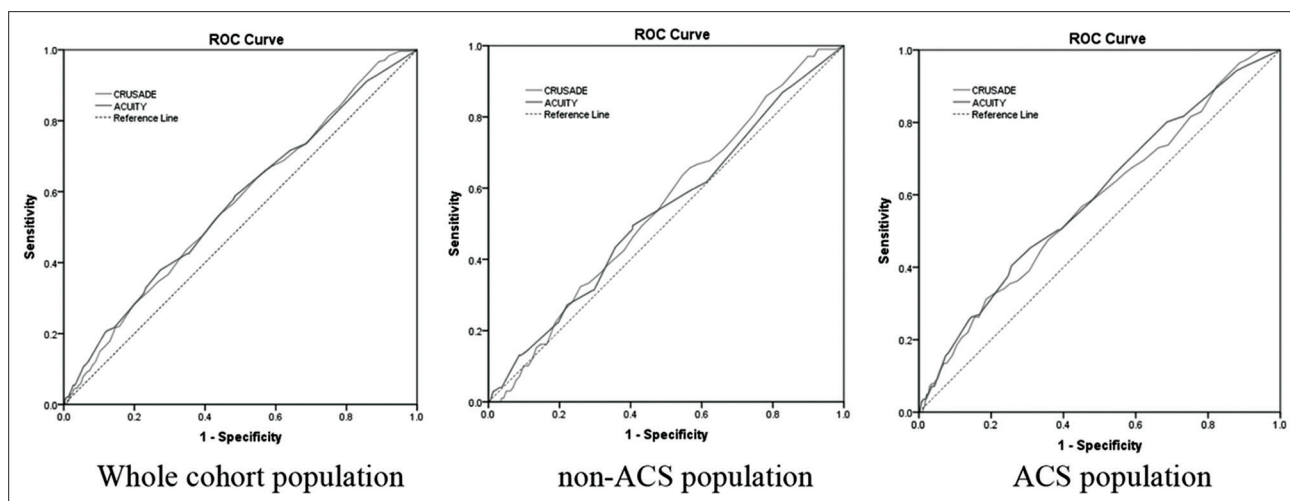
Figure 2: Comparison of predictive value of CRUSADE and ACUITY-HORIZONS scores for major bleeding. No statistically significant differences were found irrespective of whole cohort population, non-ACS population, or ACS population. CRUSADE: Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines; ACUITY-HORIZONS: Acute Catheterization and Urgent Intervention Triage Strategy and Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction; ACS: Acute coronary syndrome; ROC: Receiver operating characteristic.

patient groups, ethnic variations, use of anticoagulant drugs, durations of follow-up, and so on. Ratib et al.[10] reported an incidence of bleeding in the 30 days after PCI through TRA of only 0.2%; Mehran et al.[11] reported an out-of-hospital incidence of bleeding in the 2-year after PCI of 1.4%; whereas in the CREDO study,[12] the incidence for 1 year was higher at 8.8%.

We found that CRUSADE and ACUITY-HORIZONS scores both have predictive value for long-term risk of bleeding in Chinese patients undergoing PCI, which is consistent with the findings of Costa et al.,[7] whose patient cohort comprised European and American patients and was smaller than ours (1970 patients). Additionally, Costa et al. did not further analyze the subgroups of ACS. We also found that CRUSADE and ACUITY-HORIZONS scores had predictive value for long-term MB in the ACS, but not in the non-ACS subgroup of post-PCI patients. This discrepant result may be related to the fact that CRUSADE and ACUITY-HORIZONS scores were originally developed using only patients with ACS. In other words, the two scores appear to have clinical value overall and in the ACS subgroup; however, their predictive value is relatively limited. This may be because some bleeding risk factors that are relevant to Chinese patients treated with PCI and DAPT are not included in CRUSADE and ACUITY-HORIZONS scores. Whether introduction of more clinical factors, such as plasma markers or results of platelet function or gene testing, would improve predictive value requires further exploration and validation.

In this study, we also conducted head-to-head comparison between CRUSADE and ACUITY-HORIZONS scores and identified no significant difference between them in the overall cohort or ACS and non-ACS subgroups. Of previous studies, only that of Costa et al.[7] reported results that are similar to ours for long-term follow-up of patients after PCI. Reported predictions of risk of in-hospital

bleeding in patients with ACS according to these two scores have been inconsistent. Flores-Ríos et al.[13] reported that CRUSADE scores were better able to predict bleeding risk than ACUITY-HORRIZONS scores in 1391 patients with ST-segment elevation myocardial infarction undergoing PCI; however, Correia et al.[14] found that ACUITY-HORIZONS scores were better than CRUSADE scores in 519 patients with ACS. These discrepancies may be attributable to differences in definition of bleeding and study patients' characteristics.

In our study, we found that CRUSADE and ACUITY-HORIZONS scores were significantly higher in the MB than in the non-MB group. CRUSADE scores were 1.58 times higher in the intermediate-risk than low-risk group; however, the risk did not differ significantly between high- and low-risk groups. ACUITY-HORIZONS scores were 1.66 times higher in the high-risk than the low-risk group; however, the risk did not differ significantly between intermediate- and low-risk groups. Thus, in patients with DAPT after PCI, CRUSADE and ACUITY-HORIZONS scores do not discriminate between low-, intermediate-, and high-risk groups, which indicates a need for further analysis and adjustment of risk stratifications.

Our findings have expanded the scope of clinical application of CRUSADE and ACUITY-HORIZONS scores in assessing the long-term risk of bleeding in patients undergoing PCI.

Some limitations of our analysis should be considered. First, this study was a single-center observational study, which may limit the generalizability of our findings. Second, CRUSADE and ACUITY-HORIZONS scores are clinical metrics; whether to introduce plasma markers, platelet function, or gene testing to improve predictive accuracy requires further study.

In conclusion, CRUSADE and ACUITY-HORIZONS scores are statistically significant predictors of out-of-hospital

bleeding after PCI with DES in Chinese patients in the long term but of relatively limited practical prognostic value; thus, further studies are needed to improve predictors of bleeding. Comparison of predictive values of bleeding between CRUSADE score and ACUITY-HORIZONS score showed no significant difference.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Mauri L, Kereiakes DJ, Yeh RW, Driscoll-Shempp P, Cutlip DE, Steg PG, *et al.* Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. N Engl J Med 2014;371:2155-66. doi: 10.1056/NEJMoa1409312.
2. Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, *et al.* 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: The task force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2017;[Epub ahead of print]. doi: 10.1093/eurheartj/ehx419.
3. Steg PG, Huber K, Andreotti F, Arnesen H, Atar D, Badimon L, *et al.* Bleeding in acute coronary syndromes and percutaneous coronary interventions: Position paper by the working group on thrombosis of the European Society of Cardiology. Eur Heart J 2011;32:1854-64. doi: 10.1093/eurheartj/ehr204.
4. Eikelboom JW, Mehta SR, Anand SS, Xie C, Fox KA, Yusuf S, *et al.* Adverse impact of bleeding on prognosis in patients with acute coronary syndromes. Circulation 2006;114:774-82. doi: 10.1161/circulationaha.106.612812.
5. Subherwal S, Bach RG, Chen AY, Gage BF, Rao SV, Newby LK, *et al.* Baseline risk of major bleeding in non-ST-segment-elevation myocardial infarction: The CRUSADE (Can rapid risk stratification of unstable angina patients suppress ADverse outcomes with early implementation of the ACC/AHA guidelines) bleeding score. Circulation 2009;119:1873-82. doi: 10.1161/CIRCULATIONAHA.108.828541.
6. Mehran R, Pocock SJ, Nikolsky E, Clayton T, Dangas GD, Kirtane AJ, *et al.* A risk score to predict bleeding in patients with acute coronary syndromes. J Am Coll Cardiol 2010;55:2556-66. doi: 10.1016/j.jacc.2009.09.076.
7. Costa F, Tijssen JG, Ariotti S, Giatti S, Moscarella E, Guastaroba P, *et al.* Incremental value of the CRUSADE, ACUITY, and HAS-BLED risk scores for the prediction of hemorrhagic events after coronary stent implantation in patients undergoing long or short duration of dual antiplatelet therapy. J Am Heart Assoc 2015;4. pii: e002524. doi: 10.1161/JAHA.115.002524.
8. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, *et al.* Standardized bleeding definitions for cardiovascular clinical trials: A consensus report from the Bleeding Academic Research Consortium. Circulation 2011;123:2736-47. doi: 10.1161/CIRCULATIONAHA.110.009449.
9. Ariza-Solé A, Sánchez-Elvira G, Sánchez-Salado JC, Lorente-Tordera V, Salazar-Mendiguchía J, Sánchez-Prieto R, *et al.* CRUSADE bleeding risk score validation for ST-segment-elevation myocardial infarction undergoing primary percutaneous coronary intervention. Thromb Res 2013;132:652-8. doi: 10.1016/j.thromres.2013.09.019.
10. Ratib K, Mamas MA, Anderson SG, Bhatia G, Routledge H, De Belder M, *et al.* Access site practice and procedural outcomes in relation to clinical presentation in 439,947 patients undergoing percutaneous coronary intervention in the United Kingdom. JACC Cardiovasc Interv 2015;8:20-9. doi: 10.1016/j.jcin.2014.06.026.
11. Mehran R, Baber U, Steg PG, Ariti C, Weisz G, Witzenbichler B, *et al.* Cessation of dual antiplatelet treatment and cardiac events after percutaneous coronary intervention (PARIS): 2 year results from a prospective observational study. Lancet 2013;382:1714-22. doi: 10.1016/S0140-6736(13)61720-1.
12. Steinhubl SR, Berger PB, Mann JT 3rd, Fry ET, DeLago A, Wilmer C, *et al*. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: A randomized controlled trial. JAMA 2002;288:2411-20. doi: 10.1001/jama.288.19.2411.
13. Flores-Ríos X, Couto-Mallón D, Rodríguez-Garrido J, García-Guimaraes M, Gargallo-Fernández P, Piñón-Esteban P, *et al.* Comparison of the performance of the CRUSADE, ACUITY-HORIZONS, and ACTION bleeding risk scores in STEMI undergoing primary PCI: Insights from a cohort of 1391 patients. Eur Heart J Acute Cardiovasc Care 2013;2:19-26. doi: 10.1177/2048872612469885.
14. Correia LC, Ferreira F, Kalil F, Silva A, Pereira L, Carvalhal M, *et al.* Comparison of ACUITY and CRUSADE scores in predicting major bleeding during acute coronary syndrome. Arq Bras Cardiol 2015;105:20-7. doi: 10.5935/abc.20150058.