International Journal of General Medicine

Dovepress
Taylor & Francis Group

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ORIGINAL RESEARCH

The Combined Predictive Value of the GRACE Score and the ARC-HBR Criteria for Bleeding Risk After Percutaneous Coronary Intervention in STEMI Patients

Xiaoying Wang[1,*], Yuanyuan Ning[2,*], Xiaojuan Wang[1], Guangli Li[1], Dong Wu[1], Xiaowu Wang[3], Zhen Huang[4]

[1]Department of Pharmacy, Fuyang People's Hospital, Fuyang, Anhui, 236000, People's Republic of China; [2]Department of Clinical Laboratory, the First Affiliated Hospital of Wannan Medical College (Yijishan Hospital), Wuhu, 241000, People's Republic of China; [3]Department of Clinical Laboratory, The Second People's Hospital of Fuyang, Fuyang Infection Disease Clinical College of Anhui Medical University, Fuyang, Anhui, 236000, People's Republic of China; [4]Department of Scientific Research, Fuyang People's Hospital, Fuyang, Anhui, 236000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xiaowu Wang, Department of Clinical Laboratory, The Second People's Hospital of Fuyang, Fuyang infection Disease Clinical College of Anhui Medical University, Fuyang, Anhui, 236000, People's Republic of China, Email wangxiaowu19880218@126.com; Zhen Huang, Department of Scientific Research, Fuyang People's Hospital, Fuyang, Anhui, 236000, People's Republic of China, Email huangzhenfy@163.com

Objective: To evaluate the incremental predictive value of the Global Registry of Acute Coronary Events (GRACE) score combined with the Academic Research Consortium for High Bleeding Risk (ARC-HBR) criteria for bleeding risk after percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI).

Methods: This prospective observational study enrolled 338 STEMI patients who underwent their first PCI at Fuyang People's Hospital from January 2023 to March 2024. Bleeding events were defined according to the Bleeding Academic Research Consortium (BARC) types 1–5. Patients were stratified by GRACE score (low/middle/high) and ARC-HBR status (high/low). The predictive performance of the model was assessed using receiver operating characteristic (ROC) curves, net reclassification improvement (NRI), integrated discrimination improvement (IDI), decision curve analysis (DCA), and calibration plots. Internal validation was performed via bootstrap resampling (1,000 iterations).

Results: Bleeding occurred in 83 patients (24.56%), with 63 in-hospital events (18.64%) and 34 out-of-hospital events (10.06%). The majority were mild (BARC type 1, 82.54% in-hospital; 73.53% out-of-hospital). The combined GRACE + ARC-HBR model achieved an area under the ROC curve (AUC) of 0.774 (95% CI 0.726–0.818), compared with 0.712 (95% CI 0.660–0.759) for GRACE alone and 0.667 (95% CI 0.614–0.717) for ARC-HBR alone. Versus GRACE, the combined model showed a non-significant NRI (−0.0509; P = 0.0945) but a significant IDI (0.0560; P = 0.0006). Versus ARC-HBR, both NRI (0.3277; P = 0.0007) and IDI (0.0768; P < 0.0001) were significantly positive. DCA demonstrated the highest net benefit for the combined model across most threshold probabilities. The calibration curve yielded a Brier score of 0.147, and the Hosmer-Lemeshow test confirmed good calibration (χ^2=3.568, P=0.8938). Bootstrap internal validation produced a bias-corrected AUC of 0.775.

Conclusion: Compared with either score alone, the combination of the GRACE score and the ARC-HBR criteria provides incremental predictive value for post-PCI bleeding in STEMI patients.

Keywords: acute ST-elevation myocardial infarction, percutaneous coronary intervention, bleeding, GRACE score, ARC-HBR criteria

Introduction

Acute ST-elevation myocardial infarction (STEMI) is a life-threatening cardiovascular emergency associated with significant morbidity and mortality.[1] This condition results from prolonged interruption of myocardial blood supply, leading to extensive heart muscle damage. Early intervention is therefore critical to improve outcomes and preserve

https://doi.org/10.2147/IJGM.S605618
Received: 4 March 2026
Accepted: 23 April 2026
Published: 1 May 2026

cardiac function. Percutaneous coronary intervention (PCI) is the primary treatment for STEMI, restoring coronary blood flow and revolutionizing patient management. After PCI, long-term antiplatelet therapy is typically required to reduce recurrent thrombotic events. However, these agents also increase bleeding risk.[2] Bleeding complications-most commonly gastrointestinal, but also vascular, retroperitoneal, or intracranial-are frequent adverse effects of antiplatelet therapy, often leading to drug discontinuation and safety concerns.[3–6] Early identification of patients at high bleeding risk is essential to guide treatment and improve prognosis.[7] Several risk assessment tools exist to help clinicians tailor antiplatelet therapy. Nevertheless, current models for predicting post-PCI bleeding in STEMI patients remain suboptimal, underscoring the need for further research.

The Global Registry of Acute Coronary Events (GRACE) score is a widely used tool that predicts prognosis in acute coronary syndrome (ACS) patients by integrating multiple clinical variables, including age, heart rate, blood pressure, myocardial injury markers, renal function, cardiac arrest history, diabetes, smoking, coronary heart disease history, and heart failure signs.[8] The GRACE score is well validated for predicting short-and long-term mortality and has also proven valuable for early risk stratification in ACS.[9] However, although the GRACE score performs well for ischemic events, its sensitivity for predicting bleeding risk is limited.

Several bleeding risk assessment tools have been developed and validated for patients undergoing PCI. The CRUSADE score is one of the most widely used tools for predicting in-hospital bleeding in ACS patients. However, a recent comparative study demonstrated that the Academic Research Consortium for High Bleeding Risk (ARC-HBR) criteria had superior predictive ability for in-hospital bleeding events compared with the CRUSADE score in ACS patients undergoing PCI (AUC 0.751 vs 0.696, $P < 0.0001$), and this advantage was even more pronounced in the STEMI subgroup (AUC 0.767 vs 0.694, $P = 0.020$).[10] The HAS-BLED score, originally developed for bleeding risk assessment in atrial fibrillation patients, has also been extended to ACS populations, but its discrimination performance for bleeding in PCI patients has been suboptimal. A validation study in Chinese patients with atrial fibrillation and ACS/PCI found that the ARC-HBR score performed better than both the HAS-BLED score (0.692 vs 0.575, P=0.007) and the PRECISE-DAPT score (c-statistic: 0.692 vs 0.616) in predicting 1-year major bleeding.[11] A recent systematic review noted that existing bleeding risk models, including CRUSADE, PRECISE-DAPT, and HAS-BLED, demonstrate only moderate predictive accuracy (c-statistics 0.70–0.80) for bleeding complications in myocardial infarction patients.[12] Notably, while the GRACE score has been well-established for predicting mortality and ischemic events in ACS patients, its performance for bleeding prediction has been reported to be suboptimal compared with dedicated bleeding scores.[13] Thus, additional indicators are needed for combined use to more accurately assess bleeding risk after PCI in STEMI patients.[14–16]

The ARC-HBR criteria provide a consensus-based framework for identifying patients at high bleeding risk (HBR) undergoing PCI. Developed through collaboration among leading research organizations, regulatory authorities, and physician-scientists from the United States, Asia, and Europe, the ARC-HBR criteria focus on bleeding related to percutaneous coronary intervention.[17] These criteria have been validated in diverse populations, including patients with atrial fibrillation (AF) and ACS, as well as those receiving both oral anticoagulants (OACs) and antiplatelet therapy (APT) during PCI.[11] The ARC-HBR score effectively stratifies patients into different risk categories, enabling clinicians to make more informed decisions regarding antiplatelet and anticoagulant therapy. Moreover, when compared with other bleeding risk scores such as HAS-BLED and PRECISE-DAPT, the ARC-HBR score has shown superior predictive performance for bleeding outcomes in patients undergoing PCI who receive both OAC and APT, highlighting its added value beyond existing tools.[11]

Several risk stratification approaches combining ischemic and bleeding scores have been explored for patients undergoing PCI. These include integrating the CRUSADE score with the GRACE score for mortality prediction and comparative analyses of multiple bleeding scores in CAD cohorts.[13,18] However, the combined predictive value of the GRACE score and the ARC-HBR criteria for post-PCI bleeding in STEMI patients has not been systematically evaluated. The novelty of this study lies in its prospective validation of the incremental predictive value of combining these two tools, the GRACE score (primarily for ischemic risk) and the ARC-HBR criteria (specifically for bleeding risk), in a dedicated STEMI cohort. The aim is to explore the application value of this combined approach in predicting bleeding risk after PCI in STEMI patients. By systematically comparing the predictive performance of the combined model with that of each score alone, and by contextualizing our findings within existing bleeding risk scores (eg.,

CRUSADE, HAS-BLED, PRECISE-DAPT), we hope to provide a more accurate risk assessment method for clinical practice. This may help guide clinical decision-making, optimize individualized treatment strategies, and ultimately improve the prognosis of STEMI patients.

Materials and Methods

Study Design and Population

This was a prospective observational study. Clinical data from STEMI patients who underwent their first PCI at Fuyang People's Hospital from January 2023 to March 2024 were analyzed. Patients were categorized into bleeding and non-bleeding groups based on the occurrence of post-PCI bleeding. In-hospital bleeding was defined as any bleeding event occurring at any site during the hospitalization following PCI. Out-of-hospital bleeding was defined as any bleeding event occurring at any site within one year after discharge. The study was approved by the Ethics Committee of Fuyang People's Hospital (Approval No. 202311).

Inclusion and Exclusion Criteria

Inclusion criteria were: (1) meeting STEMI diagnostic criteria;[19] (2) age ≥18 years; (3) undergoing PCI with post-operative DAPT; (4) implantation of ≥1 sirolimus-eluting stent.

Exclusion criteria were: (1) coagulation dysfunction at admission; (2) active bleeding, peptic ulcer disease, or other DAPT contraindications; (3) concurrent oral anticoagulant use; (4) hematologic or chronic bleeding disorders; (5) lost to follow-up after discharge.

Sample Size

The primary endpoint was the occurrence of bleeding events within one year after discharge. Based on previous reports, the one-year bleeding incidence was assumed to be approximately 20%.[20] The study was designed to compare the predictive performance of the GRACE score alone versus the GRACE score combined with the ARC-HBR criteria using the area under the receiver operating characteristic curve (AUC). Assuming an AUC of 0.70 for GRACE alone,[21] an anticipated increase to 0.76 for the combined model, a sample size of at least 320 patients was estimated to provide 80% power at a two-sided α of 0.05, with an assumed correlation of 0.75 between the two ROC curves (DeLong method, PASS 15 software).

Data Collection

The following variables were extracted from electronic medical records: sex, age, smoking status, alcohol consumption, hypertension, type 2 diabetes, coronary heart disease, prior PCI, gastrointestinal disease, emergency PCI status, stroke, cancer, renal function status, Gensini score, GRACE score, and number of stents implanted, etc. At admission, key laboratory indicators were documented, including estimated glomerular filtration rate (eGFR), brain natriuretic peptide (BNP), cardiac troponin (cTn), alanine aminotransferase (ALT), creatine kinase (CK), fasting blood glucose (FBG), hemoglobin (Hb), total cholesterol (TC), and triglycerides (TG). Additionally, the patient's medication status at discharge was recorded.

Definition

The GRACE score and ARC-HBR criteria are calculated based on patients' clinical characteristics. The GRACE score incorporates multiple parameters, including age, heart rate, systolic blood pressure, serum creatinine level, Killip classification, presence of cardiac arrest at admission, elevation of cardiac necrosis markers, and ST-segment changes.[22] The total score for each patient is calculated by summing the individual scores of each prognostic variable. A GRACE score >140 is defined as high risk, a score between 109 and 140 as intermediate risk, and a score ≤108 as low risk.

The ARC-HBR criteria are divided into major and minor criteria.[17] Patients meeting at least one major criterion or at least two minor criteria are classified as high bleeding risk (HBR). Those with only one minor criterion or none are classified as non-HBR. Bleeding events were evaluated according to the Bleeding Academic Research Consortium (BARC) criteria and classified into types 1 to 5, with higher types indicating more severe bleeding.[3]

Coagulation dysfunction was defined as an International Normalized Ratio (INR) >1.5, an activated partial thromboplastin time (aPTT) >60 seconds, or thrombin time (TT) > 15 seconds.[23]

Net Reclassification Improvement (NRI): For subjects who experience the bleeding event, any "upward" movement in risk category indicates improved classification, whereas "downward" movement indicates worse classification. For subjects who do not experience the outcome event, the opposite holds: downward movement improves classification, and upward movement worsens it.[24] The Integrated Discrimination Improvement (IDI) is an extension of the NRI. It integrates reclassification improvements over all possible probability cut-offs for the outcome, allowing the assessment of improvement in model discrimination without the need to predefine risk categories.

Observation Indicators and Follow-Up

The primary observation endpoints were bleeding events during hospitalization and the first bleeding event occurring after discharge. Patients were followed up by telephone every three months after discharge, and follow-up was terminated once a bleeding event occurred, with a maximum follow-up period of one year. During follow-up, data on post-discharge bleeding events were recorded, including the time and severity of bleeding, intervention measures, readmission status, as well as the reasons, time, and place of readmission.

Statistical Analysis

Statistical analyses were performed using SPSS 26.0, MedCalc, GraphPad Prism 8.0, and Python 3.12. Continuous variables are presented as mean ± standard deviation if normally distributed, or as median with interquartile range [M(P25, P75)] if non-normally distributed. Categorical variables are expressed as frequencies and percentages [n (%)]. Comparisons between two groups were performed using the independent *t*-test or Mann–Whitney *U*-test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables. For comparisons among three or more groups, one-way analysis of variance (ANOVA) with the Student-Newman-Keuls (SNK) post hoc test was used for normally distributed data with homogeneous variances; otherwise, the Kruskal–Wallis test with pairwise comparisons was applied. For multiple pairwise comparisons of categorical variables, the Bonferroni correction was employed.

Variables with a P value < 0.10 in univariate logistic regression analysis were considered candidates for inclusion in the multivariable binary logistic regression model. Three prediction models were constructed and evaluated: the GRACE score alone, the ARC-HBR criteria alone, and a combined model integrating both scores.

The predictive performance of each model was assessed using the AUC. The DeLong method was used to compare AUCs between paired models. Incremental predictive value was further quantified by calculating the NRI and IDI. Calibration was evaluated using the Hosmer-Lemeshow goodness-of-fit test and a calibration plot with the Brier score. Decision curve analysis (DCA) was performed to assess the clinical net benefit across a range of threshold probabilities, with net benefit calculated as: (true positives / total sample size) − (false positives / total sample size) × (threshold probability / (1 − threshold probability)).

Internal validation was conducted using bootstrap resampling with 1,000 replicates. The bias-corrected AUC was derived by subtracting the mean optimism (the average difference between the AUC estimated on each bootstrap sample and the AUC of the same model applied to the original dataset) from the apparent AUC. Missing values for continuous variables were imputed using the mean substitution method.

GraphPad Prism 8.0 was used to generate bleeding risk plots. DCA, calibration curves, and bootstrap procedures were implemented in Python 3.12. A two-tailed P value < 0.05 was considered statistically significant.

Results

Baseline Characteristics

From January 2023 to March 2024, 483 STEMI patients were initially screened, and 338 were ultimately included in the analysis after exclusions and loss to follow-up (Figure 1). Patients in the GRACE high-risk group were significantly older (median 73 vs 56 years), had lower eGFR (66.59 vs 95.70 mL/min/1.73m^2), and lower hemoglobin (126.50 vs 142.00 g/L) compared with the low-risk group (all P < 0.001). The prevalence of chronic kidney disease was also higher in the high-risk

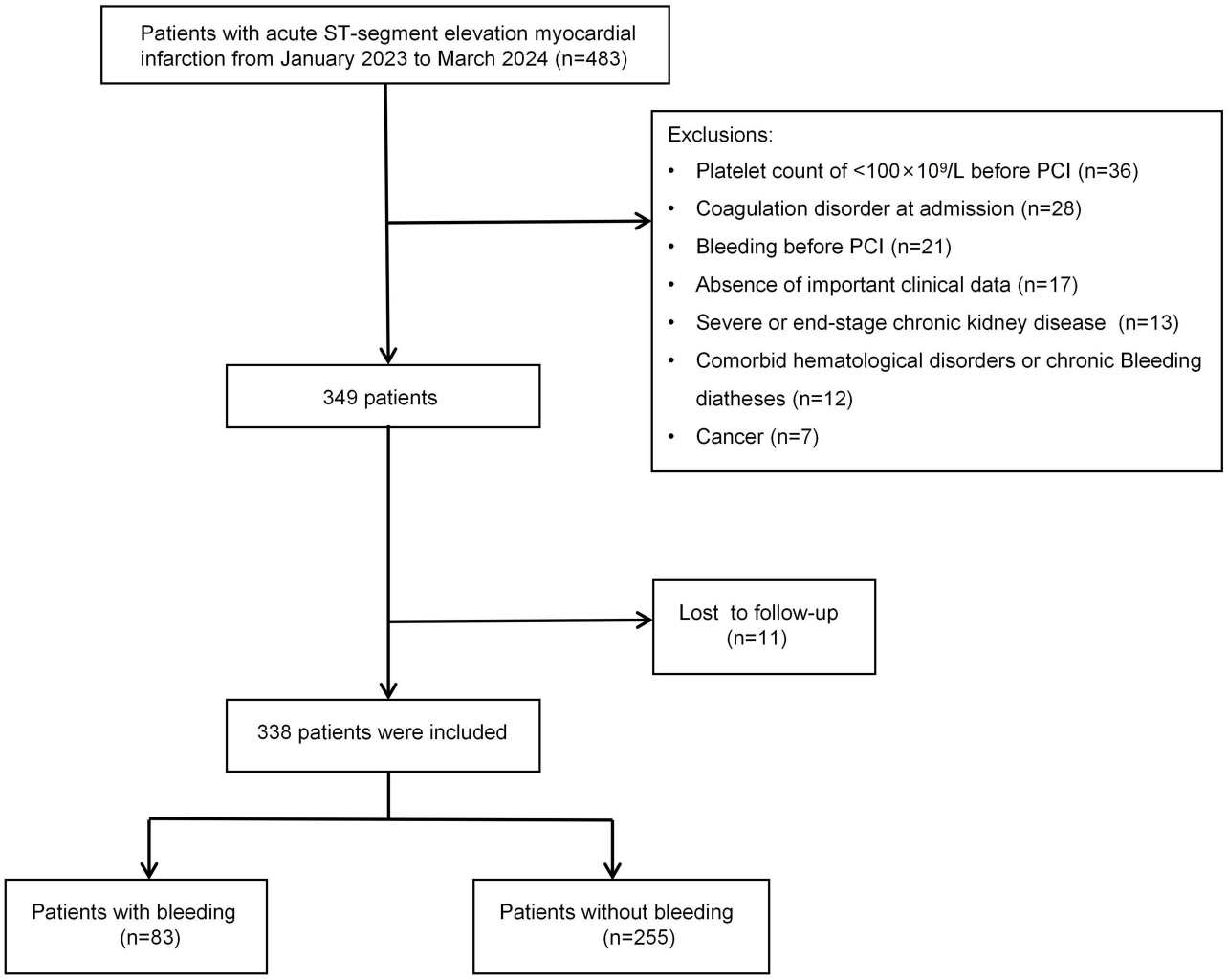

Figure 1 Inclusion and exclusion study flow diagram.

group (40.91% vs 15.25%, P < 0.001). A similar pattern was evident for ARC-HBR stratification, with high-risk patients demonstrating older age, poorer renal function, and a greater comorbidity burden. Notably, male sex, smoking, and alcohol consumption were consistently less frequent among patients classified as high-risk by either score (all P < 0.05) in Table 1.

In the bleeding group, the most prevalent major criteria were prior trauma or surgery (7.23%) and major stroke (7.23%), whereas the most common minor criteria were age ≥ 75 years (26.51%), moderate CKD (24.10%), and oral NSAID or steroid use (18.07%) in Table 2.

Bleeding Characteristics

Among the 338 patients, 83 (24.56%) experienced a bleeding event, including 63 in-hospital events (18.64%) and 34 post-discharge events (10.06%). Gastrointestinal bleeding was the predominant in-hospital event (53.97%), whereas nosebleed and gum bleeding were most frequent after discharge (29.41% and 23.53%, respectively). The majority of bleeding episodes were mild, with BARC type 1 accounting for 82.54% of in-hospital and 73.53% of out-of-hospital events. A detailed breakdown of bleeding sites and BARC classification is provided in Table 3.

Establishment and Assessment of a Bleeding Prediction Model

Univariate logistic regression identified age, hospital stay, troponin, eGFR, GRACE score, and ARC-HBR criteria as potential predictors of bleeding (P < 0.10). These variables were entered into a multivariable model, which confirmed

https://doi.org/10.2147/IJGM.S605618

Table 1 Baseline Characteristics

Variable	GRACE Score			*P-value*	ARC-HBR Criteria		*P-value*
	High-risk (>140) (n=88)	Middle-risk (109–140) (n=73)	Low-risk (≤108) (n=177)		High-risk (n=86)	Low-risk (n=252)	
Age, years	73(66.25,80.00)[a]	64(57.50,72.00)[a,b]	56(47.00,65.50)	<0.001	72.50(60.75, 79.25)	59.00(52.00,69.75)	<0.001
Male sex, n (%)	54(61.36)[a,b]	58(79.45)	140(79.09)	0.004	53(61.63)	199(78.97)	0.001
Smoking, n (%)	33(37.50)[a,b]	47(64.38)	105(59.32)	0.001	31(36.05)	154(61.11)	<0.001
Alcohol, n (%)	26(29.54)	34(46.57)	79(44.63)	0.036	26(30.23)	113(44.84)	0.017
Previous CHD, n (%)	18(20.45)[a]	6(8.22)	17(9.60)	0.020	13(15.12)	28(11.11)	0.326
Previous PCI, n (%)	8(9.09)	5(6.85)	8(4.52)	0.348	3(3.49)	18(7.14)	0.225
Hypertension, n (%)	52(59.09)	39(53.42)	97(54.80)	0.733	54(62.79)	134(53.17)	0.121
Diabetes mellitus, n (%)	21(23.86)	16(21.92)	40(22.60)	0.955	24(27.91)	53(21.03)	0.189
Chronic kidney diseases, n (%)	36(40.91)[a,b]	11(15.07)	27(15.25)	<0.001	38(44.19)	36(14.29)	<0.001
Stroke, n (%)	16(18.18)[a]	14(19.18)[a]	14(7.91)	0.014	14(16.28)	30(11.90)	0.298
Previous cancer, n (%)	3(3.41)	2(2.74)	4(2.26)	0.903	2(2.33)	7(2.78)	1.000
Emergency PCI, n (%)	40(45.45)	31(42.46)	84(47.46)	0.769	36(41.86)	119(47.22)	0.389
Gastrointestinal Diseases, n (%)	8(9.09)[a]	3(4.11)	2(1.13)	0.008	4(4.65)	9(3.57)	0.901
Gensinis score	60.50(36.25,80.00)	54.00(37.50,80.00)	56.00(42.00,86.00)	0.423	54.00(38.88,78.50)	56.00(38.50,84.00)	0.827
eGFR (mL/min*1.73m^2)	66.59(51.63,83.26)[a]	81.08(67.41,102.10)[a,b]	95.70(72.74,122.07)	<0.001	63.27(51.03,84.04)	92.99(72.00,114.57)	<0.001
BNP (pg/mL)	1840.00(707.50,2533.50)[a]	1304.00(272.00,2198.20)	1210.00(361.50,2198.20)	0.032	1754.00(715.00,2839.75)	1251.00(353.25,2198.20)	0.009
cTn (ng/mL)	29.84(6.12,50.00)[a]	19.80(4.24,50.00)	16.42(2.27,49.52)	0.045	23.28(4.89,50.00)	19.33(3.51,50.00)	0.903
ALT (U/L)	12.35(1.50,47.95)[a,b]	5.40(1.40,31.30)	5.60(1.30,33.95)	0.473	2.60(1.27,6.62)	18.45(1.50,44.37)	<0.001
CK (U/L)	748.15(151.72,1423.42)	854.80(171.25,1762.55)	496.00(133.50,1206.10)	0.300	470.50(108.67,1285.07)	708.10(168.52,1438.52)	0.098
Isozyme (U/L)	59.25(7.69,170.18)	63.23(7.54,122.42)	28.64(5.38,95.02)	0.149	29.61(3.86,120.23)	43.10(7.75,121.47)	0.013
FBG (mmol/L)	6.35(5.03,7.75)	6.17(5.11,7.75)	5.98(5.01,7.66)	0.809	6.13(5.12,7.91)	6.15(5.04,7.64)	0.643
Hb (g/L)	126.50(117.50,142.00)ab	137.00(125.00,152.00)	142.00(127.00,151.50)	<0.001	122.00(110.00,138.25)	142.00(127.00,152.75)	<0.001
TC (mmol/L)	4.50(3.49,5.19)	4.61(3.77,5.26)	4.43(3.87,5.01)	0.582	4.34(3.64,5.11)	4.58(3.81,5.08)	0.246
TG (mmol/L)	1.18(0.86,1.74)[a]	1.31(1.00,1.74)	1.66(1.05,2.17)	<0.001	1.19(0.92,1.78)	1.50(1.00,1.99)	0.102

Notes: [a]compare with low-risk GRACE score, P<0.05; [b]compare with middle-risk GRACE score, P<0.05.

Abbreviations: GRACE, Global Registry of Acute Coronary Events; ARC-HBR, Academic Research Consortium for High Bleeding Risk; CHD, coronary heart disease; PCI, percutaneous coronary intervention; eGFR, estimated glomerular filtration rate; BNP, brain natriuretic peptide; cTn, cardiac troponin; ALT, alanine aminotransferase; CK, creatine kinase; FBG, fasting blood glucose; Hb, hemoglobin; TC, total cholesterol; TG, triglyceride.

https://doi.org/10.2147/IJGM.S605618

Table 2 Distribution of ARC-HBR Criteria Components in the Study Cohort (N=338)

Major Criteria	Bleeding (N=83) n (%)	No Bleeding (N=255) n (%)
Severe CKD (eGFR <30 mL/min)	1 (1.20)	5(1.96)
Thrombocytopenia (platelet <100×10^9/L)	1 (1.20)	1(0.39)
Liver cirrhosis	1 (1.20)	0(0.00)
Active malignancy (past 12 months)	2 (2.41)	7(2.75)
Prior trauma or surgery	6(7.23)	23(9.02)
Recent history of spontaneous bleeding	2(2.41)	5(1.96)
History of spontaneous intracranial hemorrhage	1(1.20)	4(1.57)
Stroke major	6(7.23)	22(8.63)
Minor criteria		
Age ≥ 75 years	22(26.51)	46 (18.04)
Moderate CKD (eGFR 30–59 mL/min)	20(24.10)	45 (17.65)
Bleeding or transfusion minor	5 (6.02)	0 (0.00)
Use of oral NSAIDs or steroid	15 (18.07)	36(14.12)
Stroke minor	5(6.02)	11(4.31)

Abbreviations: NSAIDs, non-steroidal anti-inflammatory drugs; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease.

Table 3 Bleeding Characteristics of Patients After PCI

Major Bleeding Sites	Bleeding in-hospital (n=63)	Bleeding out-of-hospital (n=34)
Gastrointestinal bleeding, n (%)	34(53.97)	5(14.71)
Hematuria, n (%)	12(19.05)	2(5.88)
Gum bleeding, n (%)	4(6.35)	8(23.53)
Skin and soft tissue bleeding,n (%)	4(6.35)	7(20.59)
Blood in sputum, n (%)	4(6.35)	2(5.88)
Nosebleed, n (%)	5(7.94)	10(29.41)
BARC type		
Type 1, n (%)	52(82.54)	25(73.53)
Type 2, n (%)	9(14.29)	8(23.53)
Type 3, n (%)	1(1.59)	1(2.94)
Type 5, n (%)	1(1.59)	0(0.0)

Abbreviation: BARC, Bleeding Academic Research Consortium.

DAPT with aspirin plus ticagrelor (OR 2.42, 95% CI 1.04–5.65, P = 0.040), GRACE score (P < 0.001), and ARC-HBR criteria (OR 4.50, 95% CI 2.30–8.78, P < 0.001) as independent risk factors (Table 4).

The combined prediction model was formulated as: Logit (*P*)= −2.523+1.307×ARC-HBR+1.791×GRACE middle risk+1.510×GRACE high risk. The model yielded an AUC of 0.774 (95% CI 0.726–0.818) with an optimal cut-off of 0.26623, corresponding to a sensitivity of 67.47%, specificity of 77.25%, and Youden index of 0.4475 (Table 5).

Predictive Performance and Clinical Utility of the Combined Model

The ROC curves showed that the combined GRACE + ARC-HBR model achieved an AUC of 0.774 (95% CI 0.726–0.818), compared with 0.712 (95% CI 0.660–0.759) for GRACE alone and 0.667 (95% CI 0.614–0.717) for ARC-HBR alone (Figure 2A, Table 5). Compared with GRACE, the combined model yielded a non-significant NRI (−0.0509, P = 0.0945) but a significant IDI (0.0560, P = 0.0006). Compared with ARC-HBR, both NRI (0.3277, P = 0.0007) and IDI (0.0768, P < 0.0001) were significantly positive. DCA demonstrated superior net benefit for the combined model across most threshold probabilities, particularly in the mid-to-high range (Figure 2B). Calibration was satisfactory, with a Brier score of 0.147 and a Hosmer-Lemeshow test result of χ^2= 3.568 (P = 0.8938) (Figure 2C).

Table 4 Logistic Regression Analysis of Risk Factors Associated with Bleeding

Variable	Univariate Logistic Regression Analysis		Multivariate Logistic Regression Analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age, years	1.021(1.001,1.041)	0.035	0.969(0.937,1.001)	0.059
Male	1.584(0.860,2.918)	0.138		
Smoking	1.038(0.630,1.707)	0.885		
Alcohol	1.466(0.890,2.414)	0.132		
Previous CHD	1.317(0.639,2.716)	0.455		
Hypertension	0.870(0.529,1.430)	0.582		
Diabetes mellitus	1.008(0.559,1.819)	0.978		
Chronic kidney diseases	1.291(0.723,2.306)	0.387		
Stroke	1.028(0.494,2.138)	0.942		
Gastrointestinal Diseases	0.247(0.032,1.928)	0.266		
Emergency PCI	1.373(0.835,2.255)	0.210		
Hospital stay, days	1.102(1.037,1.172)	0.002	1.045(0.973,1.122)	0.229
eGFR (mL/min*1.73m^2)	0.992(0.985,0.999)	0.030	0.997(0.986,1.008)	0.568
cTn (ng/mL)	1.015(1.003,1.027)	0.012	1.006(0.993,1.02)	0.369
Hb (g/L)	0.994(0.982,1.007)	0.359		
TC (mmol/L)	0.848(0.662,1.086)	0.190		
TG (mmol/L)	1.080(0.910,1.281)	0.380		
The number of stents implanted		0.582		
1				
2	0.757(0.420,1.366)			
≥3	0.751(0.309,1.825)			
Intraoperative Tirofiban Administration	1.219(0.722,2.058)	0.459		
Aspirin combined with ticagrelor	1.961(0.949,4.053)	0.065	2.423(1.039,5.649)	0.040
Lipid-lowering drugs	1.482(0.314,6.999)	0.886		
Beta-blockers	0.676(0.341,1.340)	0.260		
Access site (radial vs femoral)	0.976(0.258,3.692)	1.000		
PPI at discharge	0.803(0.485,1.330)	0.394		
Gensinis score	0.998(0.990,1.006)	0.582		
GRACE score		<0.001		<0.001
Low risk	Ref	Ref	Ref	Ref
Middle risk	6.566(3.315,13.008)	<0.001	7.11(3.002,16.841)	<0.001
High risk	6.516(3.381,12.599)	<0.001	7.566(3.457,16.56)	<0.001
ARC-HBR criteria	4.912(2.865,8.422)	<0.001	4.497(2.304,8.779)	<0.001

Notes: Patients were divided into bleeding and non-bleeding groups based on the occurrence of post-PCI bleeding.

Abbreviations: GRACE, Global Registry of Acute Coronary Events; ARC-HBR, Academic Research Consortium for High Bleeding Risk; PCI, percutaneous coronary intervention; CHD, coronary heart disease; eGFR, estimated glomerular filtration rate; cTn, cardiac troponin; Hb, hemoglobin; TC, total cholesterol; TG, triglyceride; DAPT, dual antiplatelet therapy; PPI, proton pump inhibitor; OR, odds ratios; CI, confidence intervals.

Internal validation using bootstrap resampling (1,000 iterations) produced a bias-corrected AUC of 0.775, closely matching the apparent AUC and indicating minimal overfitting.

Kaplan-Meier Survival Curves of Bleeding Events

Kaplan-Meier curves for in-hospital and out-of-hospital bleeding stratified by GRACE and ARC-HBR risk status are shown in Figure 3. The dual high-risk group (GRACE high-risk plus ARC-HBR high-risk) exhibited significantly higher cumulative bleeding rates than all other groups, both during hospitalization (log-rank $P < 0.0001$; Figure 3A) and within one year post-discharge (log-rank $P = 0.0255$; Figure 3B). Using a 30-day landmark, 63 of the 83 bleeding events (75.90%) were classified as early (≤30 days) and 20 (24.10%) as late (>30 days). The dual high-risk group maintained significantly elevated bleeding rates across both early and late periods ($P < 0.05$; Figure 3C).

Table 5 ROC Curve Analysis Results of the GRACE Score and ARC-HBR Criteria for Bleeding Occurrence After PCI in STEMI Patients

Variable	AUC	Cut-off Value	95% CI	Sensibility	Specificity	Youden Index	P-value#	P-value*
GRACE score	0.712	0.09605	0.660–0.759	79.52	62.75	0.4226	<0.001	0.253
ARC-HBR criteria	0.667	0.1627	0.614–0.717	50.60	82.75	0.3335	<0.001	-
GRACE score combined with ARC-HBR criteria	0.774	0.26623	0.726–0.818	67.47	77.25	0.4475	-	-

Notes: #:compare with GRACE score combined with ARC-HBR criteria; *:compare with ARC-HBR criteria.
Abbreviations: GRACE, Global Registry of Acute Coronary Events; ARC-HBR, Academic Research Consortium for High Bleeding Risk; AUC, area under curve; CI, confidence interval.

Discussion

In this prospective observational study of 338 STEMI patients undergoing PCI, we found that the combination of the GRACE score and the ARC-HBR criteria improved the prediction of post-PCI bleeding compared with either score alone. The combined model achieved an AUC of 0.774 (95% CI 0.726–0.818), outperforming GRACE alone (AUC 0.712) and ARC-HBR alone (AUC 0.667). Multivariate logistic regression analysis identified DAPT with aspirin plus ticagrelor (OR 2.423), a higher GRACE score, and meeting the ARC-HBR criteria (OR 4.497) as independent risk factors for bleeding. The overall incidence of bleeding was 24.6%, with in-hospital bleeding (18.64%) being more common than out-of-hospital bleeding (10.06%). Importantly, early bleeding (≤30 days) accounted for 75.90% of all bleeding events, and the dual high-risk group had significantly higher cumulative bleeding rates in both the early and late periods. These findings suggest that integrating an ischemic risk score (GRACE) with a bleeding-specific score (ARC-HBR) provides incremental predictive value and may help clinicians tailor antithrombotic strategies for STEMI patients.

Predicting bleeding complications following PCI in STEMI patients is crucial due to their significant impact on clinical outcomes. In this clinical context, bleeding is strongly correlated with mortality, with major bleeding events linked to a 60% higher risk of in-hospital death.[25] Understanding the incidence and risk factors associated with postoperative bleeding can guide clinical decision-making and improve patient management. Our study found that the overall incidence of in-hospital bleeding after PCI in STEMI patients was 18.64%, and the incidence of gastrointestinal bleeding was 10.1%, which was higher than that reported by B. Tang et al (8.25%, 32/388).[26] In contrast, a large Turkish multicenter study (DAPT-TR) using fixed-dose aspirin plus clopidogrel in acute or chronic coronary syndromes reported much lower bleeding rates, with BARC type 1 bleeding in 3.3% and BARC type 2/3/5 bleeding in 0.6%.[27] The incidence of bleeding events during the one-year follow-up was 10.1%, slightly lower than that reported by Han Y et al (11.9%, 20/168).[6] Notably, the finding that early bleeding occurred more frequently than late bleeding in our study is consistent with the established temporal pattern of post-PCI bleeding. The mechanisms underlying early and late bleeding are fundamentally distinct. Early bleeding within 30 days is predominantly procedure-related, driven by factors such as arterial

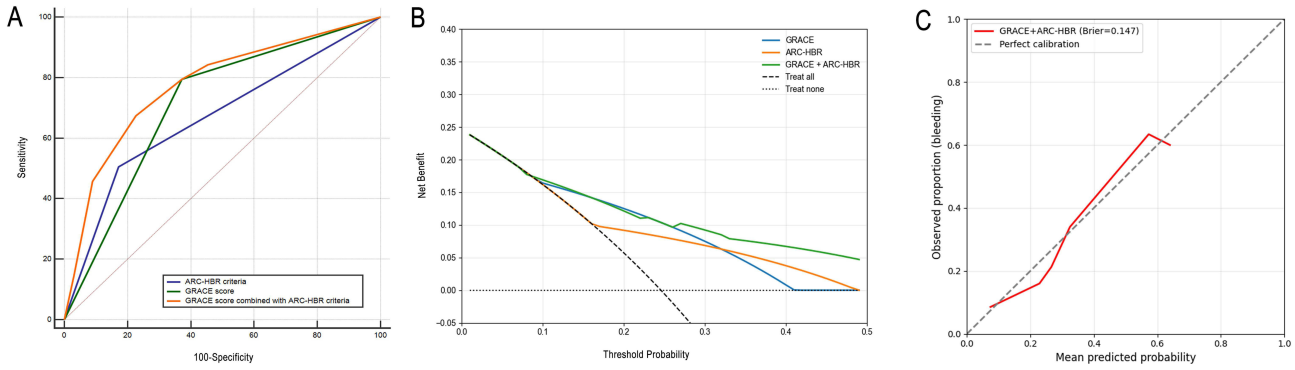

Figure 2 Predictive performance and clinical utility of the combined model. (**A**) ROC curves of the three models; (**B**) DCA curves of the three models; (**C**) Calibration curve of the GRACE score combined with ARC-HBR criteria prediction model.

https://doi.org/10.2147/IJGM.S605618

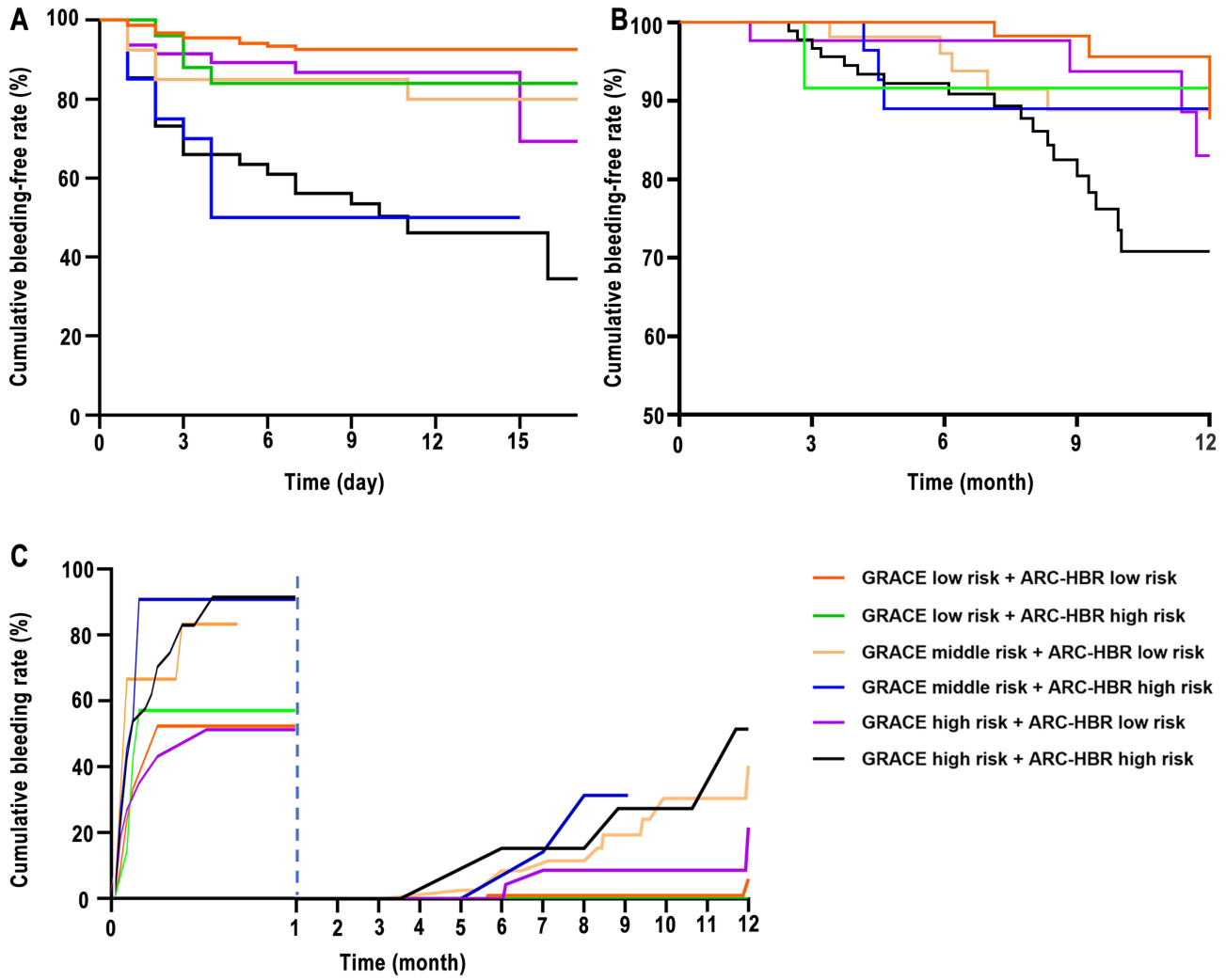

Figure 3 Prediction of post-PCI bleeding in STEMI patients using the GRACE score combined with the ARC-HBR criteria. (**A**) In-hospital bleeding; (**B**) Ou-of-hospital bleeding; (**C**) Early (≤30 days) and late (>30 days) bleeding.

access site complications, periprocedural antithrombotic therapy, intraprocedural hypotension, and the use of mechanical support devices.[2] In contrast, late bleeding beyond 30 days is primarily medication-related, associated with the cumulative effect of prolonged dual antiplatelet therapy and the ongoing balance between ischemic and hemorrhagic risks. The risk of major bleeding was significantly higher during the hospital stay than in the post-discharge, which is consistent with the findings of Stehli J et al[28] This observation highlights the need for heightened vigilance in managing patients during and immediately after PCI. Existing models, such as the GRACE score and ARC-HBR criteria, have been developed to stratify bleeding risk in patients undergoing PCI. The GRACE score incorporates various clinical parameters to predict mortality, whereas the ARC-HBR criteria specifically focus on identifying patients at high risk for bleeding complications after PCI.[29,30]

Previous studies have shown that the GRACE score, originally developed for ischemic risk stratification, also has predictive value for bleeding events. In a cohort of 1452 patients with atrial fibrillation undergoing PCI, Guo et al found that a higher GRACE score was independently associated with an increased risk of major bleeding (HR 1.012, 95% CI 1.001–1.024, P = 0.039).[31] This supports the use of the GRACE score for bleeding risk assessment. However, the predictive performance of GRACE alone for bleeding is moderate (its AUC for all-cause mortality was 0.708, while the AUC for bleeding was not reported). On the other hand, combining two bleeding-oriented scores may not provide incremental value. Kadiyala et al evaluated the joint use of PRECISE-DAPT and ARC-HBR criteria for predicting in-hospital bleeding in 3659

PCI patients and found that combining the two scores did not improve the AUC (combined AUC 0.60, P = 0.49 compared with either score alone).[32] In contrast, our study combined an ischemic risk score (GRACE) with a bleeding-specific score (ARC-HBR) and observed a significant increase in AUC from 0.712 for GRACE alone and 0.667 for ARC-HBR alone to 0.774 for the combined model. This suggests that combining ischemic and bleeding risk scores may provide greater predictive benefit than combining two tools that capture overlapping bleeding risk factors.

Studies have shown that the ARC-HBR criteria have been independently validated as predictors of bleeding at one year after PCI, providing an enhanced risk stratification framework.[33,34] In our study, we found that the combination of the GRACE score and the ARC-HBR criteria offered superior predictive performance for in-hospital and one-year bleeding events in STEMI patients after PCI. Specifically, patients classified as high-risk by the GRACE score and also as high-bleeding-risk by the ARC-HBR criteria demonstrated better predictive ability for in-hospital bleeding events. This suggests that the integrated approach not only leverages the strengths of both models but also provides a more nuanced assessment of bleeding risk, ultimately assisting clinicians in optimizing patient management strategies and improving outcomes for this vulnerable population. In this study, we compared a combined model with each single model for predicting bleeding events after percutaneous coronary intervention. The combined model improved the IDI (P=0.0006) over GRACE and both NRI (P=0.0007) and IDI (P<0.0001) over ARC-HBR. Furthermore, DCA showed that the combined model offered the highest net benefit across a clinically meaningful range of threshold probabilities. The combined model outperforms each single model in terms of net benefit across most clinically relevant thresholds. This supports its use as a decision aid for identifying patients at high bleeding risk who might require tailored antithrombotic strategies. The DCA results further emphasize that using the combined model would lead to better clinical decisions than relying on either GRACE or ARC-HBR alone.

However, our study still has certain limitations. (1) This was a single-center prospective observational study, and the results are limited to one medical institution without validation in similar patient populations at other medical facilities. (2) The sample size was relatively small, and the number of major bleeding events (BARC type 3 or 5) was too low to perform meaningful stratified analyses by bleeding severity (major vs minor bleeding). (3) There may be other unmeasured confounding factors that could affect bleeding events. (4) The GRACE score and ARC-HBR criteria, which are primarily based on clinical parameters, cannot dynamically assess bleeding risk in patients. (5) Although internal validation was performed, external validation is lacking.

In conclusion, this study demonstrates that in a prospective STEMI cohort undergoing PCI, the combination of the GRACE score and the ARC-HBR criteria provides incremental predictive value for one-year bleeding risk beyond either score alone. The combined model shows good discrimination for overall bleeding events, with numerically higher predictive performance for in-hospital bleeding, as reflected by Kaplan-Meier estimates and the predominance of early events.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author, Xiaowu Wang, on reasonable request.

Ethical Approval and Consent Statement

The study was approved by the Ethics Committee of Fuyang People's Hospital (Approval No. 202311) and conformed to the ethical guidelines of the Declaration of Helsinki. Written informed consent was obtained from each patient before enrollment.

Acknowledgments

The authors thank all participants of this study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was supported by the Anhui Provincial Health Research Project (Grant No. AHWJ2023A30162), the Fuyang City Key Research and Development Plan for Clinical Medical Research Translation Special Project (Grant No. FYZDYF2023LCYX012), the Bengbu Medical College Research Project (Grant No. 2022byzd166), and the Fuyang Vocational and Technical College-Fuyang Second People's Hospital Collaborative Research Cultivation Project (Grant No. 2025FZYXYPY12).

Disclosure

The authors have declared that no competing interests exist in this work.

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