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Association between stress hyperglycemia ratio and contrast-induced nephropathy in ACS patients undergoing PCI: a retrospective cohort study from the MIMIC-IV database

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Abstract

Background Contrast-induced nephropathy (CIN) is a significant complication in acute coronary syndrome (ACS) patients undergoing percutaneous coronary intervention (PCI). The role of the stress hyperglycemia ratio (SHR) as a predictor of CIN and mortality in these patients remains unclear and warrants investigation.

Objective To assess the relationship between SHR and CIN, as well as its impact on short-term mortality in ACS patients undergoing PCI.

Methods We conducted a retrospective cohort study using the MIMIC-IV database, including 552 ACS patients. SHR was calculated as the ratio of admission glucose to estimated average glucose from hemoglobin A1c. CIN was defined as a ≥ 0.5 mg/dL or ≥ 25% increase in serum creatinine within 48 h of PCI. Logistic regression and spline models were used to analyze the association between SHR and CIN, while Kaplan–Meier curves assessed 30-day mortality.

Results Higher SHR levels were independently associated with increased CIN risk (OR 2.36, 95% CI: 1.56–3.57, $P < 0.0001$). A J-shaped relationship was observed, with CIN risk rising sharply when SHR exceeded 1.06. SHR was also a predictor of higher 30-day mortality ($P < 0.0001$). Subgroup analysis revealed a stronger SHR-CIN association in non-diabetic patients.

Conclusion SHR is an independent predictor of CIN and short-term mortality in ACS patients undergoing PCI. It offers potential for risk stratification and clinical decision-making, especially in non-diabetic patients.

Keywords Stress hyperglycemia ratio, Contrast-induced nephropathy, Acute coronary syndrome, Percutaneous coronary intervention, Short-term mortality

Background

Acute coronary syndrome (ACS) remains a leading cause of global mortality, underscoring the necessity of effective reperfusion therapies such as percutaneous coronary intervention (PCI) [1]. PCI has markedly improved ACS management by reducing ischemic complications and enhancing survival rates. However, the use of contrast agents during the procedure elevates the risk of contrast-induced nephropathy (CIN), characterized by acute renal

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function deterioration [2]. The incidence of CIN varies widely, ranging from less than 1% to 50%, influenced by patient characteristics, comorbidities, procedural factors, and diagnostic criteria. High-risk groups, including older adults, patients with heart failure, chronic kidney disease (CKD), or diabetes combined with CKD, exhibit CIN rates up to 55% [3, 4]. CIN is associated with extended hospital stays, increased need for renal replacement therapy, and higher mortality. Currently, effective preventive strategies are lacking, highlighting the critical need for early identification of risk factors to improve outcomes in vulnerable patient populations.

In recent years, the stress hyperglycemia ratio (SHR) has emerged as a novel glycemic metric, offering a precise assessment of acute hyperglycemic states by accounting for baseline glucose control through hemoglobin A1c (HbA1c) levels [5]. Unlike absolute blood glucose measurements, SHR provides a more accurate identification and quantification of stress-induced hyperglycemia, which is particularly relevant in critically ill patients. Previous studies have demonstrated that elevated SHR is associated with adverse cardiovascular outcomes in both diabetic and non-diabetic populations [6–9]. Despite these findings, the relationship between SHR and CIN in PCI-treated ACS patients remains insufficiently explored.

Given the growing clinical interest in SHR as a prognostic indicator, we hypothesize that SHR may play a crucial role in predicting the development of CIN and mortality in ACS patients undergoing PCI. Utilizing Medical Information Mart for Intensive Care IV (MIMIC-IV) database, this study aims to investigate the relationship between SHR and CIN, as well as its impact on both short-term and long-term mortality. By exploring these associations, our research seeks to provide new insights into the prognostic value of SHR and its potential application in clinical practice, ultimately contributing to improved renal and overall clinical outcomes for high-risk patient cohorts.

Methods

Data source

This study leveraged the MIMIC-IV 3.0 database, which contains de-identified clinical data for 94,458 patients admitted to the intensive care units (ICUs) of Beth Israel Deaconess Medical Center between 2008 and 2022 [10, 11]. The database encompasses a wide range of clinical information, including demographic details, diagnoses, laboratory results, medication records, procedures, and outcomes, with a primary focus on critically ill ICU patients. Access to the MIMIC-IV 3.0 database was obtained after completing the required credentialing process via PhysioNet, which included the successful completion of the Collaborative Institutional Training Initiative (CITI) Program's "Data or Specimens Only Research" course (certification No. 63998837) and agreeing to the data use terms. As all data are de-identified, patient consent was not necessary. This research was conducted in accordance with ethical standards for utilizing publicly available de-identified datasets.

Patient selection

Patients meeting the following inclusion criteria were included in the study: (1) diagnosis of Acute Myocardial Infarction (AMI), including both ST-Elevation Myocardial Infarction (STEMI) and Non-ST Elevation Myocardial Infarction (NSTEMI), confirmed by ICD-9/10 codes; (2) first admission to the ICU during hospitalization. Patients meeting the following exclusion criteria were excluded: (1) age < 18 years; (2) ICU length of stay < 1 day; (3) did not undergo PCI during hospitalization; (4) estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73m^2, indicating end-stage renal disease (ESRD); (5) missing discharge status or follow-up data; (6) missing key clinical data, including admission blood glucose, HbA1c, or renal function (serum creatinine, urine output). Finally, a total of 552 patients were included in the MIMIC-IV database. (Fig. 1).

Data extraction and definitions

Data extraction was performed using Navicat Premium (Version 16.1.15) with SQL. The study examined various variables categorized as follows: (1) Demographics: Age, gender. (2) comorbidities (hypertension (HTN), diabetes mellitus (DM), congestive heart failure (CHF), cerebrovascular disease, atrial fibrillation (AF), chronic pulmonary disease (CPD), peripheral vascular disease (PVD)), (3) procedure information (PCI (including percutaneous transluminal coronary angioplasty, insertion of non-drug-eluting coronary artery stent, insertion of drug-eluting coronary artery stent), extracorporeal membrane oxygenation (ECMO), intra-aortic balloon pump (IABP), and continuous renal replacement therapy (CRRT)), (4) laboratory (white blood cell (WBC) count, albumin levels, serum creatinine (Scr), admission blood glucose, HbA1c, troponin T (TnT) and creatine kinase-MB (CK-MB), (5) vasoactive drugs (dobutamine, dopamine, epinephrine, norepinephrine, phenylephrine, milrinone, vasopressin), (6) Disease Severity Scores: Charlson Comorbidity Index (CCI), Acute Physiology Score III (APS III), Simplified Acute Physiology Score II (SAPS II), Oxford Acute Severity of Illness Score (OASIS), and Sequential Organ Failure Assessment (SOFA).

SHR was calculated as [(admission glucose (mg/dl))/(28.7 × HbA1c (%)−46.7)], admission glucose and HbA1c were obtained directly from MIMIC IV. This study utilizes the Modification of Diet in Renal Disease (MDRD)

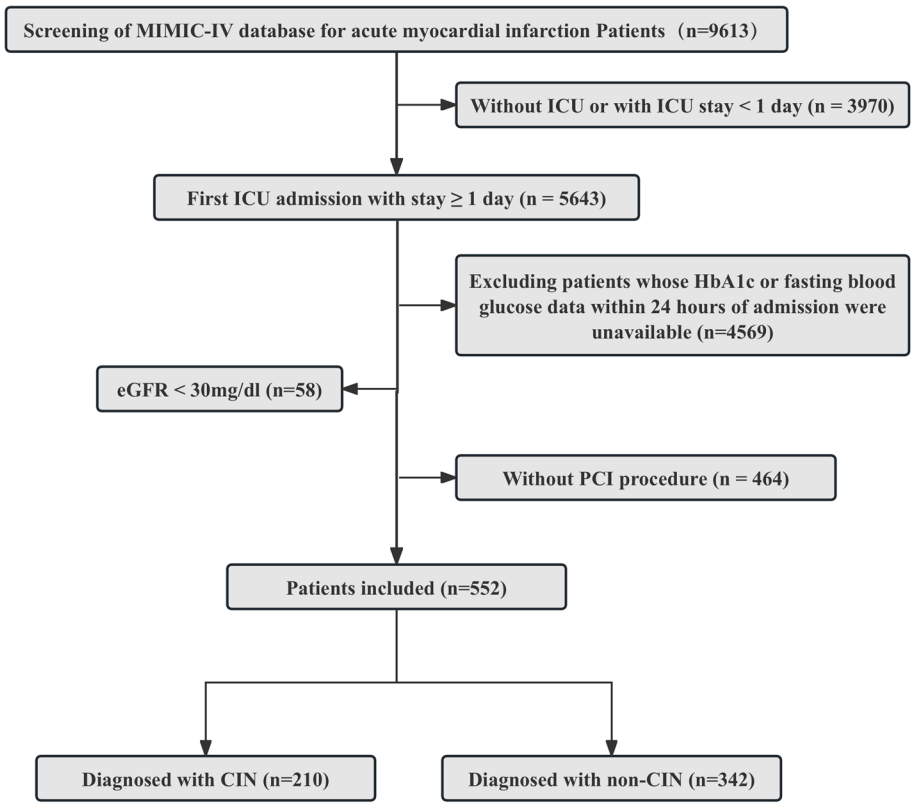

Fig. 1 Flow chart of the inclusion of the study population; PCI, percutaneous coronary intervention; CIN, contrast-induced nephropathy

equation to estimate the eGFR. The specific formula is as follows: $eGFR = 186 \times (Scr - 1.154) \times (age - 0.203) \times (0.742$ if female), where Scr refers to serum creatinine, measured in mg/dL, and age is expressed in years [12]. CIN was defined as an increase in serum creatinine of ≥ 0.5 mg/dL or $\geq 25\%$ from baseline within 48 h PCI. Baseline creatinine was determined from ICU day 1 measurements. For variables with missing values less than 20%, data imputation was performed using a random forest approach [13].

Outcomes

The primary outcome was short-term survival, defined as 30-day all-cause mortality, determined by the recorded date of death and discharge date in the MIMIC IV database.

Statistical analysis

All statistical analyses were performed using R software (version 4.4.1). Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed variables were summarized as mean ± standard deviation (SD) and compared using one-way analysis of variance (ANOVA), while non-normally distributed variables were reported as median with interquartile range (IQR) and compared using the Wilcoxon rank-sum test. Categorical variables were summarized as counts with percentages and compared using the chi-squared test. Logistic regression models were utilized to investigate the relationship between SHR and CIN, with odds ratios (ORs) and 95% confidence intervals (CIs) reported. Three models were constructed: the crude model included SHR alone; Model 1 adjusted for STEMI, diabetes mellitus (DM), and hypertension (HTN), reflecting the impact of baseline disease states on the SHR-CIN association; Model 2 incorporated additional adjustments for procedural factors, including stent placement and vessel involvement, to explore the influence of PCI complexity on CIN risk. Restricted cubic spline (RCS) regression models were applied to assess potential non-linear relationships between SHR and CIN. Knots were placed at the 25th, 50th, and 75th percentiles of the SHR distribution to ensure adequate flexibility in modeling while avoiding overfitting. A likelihood ratio test was performed to assess non-linearity, and SHR was analyzed as a continuous variable if no significant non-linear association was observed. Subgroup analyses were conducted for predefined variables, including sex, age group (<60 vs. ≥ 60 years), STEMI, DM, HTN, CHF, and stent placement status. Stratified logistic regression models were fitted for each subgroup to quantify the strength of

the SHR-CIN relationship within specific clinical strata. Baseline characteristics were compared between CIN groups and across SHR tertiles. Interaction tests were performed to evaluate whether the relationship between SHR and CIN was modified by predefined clinical variables, including DM, stent placement, and other demographic or procedural factors. Likelihood ratio tests were used to compare models with and without interaction terms, such as SHR × DM or SHR × stent placement, to test for heterogeneity in the SHR-CIN association across subgroups. A significant interaction term indicated that the effect of SHR on CIN risk varied by subgroup. Short-term survival outcomes were evaluated using Kaplan–Meier curves, with differences between groups assessed using the log-rank test. For patients with hospital stays ≤ 30 days, stratified survival analyses were conducted to account for potential confounding effects. All statistical tests were two-sided, and significance was set at $P < 0.05$.

Results

Baseline characteristics of study individuals

The study included 552 patients, with 210 in the CIN group and 342 in the non-CIN group (Table 1). SHR levels were significantly higher in the CIN group compared to the non-CIN group ($P < 0.001$). The CIN group had a higher prevalence of CHF and AF, with elevated disease severity scores, including SOFA, APS III, SAPS II, and CCI ($P < 0.05$). While no significant differences were observed in STEMI or DM between the groups, the CIN group showed significantly worse renal function, inflammatory response, and myocardial injury, as reflected by higher levels of baseline creatinine, WBC, TnT, and CK-MB ($P < 0.05$). Procedural complexity was greater in the CIN group, as evidenced by increased use of vasoactive drugs, ECMO, IABP, and CRRT ($P < 0.05$). Additionally, the CIN group experienced longer hospital and ICU stays, along with significantly higher 30-day in-hospital mortality compared to the non-CIN group ($P < 0.05$).

When stratified by SHR quartiles (Q1–Q3), SHR values demonstrated a linear increase from Q1 (0.86 [0.78–0.92]) to Q3 (1.47 [1.31–1.68]; $P < 0.0001$) (Table 2). Compared to the Q1 group, the Q3 group exhibited significantly higher prevalence of comorbidities such as CHF, DM, AF, CVD, CPD, CVD and PVD, elevated disease severity scores including SOFA, APS III, SAPS II, and CCI, as well as increased levels of myocardial injury markers (TnT, CK-MB) and inflammatory indicators (WBC) ($P < 0.05$). Additionally, renal function parameters (BUN, baseline creatinine), electrolyte levels (K), and coagulation function (INR) were markedly worsened in the Q3 group ($P < 0.05$). In terms of therapeutic interventions, the Q3 group had a significantly higher proportion of patients receiving vasoactive medications, IABP, and CRRT, and experienced longer hospital and ICU stays compared to the Q1 group ($P < 0.05$). Finally, the in-hospital mortality rate was significantly elevated in the Q3 group (21.74%) compared to the Q1 group (9.24%; $P < 0.0001$).

In summary, patients with CIN and those in the highest SHR quartile exhibited worse clinical and biochemical profiles, longer hospital and ICU stays, and higher mortality rates. These findings underscore the complex relationship between SHR and CIN, warranting further investigation.

Association between SHR and CIN

Logistic regression models demonstrated that SHR was independently associated with an elevated risk of CIN (Table 3). In the unadjusted model, each unit increase in SHR correlated with a 2.25-fold higher risk of CIN (95% CI: 1.51–3.36, $P < 0.0001$). This association remained robust after adjustment for STEMI, DM, and HTN (OR 2.39, 95% CI: 1.59–3.59, $P < 0.0001$), as well as procedural complexity factors, including stent placement and vessel involvement (OR 2.36, 95% CI: 1.56–3.57, $P < 0.0001$). When stratified by quartiles (Q1–Q3), SHR in Q3 was associated with a markedly increased risk of CIN compared to Q1 (OR 2.52, 95% CI: 1.63–3.89, $P < 0.0001$) (Fig. 2), demonstrating a clear dose–response relationship across quartiles (P for trend < 0.0001). Restricted cubic spline analysis further confirmed the J-shaped association between SHR and CIN (P-overall $= 0.0002$). When SHR exceeded the threshold value of 1.06, the incidence of CIN increased significantly. These findings highlight SHR as a continuous and independent predictor of CIN, with a critical inflection point that underscores its prognostic value (Fig. 3).

Association between SHR and LOS

In addition, our study found that patients with elevated SHR also experienced longer LOS in the hospital. The prolonged LOS likely reflects the increased complexity of managing these patients, as their critical illness often requires extended monitoring and more intensive treatments. Elevated SHR could therefore serve as a marker not only for predicting CIN and short-term mortality but also for identifying patients who are likely to experience prolonged hospitalization, further highlighting its clinical utility in predicting overall disease severity and recovery trajectory.

Subgroup analysis

To further evaluate the robustness of the association between elevated SHR levels and the risk of incident CIN, we performed subgroup analyses stratified by

Table 1 Baseline characteristics of patients stratified by the presence of CIN

Variables	Total (*n* = 552)	non-CIN (*n* = 342)	CIN (*n* = 210)	*P*
SHR	1.06(0.92,1.30)	1.03(0.90,1.20)	1.16(0.97,1.47)	< 0.0001
Sex,%				0.28
Female	178(32.25)	104(30.41)	74(35.24)	
Male	374(67.75)	238(69.59)	136(64.76)	
Age,years	67.75(59.10,77.02)	66.99(58.17,77.10)	69.17(61.58,76.96)	0.10
SOFA	2.00(1.00,5.00)	2.00(1.00,3.00)	4.00(1.25,7.00)	< 0.0001
APS3	33.00(26.00,44.00)	31.00(25.00,38.00)	38.00(30.00,52.00)	< 0.0001
SAPSII	30.00(23.00,37.00)	28.00(21.25,35.00)	34.00(26.00,44.00)	< 0.0001
OASIS	28.00(22.00,33.00)	26.00(22.00,31.00)	31.00(25.00,36.75)	< 0.0001
CCI	5.00(3.00,7.00)	5.00(3.00,7.00)	5.00(4.00,7.00)	0.01
CHF,%				< 0.01
no	296(53.62)	201(58.77)	95(45.24)	
yes	256(46.38)	141(41.23)	115(54.76)	
STEMI,%				0.14
no	150(27.17)	85(24.85)	65(30.95)	
yes	402(72.83)	257(75.15)	145(69.05)	
DM,%				0.32
no	383(69.38)	243(71.05)	140(66.67)	
yes	169(30.62)	99(28.95)	70(33.33)	
AF,%				< 0.01
no	416(75.36)	271(79.24)	145(69.05)	
yes	136(24.64)	71(20.76)	65(30.95)	
CVD,%				0.21
no	501(90.76)	315(92.11)	186(88.57)	
yes	51(9.24)	27(7.89)	24(11.43)	
CPD,%				0.47
no	441(79.89)	277(80.99)	164(78.10)	
yes	111(20.11)	65(19.01)	46(21.90)	
PVD,%				0.10
no	483(87.50)	306(89.47)	177(84.29)	
yes	69(12.50)	36(10.53)	33(15.71)	
HTN,%				0.58
no	164(29.71)	105(30.70)	59(28.10)	
yes	388(70.29)	237(69.30)	151(71.90)	
RBC,m/uL	4.09 ± 0.67	4.11 ± 0.65	4.05 ± 0.71	0.29
Hb,g/dL	12.33 ± 1.97	12.42 ± 1.94	12.17 ± 2.01	0.16
PLT,K/uL	218.00(174.00,260.00)	219.00(175.00,261.00)	211.00(173.00,257.00)	0.83
WBC,K/uL	11.50(8.80,14.43)	11.10(8.40,13.28)	12.60(9.80,16.10)	< 0.0001
BUN,mg/dL	18.00(14.00,26.00)	17.00(13.00,24.00)	20.00(14.00,30.00)	< 0.01
Na,mmol/L	138.00(137.00,140.00)	139.00(137.00,140.00)	138.00(136.00,140.00)	0.36
K,mmol/L	4.20(4.00,4.50)	4.20(4.00,4.40)	4.30(4.00,4.80)	< 0.001
INR	1.20(1.10,1.38)	1.20(1.10,1.30)	1.20(1.10,1.40)	1.00
Baseline Cr,mg/dL	0.90(0.70,1.10)	0.90(0.80,1.10)	0.90(0.70,1.18)	0.85
TnT,ng/mL	2.43(0.93,5.99)	2.25(0.90,5.37)	3.00(1.03,6.89)	< 0.01
CK_MB,ng/mL	90.00(27.00,203.05)	83.00(25.00,183.75)	106.00(36.25,257.35)	< 0.01
LOS hospital,days	5.05(3.08,8.99)	4.19(3.01,7.64)	6.51(3.83,11.19)	< 0.001
LOS ICU,days	2.17(1.46,4.04)	2.01(1.37,3.18)	3.04(1.79,5.32)	< 0.0001
Hospital mortality,%				< 0.0001
no	501(90.76)	325(95.03)	176(83.81)	

Table 1 (continued)

Variables	Total (*n* = 552)	non-CIN (*n* = 342)	CIN (*n* = 210)	*P*
yes	51(9.24)	17(4.97)	34(16.19)	
Vasoactive,%				< 0.0001
no	387(70.11)	269(78.65)	118(56.19)	
yes	165(29.89)	73(21.35)	92(43.81)	
ECMO,%				0.03
no	545(98.73)	341(99.71)	204(97.14)	
yes	7(1.27)	1(0.29)	6(2.86)	
IABP,%				0.03
no	450(81.52)	289(84.50)	161(76.67)	
yes	102(18.48)	53(15.50)	49(23.33)	
CRRT,%				< 0.001
no	539(97.64)	341(99.71)	198(94.29)	
yes	13(2.36)	1(0.29)	12(5.71)	
Stent1,%				0.15
no	335(60.69)	199(58.19)	136(64.76)	
yes	217(39.31)	143(41.81)	74(35.24)	
Stent2,%				0.25
no	459(83.15)	279(81.58)	180(85.71)	
yes	93(16.85)	63(18.42)	30(14.29)	
Stentmoere,%				0.55
no	498(90.22)	306(89.47)	192(91.43)	
yes	54(9.78)	36(10.53)	18(8.57)	
Vessel1,%				0.02
no	218(39.49)	122(35.67)	96(45.71)	
yes	334(60.51)	220(64.33)	114(54.29)	
Vessel2,%				0.90
no	497(90.04)	307(89.77)	190(90.48)	
yes	55(9.96)	35(10.23)	20(9.52)	
Vesselmoere,%				0.23
no	537(97.28)	330(96.49)	207(98.57)	
yes	15(2.72)	12(3.51)	3(1.43)	

SHR Sstress hyperglycemia ratio, *SOFA* Sequential Organ Failure Assessment, *APS3* Acute Physiology Score III, *SAPSII* Simplified Acute Physiology Score II, *OASIS* Oxford Acute Severity of Illness Score, *GCS* Glasgow Coma Scale, *CCI* Charlson Comorbidity Index, *CHF* Congestive heart failure, *STEMI* ST-elevated myocardial infarction, *DM* Diabetes mellitus, *AF* Atrial fibrillation, *CVD* Cerebrovascular disease, *CPD* Chronic pulmonary disease, *PVD* Peripheral vascular disease, *HTN* Hypertension, *RBC* Red blood cells (m/uL), *Hb* Hemoglobin (g/dL), *PLT* Platelets (K/uL), *WBC* White blood cells (K/uL), *BUN* Blood urea nitrogen (mg/dL), *Na* sodium (mmol/L), *K* Potassium (mmol/L), *INR* International normalized ratio, *Baseline Cr* Baseline creatinine (mg/dL), *TnT* Cardiac troponin T (ng/mL), *CK_MB* Creatine kinase-MB (ng/mL), *ECMO* Extracorporeal membrane oxygenation, *IABP* Intra-aortic balloon pump, *Stent1* Single stent placement during PCI, *Stent2* Two stents placed during PCI; Stentmoere, more than two stents placed during PCI; Vessel1, single vessel treated during PCI; Vessel2, two vessels treated during PCI; Vesselmoere, more than two vessels treated during PCI. Mortality refers to in-hospital mortality within 30 days of admission

demographic factors and clinical histories (Fig. 4). The positive association between SHR and CIN remained significant in most subgroups, confirming SHR's role as a reliable predictor across different clinical groups. Interaction tests using likelihood ratio tests revealed that a history of diabetes and stent implantation significantly modified the SHR-CIN relationship (interaction $P < 0.05$). Specifically, while SHR was strongly associated with CIN in non-diabetic patients, no significant relationship was observed in diabetic patients. This suggests that chronic metabolic conditions in diabetes, such as insulin resistance and renal microvascular damage, may attenuate the kidneys' response to acute hyperglycemia, reducing the predictive value of SHR in this population. Moreover, stent implantation enhanced the association between SHR and CIN. The increased procedural complexity and potential vascular injury associated with PCI may exacerbate renal injury in the presence of elevated SHR. These findings suggest that patients undergoing complex PCI procedures, particularly those with stent placement, may

Table 2 Baseline characteristics of study participants stratified by SHR

Variables	Total (*n* = 552)	Q1 (*n* = 184)	Q2 (*n* = 184)	Q3 (*n* = 184)	*P*
SHR	1.06(0.92,1.30)	0.86(0.78,0.92)	1.06(1.01,1.12)	1.47(1.31,1.68)	< 0.0001
Sex,%					0.17
Female	178(32.25)	68(36.96)	51(27.72)	59(32.07)	
Male	374(67.75)	116(63.04)	133(72.28)	125(67.93)	
Age,years	67.75(59.10,77.02)	67.55(58.66,77.04)	66.64(58.35,75.97)	68.80(61.58,77.39)	0.14
SOFA	2.00(1.00,5.00)	2.00(1.00,3.25)	2.00(1.00,3.00)	4.00(2.00,7.00)	< 0.0001
APS3	33.00(26.00,44.00)	32.00(24.00,39.00)	30.00(24.00,37.25)	39.00(31.00,54.00)	< 0.0001
SAPSII	30.00(23.00,37.00)	28.00(21.75,35.00)	28.00(21.75,33.00)	35.00(27.00,48.25)	< 0.0001
OASIS	28.00(22.00,33.00)	25.00(21.00,31.00)	26.00(22.00,32.00)	31.00(26.00,37.00)	< 0.0001
CCI	5.00(3.00,7.00)	5.00(3.00,7.00)	4.00(3.00,6.00)	6.00(4.00,7.25)	< 0.0001
CHF,%					< 0.0001
no	296(53.62)	120(65.22)	113(61.41)	63(34.24)	
yes	256(46.38)	64(34.78)	71(38.59)	121(65.76)	
STEMI,%					0.46
no	150(27.17)	56(30.43)	48(26.09)	46(25.00)	
yes	402(72.83)	128(69.57)	136(73.91)	138(75.00)	
DM,%					< 0.01
no	383(69.38)	115(62.50)	144(78.26)	124(67.39)	
yes	169(30.62)	69(37.50)	40(21.74)	60(32.61)	
AF,%					< 0.0001
no	416(75.36)	150(81.52)	152(82.61)	114(61.96)	
yes	136(24.64)	34(18.48)	32(17.39)	70(38.04)	
CVD,%					0.02
no	501(90.76)	168(91.30)	174(94.57)	159(86.41)	
yes	51(9.24)	16(8.70)	10(5.43)	25(13.59)	
CPD,%					0.02
no	441(79.89)	144(78.26)	159(86.41)	138(75.00)	
yes	111(20.11)	40(21.74)	25(13.59)	46(25.00)	
PVD,%					0.01
no	483(87.50)	166(90.22)	167(90.76)	150(81.52)	
yes	69(12.50)	18(9.78)	17(9.24)	34(18.48)	
HTN,%					0.43
no	164(29.71)	53(28.80)	61(33.15)	50(27.17)	
yes	388(70.29)	131(71.20)	123(66.85)	134(72.83)	
RBC,m/uL	4.09 ± 0.67	4.01 ± 0.63	4.20 ± 0.69	4.06 ± 0.68	0.02
Hb,g/dL	12.33 ± 1.97	12.04 ± 1.84	12.66 ± 1.94	12.28 ± 2.10	0.01
PLT,K/uL	218.00(174.00,260.00)	217.00(170.50,262.25)	218.00(175.00,256.50)	219.50(174.75,263.00)	0.98
WBC,K/uL	11.50(8.80,14.43)	9.90(8.28,11.83)	11.30(8.60,13.23)	13.90(10.70,16.23)	< 0.0001
BUN,mg/dL	18.00(14.00,26.00)	17.00(13.00,24.00)	16.00(13.00,21.00)	23.00(17.00,33.00)	< 0.0001
Na,mmol/L	138.00(137.00,140.00)	139.00(137.00,140.00)	138.00(136.00,140.00)	138.00(136.00,140.55)	0.56
K,mmol/L	4.20(4.00,4.50)	4.20(4.00,4.40)	4.20(3.98,4.40)	4.30(4.00,4.70)	< 0.001
INR	1.20(1.10,1.38)	1.20(1.10,1.30)	1.20(1.10,1.30)	1.30(1.10,1.43)	< 0.0001
Baseline Cr, mg/dL	0.90(0.70,1.10)	0.90(0.70,1.10)	0.90(0.70,1.10)	1.00(0.80,1.40)	< 0.0001
TnT,ng/mL	2.43(0.93,5.99)	1.95(0.74,4.19)	2.28(0.98,6.64)	3.21(1.31,8.24)	< 0.001
CK_MB,ng/mL	90.00(27.00,203.05)	61.90(23.75,145.00)	97.20(36.75,221.15)	110.00(29.75,258.25)	< 0.001
LOS hospital,days	5.05(3.08,8.99)	4.69(3.03,7.87)	4.13(2.89,6.95)	6.78(3.91,12.29)	< 0.0001
LOS ICU,days	2.17(1.46,4.04)	2.07(1.31,3.45)	1.92(1.40,3.12)	3.08(2.00,5.40)	< 0.0001
Hospital mortality,%					< 0.0001
no	501(90.76)	178(96.74)	179(97.28)	144(78.26)	

Table 2 (continued)

Variables	Total (*n* = 552)	Q1 (*n* = 184)	Q2 (*n* = 184)	Q3 (*n* = 184)	*P*
yes	51(9.24)	6(3.26)	5(2.72)	40(21.74)	
Vasoactive,%					< 0.0001
no	387(70.11)	138(75.00)	150(81.52)	99(53.80)	
yes	165(29.89)	46(25.00)	34(18.48)	85(46.20)	
ECMO,%					0.01
no	545(98.73)	183(99.46)	184(100.00)	178(96.74)	
yes	7(1.27)	1(0.54)		6(3.26)	
IABP,%					0.01
no	450(81.52)	153(83.15)	159(86.41)	138(75.00)	
yes	102(18.48)	31(16.85)	25(13.59)	46(25.00)	
CRRT,%					< 0.001
no	539(97.64)	183(99.46)	183(99.46)	173(94.02)	
yes	13(2.36)	1(0.54)	1(0.54)	11(5.98)	
Stent1,%					0.26
no	335(60.69)	110(59.78)	105(57.07)	120(65.22)	
yes	217(39.31)	74(40.22)	79(42.93)	64(34.78)	
Stent2,%					0.76
no	459(83.15)	150(81.52)	155(84.24)	154(83.70)	
yes	93(16.85)	34(18.48)	29(15.76)	30(16.30)	
Stentmoere,%					0.48
no	498(90.22)	168(91.30)	168(91.30)	162(88.04)	
yes	54(9.78)	16(8.70)	16(8.70)	22(11.96)	
Vessel1,%					< 0.01
no	218(39.49)	76(41.30)	57(30.98)	85(46.20)	
yes	334(60.51)	108(58.70)	127(69.02)	99(53.80)	
Vessel2,%					0.07
no	497(90.04)	164(89.13)	173(94.02)	160(86.96)	
yes	55(9.96)	20(10.87)	11(5.98)	24(13.04)	
Vesselmoere,%					0.08
no	537(97.28)	181(98.37)	181(98.37)	175(95.11)	
yes	15(2.72)	3(1.63)	3(1.63)	9(4.89)	

Table 3 Association Between SHR and CIN in Logistic Regression Models

Variables	Crude model		Model 1		Model 2	
	95%CI	*P*	95%CI	*P*	95%CI	*P*
CIN ~ SHR	2.25(1.51,3.36)	< 0.0001	2.39(1.59,3.59)	< 0.0001	2.36(1.56,3.57)	< 0.0001
CIN ~ SHRQ						
Q1	ref		ref		ref	
Q2	0.88(0.56,1.37)	0.57	0.91(0.58,1.43)	0.69	0.92(0.58,1.45)	0.72
Q3	2.36(1.55,3.61)	< 0.0001	2.44(1.59,3.73)	< 0.0001	2.52(1.63,3.89)	< 0.0001
P for trend(character2integer)		< 0.0001		< 0.0001		< 0.0001
P for trend (Median value)		< 0.0001		< 0.0001		< 0.0001

The crude model included SHR alone. Model 1 was adjusted for STEMI, DM, and HTN. Model 2 was further adjusted for STEMI, DM, HTN, stent placement, and vessel involvement

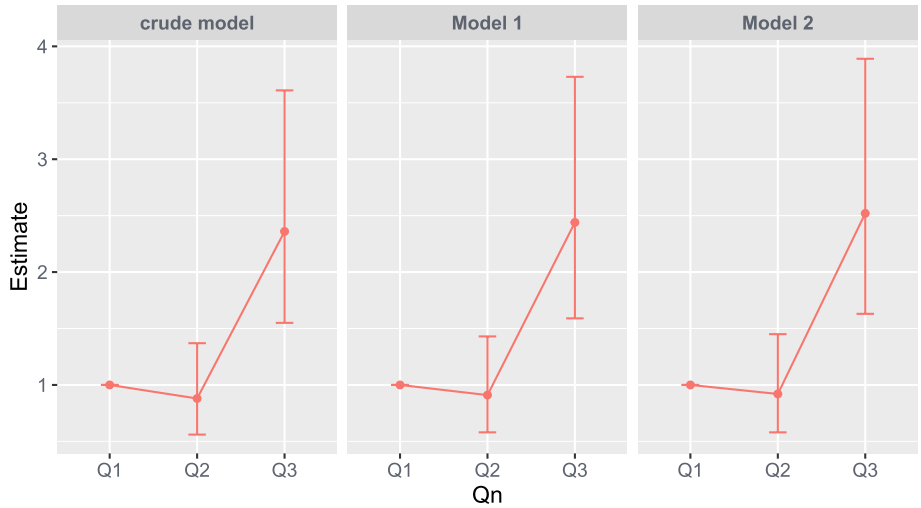

Fig. 2 Association Between SHR and CIN in Logistic Regression Models; The crude model included SHR alone. Model 1 was adjusted for STEMI, DM, and HTN. Model 2 was further adjusted for STEMI, DM, HTN, stent placement, and vessel involvement

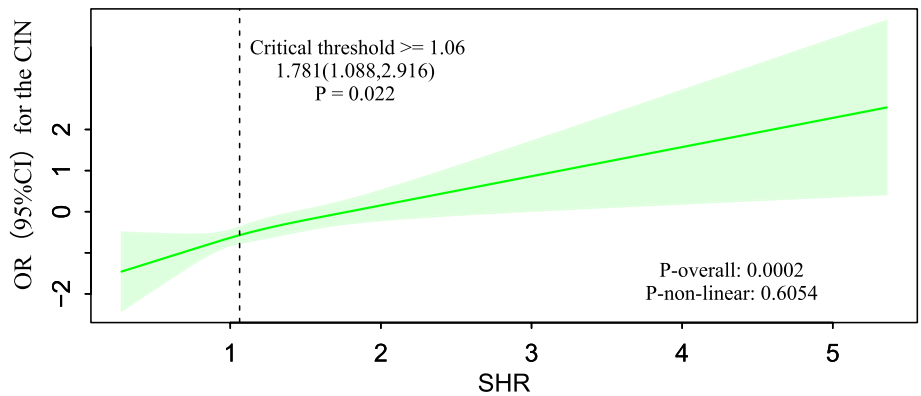

Fig. 3 RCS Analysis of SHR and CIN Association

be at higher risk for CIN when SHR levels are elevated. These results were further illustrated by forest plots, which confirmed that the SHR-CIN association was stronger in non-diabetic patients and those with stent implants. This underscores the need to consider diabetes and procedural complexity when evaluating SHR as a prognostic tool in clinical practice.

SHR and Mortality

Survival analysis revealed a significant association between SHR levels and 30-day in-hospital mortality ($P < 0.0001$; Fig. 5). Kaplan–Meier curves demonstrated a clear stratification of survival probabilities across SHR quartiles, with higher SHR values associated with increased mortality risk. Patients in the lowest SHR quartile (Q1) exhibited the highest survival probability, while those in the highest quartile (Q3) experienced a marked reduction in survival over time. The observed gradient in survival curves highlights the prognostic value of SHR as an independent predictor of short-term mortality.

Discussion

Diabetes and preoperative blood glucose levels are now recognized as independent risk factors for CIN [14, 15]. However, existing studies suggest that fluctuations in blood glucose levels are associated with higher cardiovascular event risks than sustained hyperglycemia [16, 17]. Among patients with acute coronary syndrome (ACS), the body is often in a state of intense stress, triggered by factors such as surgery, interventional therapy, and medication use. Stress responses are typically accompanied by the release of hyperglycemic hormones, including cortisol, adrenaline, and glucagon. While these hormonal responses are intended to manage short-term stress, prolonged stress states may lead to maladaptive physiological responses, particularly in ACS-PCI patients, where

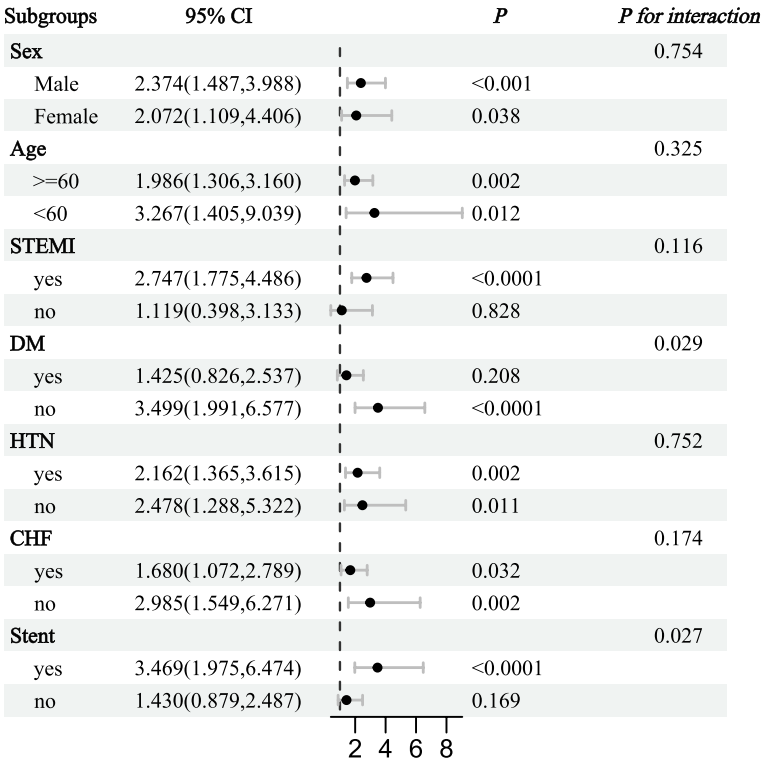

Fig. 4 Forest Plot of Subgroup Analyses for the Association Between SHR and CIN; Subgroups include sex (male, female), age (≥ 60, < 60 years), STEMI (presence or absence of ST-segment elevation myocardial infarction), DM (diabetes mellitus), HTN (hypertension), CHF (congestive heart failure), and stent placement status (yes or no). Interaction P-values indicate whether the association between SHR and CIN differs significantly among subgroups

acute hyperglycemia can exacerbate disease severity [18]. SHR reflects the extent of rapid blood glucose elevation under acute stress conditions and provides more sensitive and specific predictive information than traditional glucose levels. Therefore, SHR is a critical metric for ACS-PCI patients. Previous studies have shown that SHR correlates with disease severity and in-hospital mortality in critically ill patients [5, 19]. Additionally, it has been identified as a predictor of adverse outcomes in trauma, acute coronary syndromes, and acute ischemic stroke [9, 20–22]. Recent studies have also emphasized SHR's prognostic value in a broader clinical context. For example, a meta-analysis revealed that higher SHR values significantly increase the risks of major adverse cardiovascular and cerebrovascular events (MACCE), as well as both short-term and long-term mortality in acute myocardial infarction patients [23]. Additionally, findings from a Chinese multicenter study showed that elevated SHR is associated with adverse long-term outcomes in coronary artery disease patients, particularly those with chronic kidney disease (CKD) [24]. These studies highlight the important role of SHR in risk stratification for cardiovascular outcomes in high-risk patient populations. Moreover, recent data from the MIMIC-IV database found that elevated SHR is strongly associated with increased in-hospital and 1-year mortality in sepsis patients, further reinforcing the broad applicability of SHR as a prognostic tool [25]. Similarly, a machine learning-based study demonstrated that SHR is an independent predictor of 28-day all-cause mortality in ICU patients with CHF, outperforming traditional metrics such as blood glucose and HbA1c [26]. This illustrates the robust utility of SHR across various critical conditions.

In this study, SHR levels were significantly higher in the CIN group compared to the non-CIN group. Moreover, we observed a J-shaped linear relationship between SHR and CIN, with a sharp increase in CIN risk when SHR exceeded a threshold of 1.06. The mechanisms underlying the relationship between SHR elevation and CIN are likely multifactorial. Previous research has demonstrated that blood glucose fluctuations impair endothelial function and exacerbate inflammation, further damaging renal microvasculature and increasing CIN risk [27, 28]. Additionally, stress responses associated with ACS-PCI, particularly oxidative stress and mitochondrial dysfunction, may further predispose the kidneys to injury

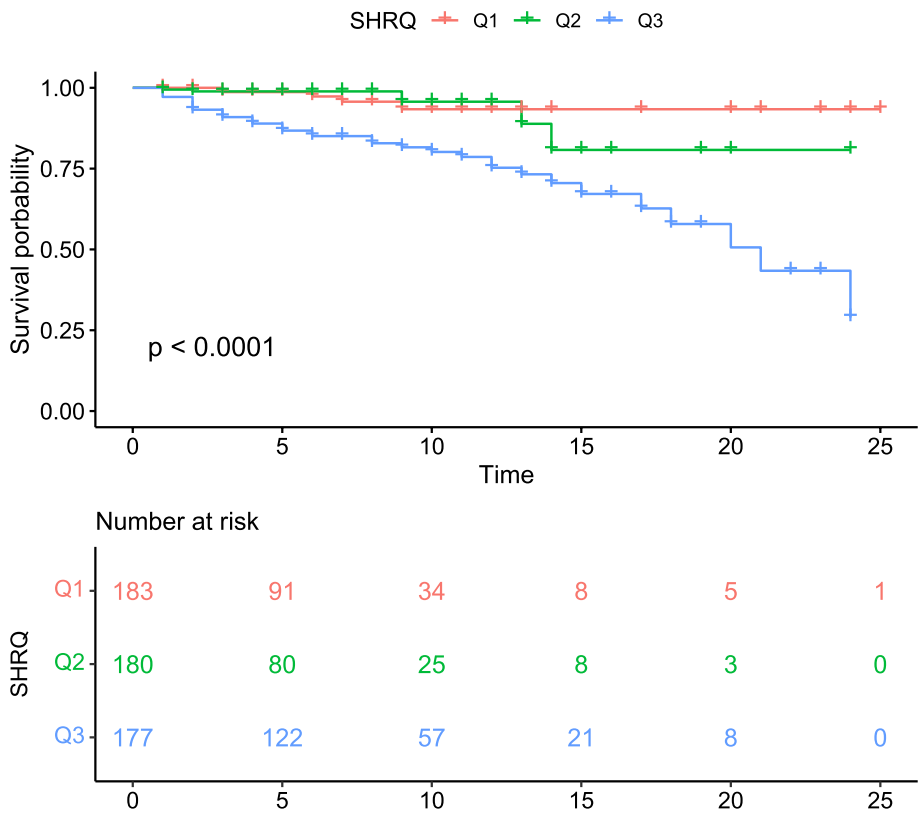

Fig. 5 Kaplan–Meier Curves for 30-Day Mortality by SHR Quartiles; Higher SHR quartiles show significantly lower survival probabilities ($P < 0.0001$); SHR, stress hyperglycemia ratio

[29–31]. Stress-induced hyperglycemia may also disrupt the balance between nitric oxide (NO) bioavailability and reactive oxygen species (ROS) accumulation in endothelial cells, leading to endothelial dysfunction and increased CIN susceptibility [32, 33]. Furthermore, hyperglycemia may stimulate advanced glycation end-products (AGEs), causing microvascular damage and subsequent glomerulosclerosis, further escalating CIN risk [34, 35].

Although the relationship between SHR and CIN was significant in the overall patient population, we found notable differences among subgroups. Notably, the association between SHR and CIN was more pronounced in non-diabetic patients. The predictive effect of stress hyperglycemia on outcomes in diabetic versus non-diabetic patients remains controversial. Some studies suggest that stress hyperglycemia predicts worse outcomes in non-diabetic patients with intracerebral hemorrhage [36–38]. The rationale for focusing on non-diabetic versus diabetic patients lies in the distinct metabolic adaptations associated with chronic hyperglycemia in diabetic patients. Prolonged exposure to high glucose levels in diabetes induces renal adaptations, including glomerular hypertrophy and increased mesangial matrix expansion, which may blunt the kidneys' sensitivity to acute glucose fluctuations [39]. Additionally, chronic hyperglycemia leads to insulin resistance and microvascular complications, further attenuating the impact of stress-induced hyperglycemia on renal function [40]. As a result, acute hyperglycemia may exert a relatively weaker effect on renal injury in diabetic patients, while in non-diabetic patients, the absence of these chronic adaptations likely amplifies the renal impact of acute glucose surges. This disparity underscores the importance of baseline metabolic states in modifying the SHR-CIN relationship and highlights the need for subgroup-specific risk assessments. Furthermore, our study also revealed that patients with stent implantation had a higher CIN risk than those without stents. These findings highlight the need for heightened vigilance regarding acute glucose fluctuations, particularly elevated SHR, in non-diabetic patients during CIN risk assessment, which may inform subsequent therapeutic decisions. This complexity emphasizes the potential role of SHR in guiding therapeutic interventions, especially in non-diabetic patients. For instance, SGLT-2 inhibitors, such as dapagliflozin and empagliflozin, have shown potential not only in reducing fasting glucose levels but

also in improving lipid profiles, such as lowering LDL cholesterol and triglycerides while increasing HDL cholesterol [41]. Further research is needed to explore how integrating SHR with the use of SGLT-2 inhibitors in predictive models may refine patient management strategies and optimize therapeutic decision-making.

Beyond CIN prediction, our study explored the short-term prognostic value of SHR in ACS-PCI patients. Our results showed that elevated SHR was associated with significantly higher short-term mortality. This finding underscores the dual importance of SHR as a biomarker for predicting both CIN and broader outcomes in ACS-PCI patients. Acute hyperglycemia impacts patient prognosis through mechanisms such as oxidative stress, endothelial dysfunction, and systemic inflammatory responses [42]. These pathological changes not only heighten CIN risk but may also contribute to multi-organ failure, increasing short-term mortality. Specifically, patients with elevated SHR often exhibit more severe pathological states [43, 44]. In our study, patients with elevated SHR presented with more comorbidities, including CHF, DM, AF, CVD, CPD, and PVD, alongside significantly higher disease scores (e.g., SOFA, SAPS II, OASIS). These factors collectively exacerbate disease severity and complicate treatment, resulting in worse outcomes. Additionally, patients with elevated SHR required more intensive interventions, such as ECMO, IABP, and CRRT, reflecting the severity of their critical illness and multi-organ dysfunction. The need for such advanced interventions further complicates recovery, emphasizing the prognostic significance of SHR.

Limitations

Our research has several limitations. First, we did not account for potential ICU complications, such as infections or exposure to nephrotoxic drugs, which may have influenced the SHR-CIN relationship. Additionally, data on fluid intake and hemodynamic status, both critical for assessing CIN risk, were not systematically collected. Hypovolemia, in particular, can exacerbate renal hypoperfusion, increasing CIN risk. The single-center design limits the generalizability of our findings, and multicenter studies are needed to validate these results. Moreover, our analysis focused on short-term outcomes, while long-term effects, such as chronic kidney disease or overall survival, were not assessed. Another limitation is the significant missing data for BMI (> 20%), which led to its exclusion from the analysis. As BMI may influence SHR's predictive value, its omission could have impacted our findings. Finally, the severity and progression of comorbidities were not fully considered, which may have confounded the results. Future studies should address these factors to provide a more comprehensive understanding of SHR's prognostic role.

Future directions

SHR holds promise as a routine clinical monitoring tool, aiding in the early identification of high-risk PCI patients and guiding personalized treatment, especially in non-diabetic individuals. Future research should further explore SHR's clinical application. Moreover, as BMI may influence stress-induced hyperglycemia and the predictive accuracy of SHR, it is important to investigate its impact across different body types. Furthermore, right ventricular infarction, through increased right heart load and hypovolemia, may elevate CIN risk. Research should also evaluate the predictive value of SHR in this specific subgroup of patients.

Conclusion

In conclusion, the SHR emerges as a significant and independent predictor of CIN and short-term mortality in ACS patients undergoing PCI. These findings underscore the importance of acute glycemic stress as a key factor influencing renal and overall patient outcomes in the context of PCI. SHR holds promise as a valuable biomarker for risk stratification and guiding preventive interventions, thereby contributing to enhanced clinical management and improved patient prognosis. Continued research is essential to validate these findings and explore targeted strategies to mitigate the adverse effects of stress-induced hyperglycemia in this vulnerable patient population.

Abbreviations

ACS	Acute Coronary Syndrome
AF	Atrial Fibrillation
AMI	Acute Myocardial Infarction
ANOVA	Analysis of Variance
APS3	Acute Physiology Score III
BMI	Body Mass Index
BUN	Blood Urea Nitrogen (mg/dL)
CCI	Charlson Comorbidity Index
CHF	Congestive Heart Failure
CKD	Chronic Kidney Disease
CK-MB	Creatine Kinase-MB (ng/mL)
CIN	Contrast-Induced Nephropathy
CPD	Chronic Pulmonary Disease
CRRT	Continuous Renal Replacement Therapy
CVD	Cerebrovascular Disease
DM	Diabetes Mellitus
ECMO	Extracorporeal Membrane Oxygenation
eGFR	Estimated Glomerular Filtration Rate
GCS	Glasgow Coma Scale
Hb	Hemoglobin (g/dL)
HbA1c	Hemoglobin A1c
HTN	Hypertension
IABP	Intra-Aortic Balloon Pump
ICU	Intensive Care Unit
INR	International Normalized Ratio
IQR	Interquartile Range

K	Potassium (mmol/L)
LOS	Length of Stay
MACCE	Major Adverse Cardiovascular and Cerebrovascular Events
Na	Sodium (mmol/L)
OASIS	Oxford Acute Severity of Illness Score
OR	Odds Ratio
PCI	Percutaneous Coronary Intervention
PLT	Platelets (K/uL)
PVD	Peripheral Vascular Disease
RCT	Randomized Controlled Trial
RBC	Red Blood Cells (m/uL)
RCS	Restricted Cubic Spline
SAPSII	Simplified Acute Physiology Score II
SHR	Stress Hyperglycemia Ratio
SOFA	Sequential Organ Failure Assessment
STEMI	ST-Elevated Myocardial Infarction
TnT	Cardiac Troponin T (ng/mL)
WBC	White Blood Cells (K/uL)
Stent1	Single stent placement during PCI
Stent2	Two stents placed during PCI
Stentmoere	More than two stents placed during PCI
Vessel1	Single vessel treated during PCI
Vessel2	Two vessels treated during PCI
Vesselmoere	More than two vessels treated during PCI

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Authors' contributions
Yanlong Zhao contributed to the data collection, analysis, and drafting of the manuscript. Yuanyuan Zhao and Shuai Wang participated in manuscript writing and provided additional edits. Zhenxing Fan, Yanling Wang, and Fangyan Liu guided the overall structure of the article and assisted in figure preparation. Zhi Liu supervised the study, critically reviewed and revised the manuscript, and provided essential guidance in writing. All authors have read and approved the final manuscript. Each author agrees to be personally accountable for their own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even if not directly contributed by them, are appropriately investigated and resolved.

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Data Availability
The datasets used in this study are publicly available from the MIMIC-IV database [https://doi.org/10.13026/hxp0-hg59]. Access to the database requires registration and successful completion of the CITI program.

Declarations

Ethics approval and consent to participate
This study was conducted using the publicly available, de-identified Medical Information Mart for Intensive Care IV (MIMIC-IV) database, which does not require individual patient consent. Ethical approval for the use of the MIMIC-IV database was obtained by completing the Collaborative Institutional Training Initiative (CITI) Program's "Data or Specimens Only Research" course (Certification No. 63998837).

Consent for publication
This study does not include any data from individual persons.

Competing interests
The authors declare no competing interests.

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