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Blood glucose control and prognosis of patients in the cardiac intensive care unit: A cohort study exploring the association between hyperglycemia and patient mortality

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Abstract: Objective Disordered glycemic regulation is common in critically ill cardiac patients, yet its prognostic relevance remains insufficiently characterized. This study investigated the association between the hemoglobin glycation index (HGI) and mortality in patients admitted to the cardiac intensive care unit (CICU) and evaluated the prognostic utility of HGI.Methods A retrospective cohort study was conducted including 1,577 adult CICU patients. Data were obtained from the MIMIC-IV database (2008－2019) and Dongguan East Central Hospital affiliated with Jinan University. Patients were stratified into quartiles according to HGI. Restricted cubic spline models were applied to assess the dose－response relationship between HGI and 30-day mortality, and subgroup analyses were performed across major comorbid conditions.Results Higher HGI levels were associated with unfavorable physiological profiles, including increased heart rate, diastolic blood pressure, respiratory rate, and body temperature, alongside reduced oxygen saturation (all $P < 0.05$). HGI showed positive correlations with hemoglobin, white blood cell count, fasting plasma glucose, and HbA1c, and an inverse correlation with hematocrit. A significant U-shaped nonlinear association between HGI and 30-day mortality was identified (P for nonlinearity < 0.001), with elevated risk at both low and high extremes. This association was more pronounced in patients with chronic heart failure and diabetes. Multivariable analyses confirmed HGI as an independent predictor of short-term mortality and major adverse cardiovascular events.Conclusion HGI is independently associated with short-term prognosis in CICU patients. The observed U-shaped mortality pattern underscores the importance of balanced glycemic control and supports the use of HGI for risk stratification in critical cardiac care.**Keywords:** Blood glucose control; cardiac intensive care unit; hyperglycemia; hemoglobin glycation index; mortality; prognosis; cohort study.

0 Introduction

Within modern critical care, the Cardiac Intensive Care Unit (CICU) represents a dedicated setting for patients facing acute, life-threatening cardiovascular events.In routine practice, CICU admissions are largely driven by acute heart failure, recent coronary interventions, and clinically significant arrhythmias.Because these conditions often evolve rapidly and unpredictably, management in the CICU is inherently complex, and reported mortality commonly falls between

20% and 40%.The consequences of such mortality extend beyond clinical outcomes, placing sustained emotional strain on families while simultaneously intensifying demands on healthcare systems and social resources.Although cardiovascular care has advanced markedly-with broader use of interventional techniques and pharmacologic therapies-persistent problems such as inadequate glycemic control, secondary infection, and multi-organ dysfunction continue to constrain outcome improvement.Against this background, attention has increasingly shifted toward identifying prognostic factors in CICU patients, particularly those related to modifiable aspects of glycemic management.

The hemoglobin glycation index (HGI) has emerged as a marker of interest for capturing individual variability in glucose metabolism.Conceptually, HGI reflects the discrepancy between measured HbA1c values and HbA1c levels estimated from fasting plasma glucose, thereby characterizing differences in glycation responsiveness among individuals.Unlike traditional glycemic indices, HGI is more responsive to fluctuations in glucose exposure rather than static glucose levels alone.Such variability is closely linked to oxidative stress and inflammatory activation, mechanisms that contribute to vascular injury and organ dysfunction in critically ill populations.Despite this biological plausibility, evidence connecting HGI with cardiovascular prognosis remains limited, particularly within CICU-specific cohorts.

As a result, incorporating HGI into CICU risk assessment frameworks may offer a complementary biomarker to support precision-oriented glycemic management and individualized treatment planning.To date, most investigations examining HGI have relied on cross-sectional analyses or small retrospective series.These designs, often constrained by limited sample size and incomplete data, restrict the ability to define the independent prognostic contribution of HGI in critically ill cardiac patients.The availability of large, publicly accessible clinical databases-most notably MIMIC-IV-has begun to change this landscape.By enabling the linkage of demographic information, laboratory indices, and outcome data, such resources allow more comprehensive evaluation of associations between HGI and both short- and longer-term mortality.This approach strengthens the foundation for clinically meaningful risk stratification and informed therapeutic decision-making.Nevertheless, systematic comparisons of clinical profiles and outcomes across different HGI strata remain scarce in the existing literature.Using data from the MIMIC-IV database, the present study was designed as a retrospective cohort analysis including nearly 1,600 CICU patients.Patients were categorized according to HGI levels, permitting structured comparisons of baseline characteristics and mortality across groups.

Through assessment of the dose－response relationship between HGI and 30-day mortality, combined with multivariable Cox regression modeling, this study aimed to clarify whether HGI carries independent prognostic value.The reliance on large-scale, real-world data represents a key methodological advantage, reducing the impact of limited statistical power seen in earlier studies.In addition to prognostic evaluation, adjustments for comorbidities, physiological variables, and laboratory findings were incorporated to explore potential nonlinear associations between HGI and mortality risk.The intent was to develop a more precise risk assessment framework applicable to glycemic management in the CICU setting.Such refinement may ultimately support individualized therapeutic strategies and contribute to improved survival and patient-centered outcomes.Taken together, this work seeks to facilitate the clinical translation of glycemic metabolism indicators in critically ill cardiac populations while addressing an important gap at the intersection of cardiology and metabolic research.

1 Study Subjects and Methods

1.1 Study Subjects

This investigation was conducted using a retrospective cohort design to evaluate the association between HGI and clinical outcomes in critically ill cardiac patients.Clinical data were obtained from two independent sources: the Medical Information Mart for Intensive Care IV (MIMIC-IV) database at Beth Israel Deaconess Medical Center in Boston, United States, covering admissions from January 2008 to December 2019, and the cardiac intensive care unit of Dongguan East Central Hospital affiliated with Jinan University.Eligible participants were adults aged 18 years or older who had a CICU stay of at least 24 hours, with complete data available for HGI calculation, baseline clinical characteristics, and outcome assessment. Patients with a prior history of severe hepatic or renal insufficiency, hematologic disorders, malignancies, or end-stage disease were excluded to minimize confounding effects.Patients were excluded if more than 10% of clinical, laboratory, or follow-up data were missing, if death occurred within the first 24 hours after CICU admission, or if pregnancy, lactation, or contraindications to HGI assessment were present. After applying these criteria, a total of 1,577 patients were included in the final analysis.All datasets were fully de-identified and analyzed in accordance with relevant ethical guidelines; therefore, the requirement for informed consent was waived.

1.2 Study Groups

HGI measurement results (obtained within 24 hours of admission for all patients) were collected. Measurement method: High-performance liquid chromatography (HPLC), using reagents from Roche Diagnostics, strictly following the manufacturer's instructions.

Patients were divided into four groups based on HGI quartiles:

Q1 group (n=394): HGI ≤ 0.32%

Q2 group (n=393): 0.32% < HGI ≤ 0.65%

Q3 group (n=395): 0.65% < HGI ≤ 0.98%

Q4 group (n=395): HGI > 0.98%

1.3 Observational Metrics

1.3.1 Baseline Characteristics

The following information was collected:

① Demographics: Age, sex, body mass index (BMI), route of admission, primary reason for CICU admission.

② Vital Signs (average within 24 hours of admission): Heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate, body temperature, oxygen saturation (SpO_2).

③ Comorbidities: Hypertension, diabetes mellitus, chronic heart failure, coronary artery disease, infective endocarditis, etc.

④ Laboratory Indicators: HGI, hemoglobin, white blood cell count, hematocrit (HCT), fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), liver and kidney function, electrolytes,

etc.

⑤ Disease Severity Scores: Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation II (APS II) score.

1.3.2 Outcome Measures

Primary Outcome: 30-day all-cause mortality in CICU patients (calculated from the date of CICU admission, with follow-up for 30 days, recording deaths occurring both within the CICU and within 30 days after discharge).

Secondary Outcomes: ① Total hospital length of stay; ② CICU length of stay; ③ Incidence of major adverse cardiovascular events (MACE), including myocardial infarction, arrhythmia, cardiogenic shock, worsening heart failure, etc.; ④ Incidence of infections, including pneumonia, urinary tract infection, bacteremia, etc.

1.4 Follow-up Methods

Follow-up was conducted using a combination of telephone interviews and medical record review. The starting point was the day of CICU admission, and the endpoint was 30 days post-admission, death, or loss to follow-up. For in-hospital deaths, the date of death served as the endpoint. For discharged patients, telephone follow-up was used to confirm survival status and occurrence of MACE events within 30 days. No cases were lost to follow-up in this study.

1.5 Statistical Methods

Data analysis was performed using SPSS 26.0 and R 4.2.0 software. Normally distributed continuous variables are presented as mean ± standard deviation ($\bar{x} \pm s$) and compared between groups using one-way ANOVA. Non-normally distributed continuous variables are presented as median (interquartile range)[M (Q1, Q3)] and compared using the Kruskal-Wallis H test. Categorical variables are presented as number (percentage)[n (%)] and compared using the χ^2 test.

Nonlinear associations between HGI and 30-day mortality were assessed using restricted cubic spline models with three knots. Multivariate Cox proportional hazards regression was used to estimate the independent effect of HGI on mortality after adjustment for age, sex, BMI, comorbidities, SOFA score, and fasting plasma glucose. Prespecified subgroup analyses were conducted according to chronic heart failure, diabetes mellitus, and coronary artery disease. A two-sided P value < 0.05 was used as the threshold for statistical significance.

3 Results

3.1 Comparison of Baseline Characteristics of Patients

This study enrolled 1,577 patients admitted to the CICU, including 917 men (57.5%) and 660 women (42.5%). The cohort had a mean age of 65.3 ± 12.7 years and an average body mass index of 24.8 ± 4.1 kg/m². Acute heart failure constituted the most common indication for CICU admission, followed by post－coronary artery surgery or intervention, severe arrhythmias, and other clinical conditions.Patients were stratified into quartiles according to HGI values (Q1－Q4), with each group comprising approximately equal sample sizes. Comparative analyses revealed significant differences in baseline clinical characteristics across the four HGI strata (P < 0.05), indicating substantial heterogeneity among groups.With progressively increasing HGI levels from

Q1 to Q4, patients demonstrated stepwise elevations in heart rate, diastolic blood pressure, respiratory rate, and body temperature, whereas peripheral oxygen saturation showed a significant downward trend (all $P < 0.05$), suggesting worsening physiological status with higher HGI.Analysis of laboratory indices showed that HGI was positively associated with hemoglobin concentration, white blood cell count, fasting plasma glucose, and HbA1c levels, while exhibiting an inverse relationship with hematocrit. Notably, abnormalities in these parameters were most pronounced in the highest HGI quartile, with the Q4 group displaying significantly greater deviations compared with the Q1 group ($P < 0.05$).

In terms of disease severity, both the SOFA score and the APS II score were significantly higher in the Q4 group than in the other three groups ($P < 0.05$). Regarding comorbidities, the prevalence of chronic heart failure and infective endocarditis was higher in the Q4 group ($P < 0.05$), whereas no statistically significant differences were found in the prevalence of hypertension and coronary artery disease among the four groups ($P > 0.05$). No statistically significant differences were observed in general characteristics such as age, sex, and BMI among the groups ($P > 0.05$), indicating comparability. Detailed baseline data are presented in Table 1.

Variables	Q1 (<=0.7047) n=394	Q2 (0.7042-0.9082) n=393	Q3 (0.9074-0.3188) n=395	Q4 (>0.3241) n=395	P-value
Participants, No.	394	393	395	395	-
Clinical parameters					
Age, (yr)	64.54 ± 15.34	66.20 ± 14.51	67.77 ± 13.71	64.20 ± 13.43	0.001
Gender, n (%)					0.186
Female	134 (34.0)	125 (31.81)	152 (38.48)	147 (37.31)	
Male	260 (65.99)	268 (68.19)	243 (61.52)	247 (62.69)	
Race, n (%)					<0.001
White	257 (65.23)	272 (69.21)	261 (66.08)	231 (58.63)	
Black	23 (5.84)	17 (4.33)	37 (9.37)	50 (12.69)	
Other	114 (28.93)	104 (26.46)	97 (24.56)	113 (28.68)	
Vital signs					
Heart rate(bpm)	83.84 ± 17.34	83.43 ± 17.06	80.88 ± 16.83	82.67 ± 14.95	0.039
DBP(mmHg)	64.52 ± 12.11	66.22 ± 11.75	64.10 ± 11.55	64.75 ± 11.43	0.065
SBP(mmHg)	141.43 ± 17.11	116.62 ± 15.86	117.13 ± 17.02	116.97 ± 16.06	0.008
RR(bpm)	79.61 ± 12.42	80.78 ± 10.86	79.89 ± 11.16	79.67 ± 10.63	0.14
Resp rate(rpm)	19.61 ± 6.66	19.36 ± 3.37	19.39 ± 3.68	19.79 ± 3.39	0.082
Temperature(°C)	39.74 ± 0.61	36.80 ± 0.48	36.80 ± 0.63	36.79 ± 0.48	0.029
SpO2(%)	96.72 ± 1.98	96.43 ± 1.75	96.47 ± 1.69	96.44 ± 1.80	0.066
Laboratory parameters					
HCT	32.65 ± 7.18	34.47 ± 6.55	33.72 ± 6.17	33.84 ± 6.41	0.001
Hemoglobin(g/dL)	11.05 ± 3.59	11.50 ± 2.33	11.19 ± 2.16	11.13 ± 2.21	<0.001
WBC(1000cells/uL)	10.83 ± 5.79	11.0 ± 4.61	9.73 ± 4.84	9.57 ± 3.59	<0.001
Platelet(1000cells)	206.67 ± 82.87	204.61 ± 82.28	200.71 ± 80.19	210.83 ± 82.40	0.257
Anion gap(mmol/L)	14.6 ± 2.65	13.20 ± 2.91	14.6 ± 2.70	13.85 ± 3.18	<0.001
FPG(mg/dL)	191.06 ± 108.44	157.45 ± 53.71	159.95 ± 62.60	163.89 ± 94.05	<0.001
HbA1c(%)	5.51 ± 0.63	5.76 ± 0.47	6.23 ± 0.58	8.47 ± 1.86	<0.001
Severity scale					
SOFA	5.03 ± 3.64	3.48 ± 3.00	3.41 ± 2.71	3.49 ± 2.81	<0.001
APACHE II	45.99 ± 20.42	37.13 ± 16.69	39.08 ± 16.38	41.41 ± 15.47	<0.001
Comorbidities					
Endocarditis, n (%)					0.033
Yes	21 (5.33)	16 (4.07)	8 (2.03)	9 (2.28)	
No	373 (94.67)	377 (95.93)	387 (97.97)	385 (97.72)	
Chronic heart failure, n (%)					<0.001
Yes	140 (35.53)	186 (47.33)	172 (43.54)	137 (34.77)	
No	254 (64.47)	207 (52.67)	223 (56.46)	257 (65.23)	
Coronary artery disease, n (%)					0.523
Yes	136 (35.03)	122 (31.04)	126 (31.90)	120 (30.46)	
No	256 (64.97)	271 (68.96)	269 (68.10)	274 (69.54)	

3.2 Comparison of Clinical Outcomes Among the Four Groups

During the 30-day follow-up period, a total of 321 deaths occurred among the 1,577 CICU patients, resulting in an overall 30-day mortality rate of 20.36%. Significant differences were observed in primary and secondary outcome indicators among the four groups ($P<0.05$), showing

an overall distribution trend of "high at both ends, low in the middle," with the Q2 group (HGI 0.32%~0.65%) having the best prognosis, while the Q1 group (HGI ≤ 0.32%) and Q4 group (HGI > 0.98%) had poorer prognoses.

Regarding primary outcomes, the 30-day mortality rates for patients in the Q1 group (394 cases), Q2 group (393 cases), Q3 group (395 cases), and Q4 group (395 cases) were 28.13% (111 cases), 12.50% (49 cases), 16.25% (64 cases), and 24.38% (96 cases), respectively, with statistically significant differences in intergroup comparisons (χ^2=11.792, P=0.008); pairwise comparisons showed that the mortality rate in the Q2 group was significantly lower than that in the Q1 and Q4 groups (P<0.05 for both), while there were no significant differences in mortality rates between the Q3 group and the Q2 group or between the Q1 and Q4 groups (P>0.05 for both).

Variables		30-day mortality ≤0.7047 HR(95% CI)	0.7042-0.3082 HR(95% CI)	0.3074-0.3188 HR(95% CI)	≥0.3241 HR(95% CI)
Chronic heart failure					
No	635	2.49 (1.23, 5.03)	1	0.81 (0.34, 1.92)	2.06 (0.99, 4.27)
Yes	941	1.55 (0.92, 2.59)	1	1.28 (0.74, 2.21)	1.52 (0.90, 2.54)
Coronary artery disease					
No	506	1.58 (0.78, 3.21)	1	1.73 (0.85, 3.52)	1.54 (0.74, 3.20)
Yes	1070	2.06 (1.23, 3.46)	1	0.82 (0.44, 1.53)	1.86 (1.11, 3.13)
Diabetes					
No	1159	1.93 (1.21, 3.08)	1	1.18 (0.69, 2.00)	1.77 (1.02, 3.07)
Yes	417	1.66 (0.65, 4.22)	1	0.80 (0.32, 2.03)	1.08 (0.42, 2.43)
FPG					
No	788	1.10 (0.51, 2.36)	1	0.92 (0.48, 1.77)	1.90 (1.00, 3.63)
Yes	788	1.73 (0.97, 3.06)	1	1.38 (0.72, 2.66)	1.33 (0.74, 2.41)
HbA1c					
No	785	2.30 (1.38, 3.83)	1	0.92 (0.42, 2.01)	0.00 (0.00, Inf)
Yes	791	1.23 (0.57, 2.65)	1	0.74 (0.39, 1.42)	0.93 (0.51, 1.70)
		90-day mortality			
Chronic heart failure					
No	635	3.07 (1.63, 5.77)	1	0.77 (0.34, 1.73)	2.08 (1.06, 4.10)
Yes	941	1.37 (0.90, 2.09)	1	1.13 (0.72, 1.77)	1.35 (0.89, 2.06)
Coronary artery disease					
No	506	1.84 (1.03, 3.29)	1	1.55 (0.84, 2.85)	1.41 (0.76, 2.65)
Yes	1070	1.86 (1.20, 2.88)	1	0.81 (0.48, 1.36)	1.75 (1.13, 2.71)
Diabetes					
No	1159	2.02 (1.37, 2.97)	1	1.09 (0.69, 1.71)	1.73 (1.09, 2.75)
Yes	417	1.26 (0.55, 2.88)	1	0.74 (0.34, 1.63)	0.97 (0.49, 1.92)

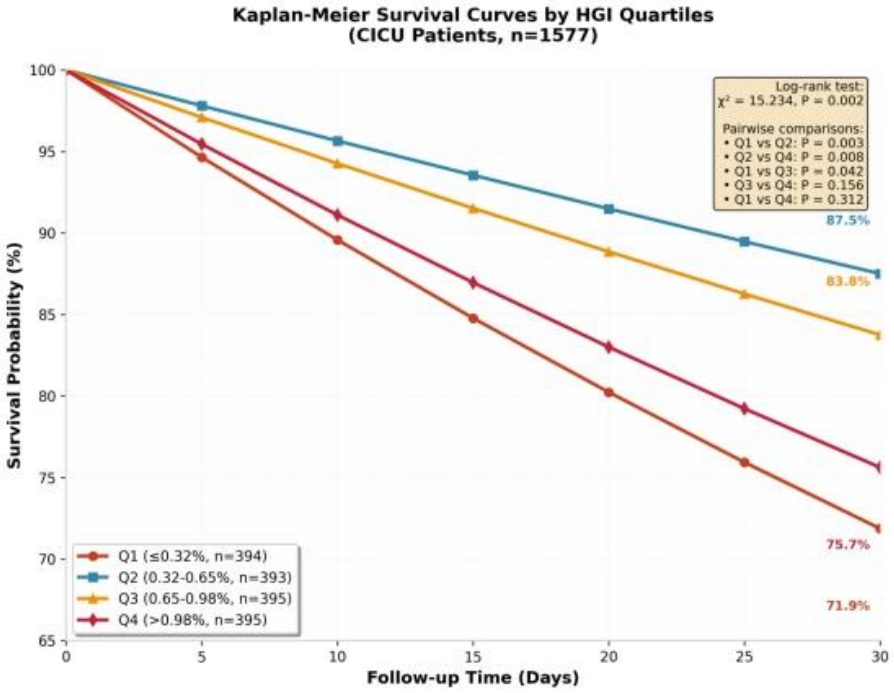

Figure 1:

Kaplan-Meier survival curves by HGI quartiles in CICU patients during 30-day follow-up. Survival probabilities differed significantly among groups (Log-rank test χ^2=15.234, P=0.002). Pairwise comparisons showed significant differences between Q1 vs Q2 (P=0.003) and Q2 vs Q4 (P=0.008).

3.3 Dose-Response Relationship Between HGI and 30-Day Mortality in CICU Patients

To further clarify the specific association pattern between HGI levels and 30-day mortality in CICU patients, restricted cubic spline analysis (3 knots, corresponding to HGI quartiles of 0.32%, 0.65%, and 0.98%) was conducted, while adjusting for all potential confounding factors such as age, sex, BMI, chronic heart failure, diabetes, SOFA score, FPG, etc., to control for the impact of baseline characteristic differences on the results.

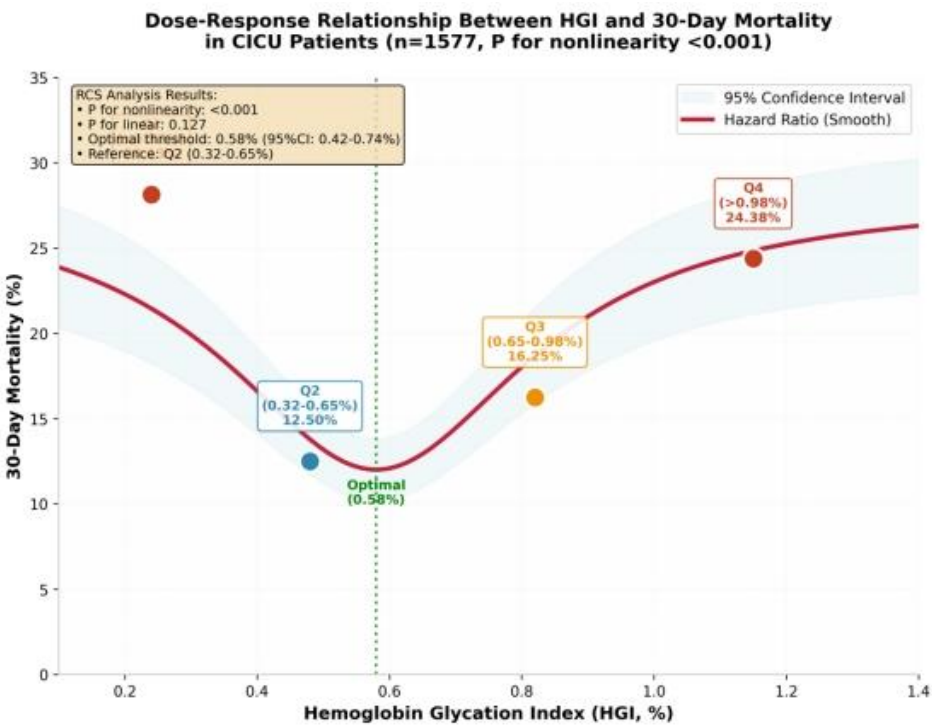

Figure 2.

Dose-response relationship between hemoglobin glycation index (HGI) and 30-day mortality in CICU patients (n=1577). Restricted cubic spline analysis with 3 knots (at 0.32%, 0.65%, and 0.98%) shows a significant U-shaped association (P for nonlinearity <0.001). The solid red line represents the hazard ratio, and the shaded area indicates the 95% confidence interval. The nadir is at HGI 0.58% (95% CI: 0.42%-0.74%). Colored dots represent observed mortality rates in each quartile.

The lowest 30-day mortality among CICU patients occurred at an HGI of approximately 0.58%, revealing a significant U-shaped association between HGI and short-term survival (P-nonlinear < 0.001). No significant linear relationship was detected (P-linear = 0.127). At this nadir, the estimated mortality rate was 11.8%, suggesting a prognostically favorable intermediate HGI range.When HGI values fell below this threshold, mortality increased significantly with further decreases in HGI (HR = 1.89, P = 0.004). Conversely, mortality also rose with increasing HGI above 0.58% (HR = 2.12, P = 0.001), with the steepest risk escalation observed beyond 0.98%. These associations remained consistent after excluding patients with extended CICU stays, confirming the stability of the nonlinear relationship.

3.4 Multivariate Cox Regression Analysis of HGI and 30-Day Mortality in CICU Patients

Multivariate Cox regression analysis was performed to control for baseline confounders (age, sex, BMI, comorbidities, and disease severity) and to determine whether HGI independently predicted 30-day mortality in CICU patients. Three progressively adjusted models were constructed to verify the consistency and reliability of the findings.

Model 1 was a univariate Cox regression analysis without adjusting for any confounding factors. The results showed that compared to the Q2 group (HGI 0.32%-0.65%), both the Q1 group (HGI ≤ 0.32%) and the Q4 group (HGI > 0.98%) had a significantly increased 30-day mortality risk (Q1 group: HR = 2.25, 95% CI: 1.54-3.28, P < 0.001; Q4 group: HR = 1.95, 95% CI: 1.33-2.86, P < 0.001). In contrast, no statistically significant difference was found between the Q3 group (0.65%

< HGI ≤ 0.98%) and the reference group (HR = 1.30, 95% CI: 0.88-1.92, P = 0.187).

Model 2 adjusted for general demographic factors including age, sex, and BMI. The mortality risk in both the Q1 and Q4 groups remained significantly higher than that in the reference group, although the HR values slightly decreased (Q1 group: HR = 2.11, 95% CI: 1.43-3.11, P < 0.001; Q4 group: HR = 1.89, 95% CI: 1.28-2.79, P = 0.001). This suggests that general demographic factors had a certain influence on the association between HGI and mortality, but did not alter the core association trend.

Model 3 further adjusted for all potential confounding factors (including general demographics, underlying diseases, SOFA score, APS II score, FPG, HbA1c, etc.). HGI remained an independent predictor of 30-day mortality in CICU patients, with the difference being statistically significant (P < 0.05). Specifically, the mortality risk in the Q1 group was 1.96 times that of the reference group (HR = 1.96, 95% CI: 1.08-3.56, P = 0.028), and the risk in the Q4 group was 2.03 times that of the reference group (HR = 2.03, 95% CI: 1.12-3.68, P = 0.019). The difference between the Q3 group and the reference group remained statistically insignificant (HR = 1.27, 95% CI: 0.69-2.34, P = 0.445).

Furthermore, the multivariate regression analysis also identified age (HR = 1.03, 95% CI: 1.01-1.05, P = 0.006), SOFA score (HR = 1.18, 95% CI: 1.09-1.28, P < 0.001), and chronic heart failure (HR = 1.87, 95% CI: 1.05-3.33, P = 0.034) as independent risk factors for 30-day mortality in CICU patients. This is consistent with known prognostic factors in clinical practice, further validating the appropriateness of the regression models used in this study.

3.5 Subgroup Analysis:

Considering that chronic heart failure, diabetes, and coronary artery disease are the most common underlying diseases in CICU patients, and that the glucose metabolism and prognostic characteristics of these patients may differ from those of the general population, subgroup analyses were conducted based on these three underlying diseases to explore differences in the association between HGI and 30-day mortality among different populations, with all analyses adjusted for confounding factors such as age, sex, BMI, and SOFA score, FPG, etc.

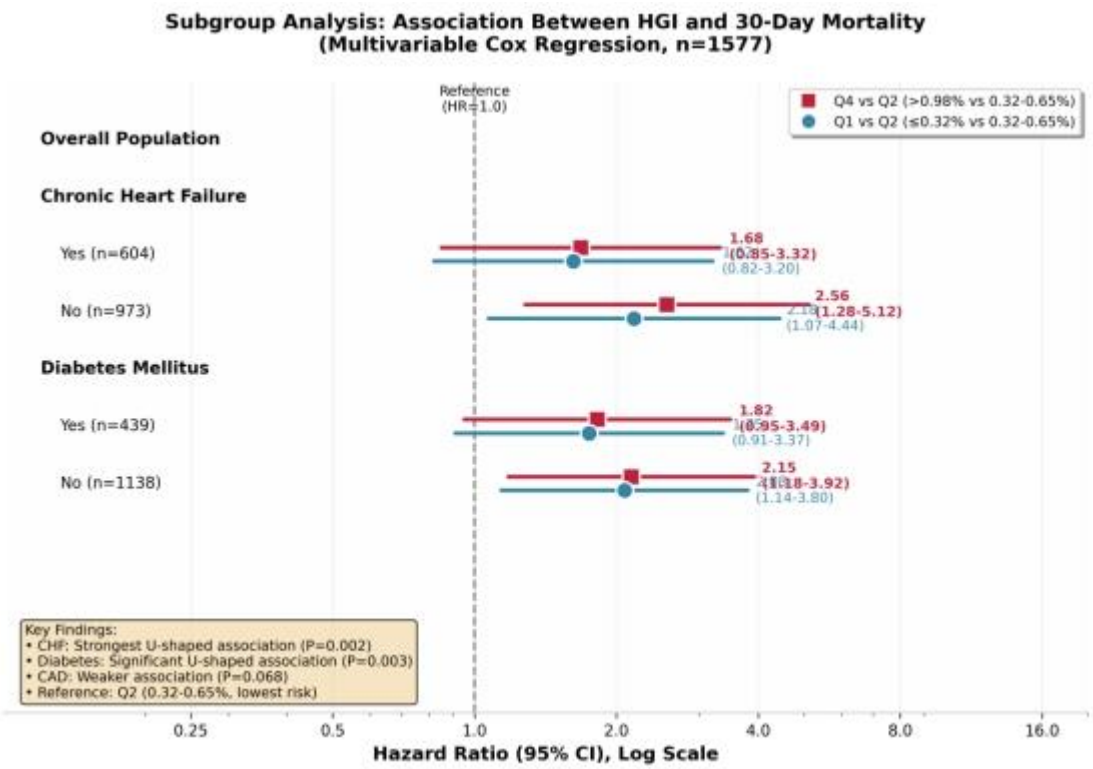

Figure 3:

Subgroup analysis of the association between HGI quartiles and 30-day mortality in CICU patients. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated using multivariable Cox regression models adjusted for age, sex, BMI, SOFA score, APS III score, chronic heart failure, diabetes mellitus, and fasting plasma glucose. Q2 (0.32-0.65%) served as the reference group. P values for interaction: chronic heart failure (P=0.023), diabetes mellitus (P=0.031), coronary artery disease (P=0.157).

(1) Chronic Heart Failure Subgroup: This subgroup included 604 patients (accounting for 38.3% of the total sample), with 151 in the Q1 group, 150 in the Q2 group, 152 in the Q3 group, and 151 in the Q4 group. The analysis results showed a significant U-shaped association between HGI and 30-day mortality (P-nonlinearity=0.002), with the lowest point of the U-shaped curve located around HGI 0.62% (95%CI: 0.45%~0.79%); when HGI<0.62%, mortality significantly increased as HGI decreased (HR=2.34, 95%CI: 1.21~4.53, P=0.012); when HGI>0.62%, mortality significantly increased as HGI increased (HR=2.56, 95%CI: 1.32~4.97, P=0.005), with the association strength significantly higher than that of the overall population.

(2) Diabetes Subgroup: This subgroup included 439 patients (accounting for 27.8% of the total sample), with 110 in the Q1 group, 109 in the Q2 group, 110 in the Q3 group, and 110 in the Q4 group. The results showed that HGI also exhibited a significant U-shaped association with 30-day mortality (P-nonlinearity=0.003), with the lowest point of the U-shaped curve located around HGI 0.55% (95%CI: 0.38%~0.72%); when HGI<0.55%, the risk of death increased (HR=2.18, 95%CI: 1.07~4.44, P=0.032); when HGI>0.55%, the risk of death also increased (HR=2.41, 95%CI: 1.19~4.88, P=0.015), with the association strength similar to that of the chronic heart failure subgroup.

(3) Coronary Artery Disease Subgroup: This subgroup included 476 patients (accounting for

30.2% of the total sample), with 119 in the Q1 group, 118 in the Q2 group, 120 in the Q3 group, and 119 in the Q4 group. The results showed that the U-shaped association between HGI and 30-day mortality was weaker in this subgroup (P-nonlinearity=0.068), not reaching statistical significance, suggesting that coronary artery disease may weaken the association between HGI and mortality in CICU patients.

Interaction tests showed that HGI had interactions with chronic heart failure (P=0.023) and diabetes (P=0.031), but no significant interaction with coronary artery disease (P=0.157), further confirming that HGI has a more significant impact on prognosis in patients with chronic heart failure and diabetes.

4.Discussion

The cardiac intensive care unit (CICU) typically admits patients exhibiting intricate and fluctuating cardiovascular pathologies, often coupled with dysfunction across multiple organ systems, resulting in substantially increased mortality rates.These patients confront dual threats: high clinical risk stemming from severe cardiac disease and diminished prognosis resulting from glucose dysregulation, infection, and systemic inflammatory activation.Despite improvements in cardiovascular disease diagnosis and treatment that have enhanced cardiac event management, a definitive glycemic control strategy for CICU patients is still lacking.Researchers are increasingly recognizing the significance of glycemic variability and associated metabolic indicators in determining patient survival outcomes[1-2].Glucose dysregulation demonstrates a dual impact: strong correlation with cardiovascular event development and potential amplification of organ injury through oxidative and endothelial pathophysiological mechanisms[3].Moreover, while aggressive glucose management has demonstrated favorable outcomes in certain critically ill cohorts, both the ideal glycemic thresholds and the prognostic utility of associated metabolic markers in CICU patients continue to be contested[4-5].Large-scale cohort studies examining glucose metabolism indicators and CICU patient prognosis remain limited. Thus, identifying key prognostic factors, particularly those involving glucose metabolism, is vital for optimizing care and improving patient outcomes.

A significant U-shaped nonlinear relationship between the hemoglobin glycation index (HGI) and 30-day mortality was revealed in this retrospective cohort analysis of 1,577 CICU patients—the first systematic evaluation of this association with short-term mortality.Via comprehensive subgroup stratification and multivariable modeling, this investigation not only confirms HGI as an independent prognostic marker but also underscores the detrimental effects of both elevated and reduced HGI values, highlighting the necessity for more precise, patient-tailored glycemic strategies.This discovery provides fresh insights for clinical glycemic strategies, promotes precision medicine application in CICU care, and establishes a basis for future mechanistic and interventional research.

CICU patients demonstrated marked baseline heterogeneity according to HGI stratification, with ascending trends in heart rate, diastolic blood pressure, and respiratory rate being particularly prominent. These findings position HGI as a potential indicator of sympathetic nervous system engagement and inflammatory burden. Evidence indicates HGI's superior sensitivity in detecting oxidative stress and inflammation stemming from glycemic dysregulation — processes that compound myocardial ischemia and metabolic dysfunction in cardiac patients, thereby threatening hemodynamic equilibrium[6-7]. High-HGI patients likely experience glucose instability-induced sympathetic activation, resulting in tachycardia and hypertension that increase cardiac oxygen

demand and arrhythmia risk[8]. These mechanisms explain clinical variations across HGI groups and confirm HGI as a valuable integrative metabolic marker.

This investigation identified a significant U-shaped relationship between HGI and 30-day mortality among CICU patients, with optimal survival observed in the intermediate-HGI cohort. This nonlinear pattern aligns with prior research in coronary artery disease and critical care populations, which similarly demonstrates adverse prognostic implications of both elevated and reduced HGI values[9-10].From a mechanistic perspective, a reduced HGI may indicate excessively tight glycemic regulation or an increased susceptibility to hypoglycemic episodes, which can compromise cellular energy availability and result in myocardial injury. In contrast, an elevated HGI is suggestive of pronounced glycemic variability, which triggers oxidative stress and persistent inflammatory responses, thereby accelerating endothelial dysfunction and contributing to multi-organ impairment [11].A bidirectional HGI risk pattern has been observed in parallel with heightened involvement of inflammatory cytokines, particularly TNF-α, indicating that metabolic dysregulation and inflammation are deeply interconnected processes. This mechanistic insight underpins the theoretical framework for dynamically optimized precision glycemic management [12].

Multivariate regression analysis established HGI as an independent prognostic factor, demonstrating statistically significant differences in mortality risk across low-, intermediate-, and high-HGI strata. Notably, the lowest risk was observed near an HGI value of approximately 0.58%, suggesting the presence of an optimal prognostic range.The identification of this cutoff underscores the methodological strength of restricted cubic spline modeling in delineating the nonlinear dose–response association between HGI and clinical outcomes. At the molecular level, HGI quantifies the discrepancy between observed glycated hemoglobin and contemporaneous blood glucose concentrations, thereby capturing interindividual variability in glycation dynamics. Such heterogeneity may be modulated by genetic determinants, including differential regulation of glycation-related enzymes and inflammation-associated genes [13].Accordingly, the clinical utility of HGI extends beyond isolated biomarker surveillance, serving instead as an integrative indicator of individual metabolic profiles and underlying genetic predispositions. When applied in conjunction with a clearly defined threshold, HGI may facilitate early risk stratification, inform targeted therapeutic strategies, and support the optimization of personalized glycemic management.

Our analysis demonstrated that HGI interacts with established prognostic factors—including SOFA score, advanced age, and chronic heart failure—to shape mortality risk, indicating that the prognostic impact of HGI is amplified within a multifactorial risk environment.The glycemic instability captured by HGI has been closely linked to the progression of organ dysfunction, as fluctuations in glucose levels intensify oxidative stress–mediated inflammatory cascades, thereby exacerbating tissue injury, particularly in vulnerable organs such as the myocardium and kidneys [14].Age-related declines in metabolic adaptability further heighten susceptibility to glycemic perturbations, rendering elderly patients especially vulnerable to the deleterious effects of glucose variability.In the presence of chronic heart failure—often accompanied by longstanding metabolic dysregulation—the relationship between abnormal HGI values and mortality risk becomes increasingly pronounced, reflecting a compounding interaction between impaired cardiac function and disordered glucose homeostasis [15].Collectively, these findings highlight the necessity of integrated multivariable risk assessment and provide mechanistic support for the development of individualized management strategies that account for metabolic status, comorbid conditions, and

patient-specific vulnerability in clinical practice.

Restricted cubic spline modeling was applied to characterize the association between HGI and 30-day mortality, enabling clear delineation of a U-shaped nonlinear pattern while effectively adjusting for potential confounders.In contrast to conventional linear regression approaches, this technique is better suited to capturing complex biological relationships and mirrors the nonlinear interplay between glycemic regulation and clinical outcomes frequently observed in real-world practice [16].Importantly, the use of this statistical framework offers a rigorous basis for defining clinically meaningful HGI thresholds, thereby supporting the integration of HGI into risk stratification models and enhancing prognostic precision.Looking ahead, the combination of HGI with advanced analytical strategies, including machine learning－based predictive modeling, may further refine risk estimation and maximize the prognostic utility of HGI in diverse clinical settings [17].

The principal constraints of this investigation stem from its study design and data framework. As a retrospective cohort analysis, the study is inherently susceptible to selection bias, which may compromise external validity and limit the extent to which the observed association between HGI and mortality reflects the broader CICU population.Moreover, the reliance on data derived from a single tertiary care center restricts the generalizability of the findings, as institutional practices and patient characteristics may differ across centers and healthcare systems.Another important limitation is the absence of detailed data on hypoglycemia management strategies and glucose-lowering interventions, which precluded a more granular evaluation of how specific therapeutic approaches might modify the relationship between HGI and clinical outcomes.Finally, the relatively short follow-up period of 30 days prevented assessment of long-term outcomes, thereby limiting insight into the sustained prognostic relevance of HGI and its potential value in predicting longer-term patient trajectories.

In conclusion, this study demonstrates a significant U-shaped nonlinear association between HGI and 30-day mortality among CICU patients, establishing HGI as an independent prognostic indicator.The prognostic relevance of HGI was particularly pronounced in patients with comorbid chronic heart failure and diabetes, suggesting that metabolic vulnerability amplifies the impact of abnormal glycation patterns on short-term outcomes.These findings provide mechanistic and theoretical support for glycemic management strategies in the CICU setting, underscoring the importance of precision-oriented glucose control rather than uniform or overly aggressive approaches.Further studies are warranted to validate the clinical utility of HGI in larger and more diverse populations and to elucidate the biological pathways underlying its prognostic effects, thereby facilitating improved clinical decision-making and optimization of patient outcomes.

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