

Article

Poor Glycemic Control Predicts Higher Mortality in Critically Ill Patients with COVID-19 and Hyperglycemia

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Abstract

Purpose: Hyperglycemia frequently occurs in critically ill patients with COVID-19 and may worsen outcomes. This study evaluated the prevalence, predictors, and clinical impact of poor glycemic control in severe and critical cases. **Methods:** We conducted a retrospective observational study of 338 ICU patients with COVID-19 and hyperglycemia at a tertiary center in Vietnam (August 2021–February 2022). Nearly 15,000 bedside glucose measurements were analyzed. Patients were classified into well-controlled or poorly controlled groups based on mean glucose levels (140–180 mg.dL^{−1} target). Logistic regression identified predictors of poor control. The primary outcome was in-hospital mortality. Propensity score matching (PSM) and multivariable Cox regression were performed to adjust for confounders. **Results:** Poor glycemic control occurred in 79% of patients. Independent predictors included invasive mechanical ventilation, elevated admission glucose, pre-existing diabetes, HbA1c > 7.0%, and prolonged corticosteroid exposure. After PSM, mortality was higher in the poorly controlled group compared to the well-controlled group (54.8% vs. 35.5%, $p = 0.047$). Cox regression confirmed poor glycemic control as an independent predictor of death (adjusted hazard ratio [HR] 1.61, 95% confidence interval [CI] 1.01–2.55, $p = 0.045$). **Conclusions:** Poor glycemic control is common and strongly associated with excess mortality in critically ill COVID-19 patients. Prolonged corticosteroid use emerged as a modifiable risk factor. Careful glucose monitoring and tailored steroid management are warranted to improve outcomes.

Keywords: COVID-19; hyperglycemia; glycemic control; corticosteroids; critically ill patients



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1. Introduction

Since its emergence in December 2019, the COVID-19 pandemic, caused by SARS-CoV-2, has resulted in nearly 800 million confirmed infections and more than seven million deaths worldwide [1]. Although initially considered a respiratory illness, COVID-19 is now recognized as a multisystem disease characterized by immune dysregulation, cytokine storm, and systemic inflammation. In this context, hyperglycemia has emerged as a common and clinically significant complication, strongly associated with poor outcomes [2].

The mechanisms of hyperglycemia in severe COVID-19 are multifactorial, including stress-induced insulin resistance, pancreatic β -cell dysfunction, and the frequent use of corticosteroids. These processes contribute to glycemic instability and make management particularly difficult in intensive care units (ICUs), especially in resource-limited settings. In developing countries, hyperglycemia affects up to three-quarters of severe and critical COVID-19 patients [3,4]. It has been linked to acute respiratory distress syndrome (ARDS), secondary infections, renal injury, prolonged ICU stay, and increased mortality, regardless of prior diabetes status [3,5]. Surprisingly, among patients with COVID-19 and hyperglycemia, those with new-onset hyperglycemia had worse outcomes than those with pre-existing type 2 diabetes [3]. This finding likely reflects biological and adaptive mechanisms. Clinical risk appears to be driven by relative hyperglycemia, representing an acute deviation from baseline glycemia rather than absolute glucose levels [6]. Chronic diabetes may confer partial cellular adaptation to hyperglycemia-induced oxidative stress and inflammatory signaling [7]. In contrast, stress hyperglycemia in previously normoglycemic patients likely indicates a heightened neuroendocrine and inflammatory stress response and greater underlying organ dysfunction, functioning primarily as a marker of disease severity [8].

While previous studies have described hyperglycemia in COVID-19, few have focused specifically on glycemic control and its determinants in the ICU. Factors such as systemic inflammation, corticosteroid-induced insulin resistance, and rapidly changing clinical status create a highly unstable metabolic environment where standard glucose management strategies often fail [9–11]. Evidence suggests that better glucose control improves survival: Zhu et al. reported reduced mortality in patients with well-controlled glucose [12], and Kapoor et al. showed the difficulty of maintaining target blood glucose in ICU patients with COVID-19, with outcomes favoring those who achieved control [13]. However, data remain limited on new-onset hyperglycemia and the cumulative effects of corticosteroid therapy on glycemic stability. Therefore, a deeper exploration of the mechanisms underlying poor glycemic control in critically ill patients with COVID-19, as well as the prognostic impact of poorly controlled hyperglycemia, is essential to advance our understanding of COVID-19-related metabolic dysregulation and to better prepare healthcare systems for future pandemics with similar characteristics.

We hypothesized that glycemic control is difficult to achieve in severe and critical COVID-19 patients with hyperglycemia, and that poor control is associated with worse outcomes. This study therefore aimed to (1) determine the prevalence and predictors of poorly controlled hyperglycemia and (2) assess its impact on clinical outcomes. By leveraging a large dataset of nearly 15,000 bedside glucose measurements in 338 patients, together with standardized ICU protocols, we sought to provide robust evidence from a resource-limited setting during the peak of the pandemic in southern Vietnam.

2. Materials and Methods

2.1. Study Designs and Patients

This retrospective observational study was conducted at the Intensive Care Center for COVID-19 (UCICC), University Medical Center Ho Chi Minh City, Vietnam, during the fourth pandemic wave (August 2021–February 2022) [3]. The study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines to ensure methodological transparency and rigorous reporting [14].

Eligible participants were adults (≥ 18 years) admitted to the ICU with severe COVID-19 who developed hyperglycemia during their ICU stay. All cases of SARS-CoV-2 infection were confirmed by RT-PCR according to WHO standards [15]. Severe COVID-19 was defined as the presence of at least one of the following: oxygen saturation $< 90\%$ in room air, severe pneumonia, or signs of severe respiratory distress, according to World Health

Organization guidelines [16]. Exclusion criteria included type 1 diabetes, death within 24 h of ICU admission, pregnancy, and missing key treatment or outcome data.

2.2. Hyperglycemia and Glycemic Control

Definitions of hyperglycemia vary across studies, including thresholds based on admission glucose or HbA1c levels. To closely monitor metabolic status, we performed regular bedside capillary blood glucose (BG) measurements throughout ICU admission using Accu-Chek Guide® (Roche Diabetes Care, Mannheim, Germany) or Medisafe Fit C® (Terumo Corporation, Tokyo, Japan). Hyperglycemia was defined as ≥ 180 mg.dL⁻¹ on at least two occasions within 24 h [17].

Two phenotypes were identified: (1) pre-existing type 2 diabetes (T2DM), determined by prior diagnosis or HbA1c $\geq 6.5\%$; and (2) new-onset hyperglycemia in patients without known diabetes. Details of standardized protocols for BG monitoring and management are provided in Supplementary S1.

Glycemic control status was categorized according to mean BG during ICU stay:

- Well-controlled: 140–180 mg.dL⁻¹;
- Poorly controlled: outside this range [17,18].

Stability of glycemic control was evaluated using mean BG, range, standard deviation (SD), coefficient of variation (CV), and time in range (TIR). SD and CV reflect glucose variability, whereas TIR represents the proportion of time spent within the target range. Larger range, SD, and CV values indicate greater instability, while higher TIR reflects more effective control. Hypoglycemia was not used as a criterion for group assignment; however, hypoglycemic episodes would indirectly reduce mean BG and TIR, thereby classifying patients into the poorly controlled group. Although frequent bedside capillary BG measurements were performed, mean BG was used for categorization and may not fully capture short-term glycemic variability.

2.3. Data Collection

Data were systematically retrieved from electronic medical records. Demographic variables included age, sex, body mass index (BMI), and vaccination status. Clinical characteristics comprised comorbidities such as hypertension, coronary artery disease, chronic obstructive pulmonary disease, chronic kidney disease, chronic liver disease, and pre-existing T2DM.

Laboratory data included blood glucose levels, HbA1c, inflammatory markers (C-reactive protein [CRP], ferritin, D-dimer), and organ function parameters (creatinine, aspartate aminotransferase [AST], alanine aminotransferase [ALT]). Cytokine storm syndrome (CSS) was identified by elevated lymphocytes, D-dimer, lactate dehydrogenase, ferritin, and CRP, consistent with previously described hyperinflammatory phenotypes in severe COVID-19 [19]. Systemic inflammatory response syndrome (SIRS) was assessed using standard clinical criteria: body temperature, white blood cell count, respiratory rate, and heart rate [20].

Treatment-related variables included corticosteroid therapy (CST), insulin use, and the requirement for invasive mechanical ventilation (IMV).

2.4. Outcome Measurements

The primary outcome was in-hospital mortality, defined as death occurring during the ICU stay.

Secondary outcomes were composite complications, defined as the occurrence of at least one major adverse event during ICU admission. These included the following:

- Bacterial pneumonia: symptoms of lower respiratory tract infection with a positive sputum culture;
- Bacteremia: confirmed by positive blood culture;
- Septic shock: defined according to SEPSIS-3 criteria [21];
- Acute kidney injury (AKI): diagnosed using KDIGO 2012 guidelines [22];
- Metabolic complications: hypoglycemia, diabetic ketoacidosis, and hyperosmolar hyperglycemic state, defined according to American Diabetes Association standards [17,23].

2.5. Statistical Analysis

All analyses were performed using R software (version 4.3.2; R Foundation for Statistical Computing, Vienna, Austria) within the RStudio environment (version 2024.04.0+735). For descriptive and comparative statistics, analyses were conducted using an available-case approach, whereby each variable was analyzed among patients with non-missing values.

Descriptive statistics were reported as frequencies and percentages for categorical variables. Quantitative variables were tested for normality using the Shapiro–Wilk or Kolmogorov–Smirnov tests and described as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), as appropriate.

Comparative analyses used the Chi-square test or Fisher’s exact test for categorical variables, and the independent *t*-test or Mann–Whitney U test for continuous variables, depending on distribution.

Multivariable logistic regression was employed to identify factors associated with poor glycemic control, expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Candidate variables included those significant in univariate analyses as well as clinically relevant factors (e.g., age, sex). Missing laboratory data were handled using indicator variable coding based on established clinical thresholds, with values above the prespecified cutoff classified as positive. Multicollinearity among covariates was assessed using variance inflation factors (VIFs) for multivariable regression models, with a threshold of 5 considered acceptable.

A two-sided *p*-value < 0.05 was considered statistically significant.

2.6. Propensity Score Matching and Survival Analysis

To reduce baseline imbalances between groups, propensity score matching (PSM) was applied. Covariates included age, sex, procalcitonin, comorbidities, cytokine storm syndrome (CSS), corticosteroid therapy (CST), PaO₂/FiO₂ ratio, hyperglycemia phenotype, and requirement for invasive mechanical ventilation (IMV). Propensity scores were estimated using logistic regression, and patients were matched using nearest-neighbor matching with a caliper width of 0.1 of the standard deviation of the logit-transformed score, as implemented in the *MatchIt* package (R), a method shown to minimize bias in observational studies [24].

Propensity scores were estimated using complete cases only, because full data on all matching covariates were required. The quality of matching was assessed by examining absolute standardized mean differences (aSMDs), with values < 0.1 considered indicative of good balance [25].

For sensitivity analysis, multivariable Cox proportional hazards models were fitted in the unmatched cohort using the *survival* package (R) to validate associations between glycemic control and in-hospital mortality, with results expressed as hazard ratios (HRs) and 95% confidence intervals (CIs). The proportional hazards assumption was assessed using Schoenfeld residuals; if violations were detected, the corresponding variables were handled by stratification. In addition, Kaplan–Meier survival curves with log-rank tests

were generated to visualize mortality differences between groups, and adjusted estimates from the Cox models were overlaid to improve interpretability. Prespecified subgroup analyses were performed using the primary Cox proportional hazards model, stratified by clinically relevant subgroups, with interaction terms included to assess effect modification (p for interaction).

2.7. Ethical Considerations

This retrospective study did not affect patient diagnosis, treatment, or follow-up. The study complied with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board of University of Medicine and Pharmacy at Ho Chi Minh City (Approval No. 854/HĐĐĐ-ĐHYD, issued 28 September 2023). The requirement for informed consent was waived due to the retrospective nature of the study.

3. Results

3.1. Patients and Treatments

Figure 1 presents the study flow diagram. Among 529 patients with severe or critical COVID-19 admitted to the ICU and BG was monitored throughout the ICU stay. Of these, 338 patients developed hyperglycemia and were included in the analysis of prevalence and predictors of poor glycemic control. After PSM, 124 patients were retained for outcome comparisons.

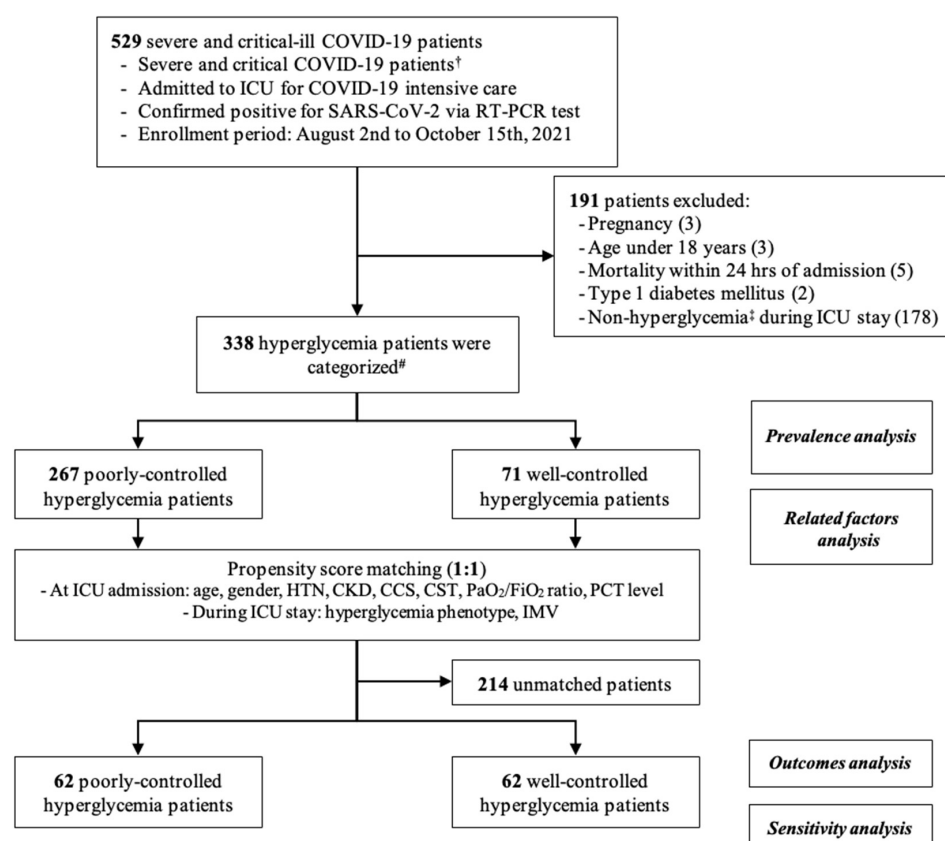


Figure 1. Flow chart of this study. Annotations: [†] Severe and critically ill COVID-19 patients were diagnosed based on positive SARS-CoV-2 RT-PCR tests according to WHO interim guidelines. [#] Mean glucose levels were calculated as the average of capillary blood glucose (BG) values during ICU stay, with the target range defined as 140–180 mg·dL⁻¹. [‡] Non-hyperglycemia during the ICU stay was defined as patients who did not meet the hyperglycemia criterion of blood glucose ≥ 180 mg·dL⁻¹ on at least two measurements within any 24 h period. Abbreviations: CKD, chronic kidney disease;

CSS, cytokine storm syndrome; CST, corticosteroid therapy; HTN, hypertension; ICU, intensive care unit; IMV, invasive mechanical ventilation; PaO₂/FiO₂, partial pressure of arterial oxygen to fraction of inspired oxygen ratio; PCT, pro-calcitonin levels; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 1 presents the baseline characteristics of the study population. The study cohort had a mean age of 64.9 years, with 59.5% female and 91.7% unvaccinated. Hypertension (64.5%) and T2DM (60.9%) were the most common comorbidities, although both were less frequent in the well-controlled group. At ICU admission, patients presented with compromised respiratory function, reflected by high respiratory rates, low oxygen saturation, and reduced PaO₂/FiO₂ ratios. Laboratory findings demonstrated elevated markers of inflammation (D-dimer, ferritin, IL-6, CRP) and infection (WBC, PCT), as well as features consistent with CSS and SIRS. The poorly controlled group had significantly higher HbA1c levels (7.3% vs. 6.4%, $p < 0.001$) and greater BG variability, reflected by wider range, higher SD and CV, and lower TIR.

Table 1. Demographics, baseline characteristics, and BG monitoring of the study population.

Variables	Total (<i>n</i> = 338)	Poorly Controlled (<i>n</i> = 267)	Well-Controlled (<i>n</i> = 71)	<i>p</i> -Value
Demographics				
Age, years old	64.9 ± 14.3	65.2 ± 14.1	63.7 ± 15.2	0.458
Male, <i>n</i> (%)	137 (40.5)	100 (37.5)	37 (52.1)	0.036
BMI, kg.m ⁻²	24 (22–26)	24 (22–27)	23 (20–25)	0.035
Vaccinated, <i>n</i> (%)	28 (8.3)	23 (8.6)	5 (7.0)	0.853
Comorbidities				
HTN, <i>n</i> (%)	218 (64.5)	180 (67.4)	38 (53.5)	0.042
CVD, <i>n</i> (%)	56 (16.6)	44 (16.5)	12 (16.9)	1.000
COPD, <i>n</i> (%)	22 (6.5)	17 (6.4)	5 (7.0)	1.000
CKD, <i>n</i> (%)	33 (9.8)	31 (11.6)	2 (2.8)	0.024
CLD, <i>n</i> (%)	14 (4.1)	9 (3.4)	5 (7.0)	0.296
T2DM, <i>n</i> (%)	206 (60.9)	192 (71.9)	14 (19.7)	<0.001
Clinical and laboratory features				
HR, bpm	93 (82–107)	95 (83–109)	90 (80–100)	0.017
SBP, mmHg	130 (111–140)	130 (112–140)	129 (110–140)	0.567
RR, bpm	25 (22–30)	25 (22–30)	24 (22–30)	0.716
Temp ≥ 38 °C, <i>n</i> (%)	22 (6.5)	17 (6.4)	5 (7.0)	1.000
SpO ₂ , (%)	92 (84–96)	92 (84–96)	93 (87–96)	0.852
HbA1c, (%)	7.1 (6.4–8.6)	7.3 (6.6–9.0)	6.4 (5.9–6.8)	<0.001
D-dimer, ng.mL ⁻¹	1374 (727–2987)	1305 (675–2981)	1779 (999–3264)	0.104
Ferritin, ng.mL ⁻¹	1140 (705–1676)	1140 (718–1676)	1096 (698–1881)	0.783
Interleukin-6, pg.mL ⁻¹	24.6 (12.9–66.3)	25.4 (12.9–75.2)	21.8 (12.9–48.8)	0.317
CRP, mg.L ⁻¹	64 (29–118)	57 (28–115)	79 (36–122)	0.212
Anti-Xa, IU.mL ⁻¹	0.5 ± 0.3	0.5 ± 0.3	0.5 ± 0.3	0.809
Creatinine, mg.dL ⁻¹	0.9 (0.7–1.2)	0.9 (0.7–1.2)	0.8 (0.7–1.1)	0.043
eGFR, mL/min/1.73 m ²	73.9 ± 35.3	71.3 ± 34.6	83.6 ± 36.3	0.012
AST, IU.L ⁻¹	56 (33–90)	52 (32–83)	71 (40–95)	0.021
ALT, IU.L ⁻¹	43 (27–68)	41 (26–66)	49 (36–86)	0.005
Fibrinogen, g.L ⁻¹	5.0 (4.2–5.9)	5.0 (4.2–5.9)	5.0 (3.8–5.8)	0.246
WBC, K.uL ⁻¹	9.7 (6.8–13.5)	9.5 (6.8–12.9)	10.3 (7.1–14.7)	0.329
PCT ≥ 0.5 ng.mL ⁻¹ , <i>n</i> (%)	126 (37.3)	102 (38.2)	24 (33.8)	0.587
PaO ₂ /FiO ₂ ratio	124 (89–205)	130 (89–221)	110 (87–159)	0.091
SIRS, <i>n</i> (%)	228 (67.5)	182 (68.2)	46 (64.8)	0.691
CSS, <i>n</i> (%)	230 (68.0)	182 (68.2)	48 (67.6)	1.000

Table 1. Cont.

Variables	Total (n = 338)	Poorly Controlled (n = 267)	Well-Controlled (n = 71)	p-Value
Respiratory support, n (%)				
- Cannula	63 (18.7)	52 (19.4)	11 (15.5)	0.455
- NRB mask	41 (12.1)	33 (12.4)	8 (11.3)	
- NIV or HFNC	148 (43.8)	111 (41.6)	37 (53.0)	
- IMV	86 (25.4)	71 (26.6)	15 (21.1)	
BG during ICU stay				
On admission, mg.dL ⁻¹	211 (146–324)	237 (146–357)	164 (145–208)	<0.001
Mean, mg.dL ⁻¹	208 (180–246)	221 (199–263)	166 (158–174)	<0.001
Median, mg.dL ⁻¹	197 (171–238)	212 (188–257)	158 (149–168)	<0.001
Maximum, mg.dL ⁻¹	387 ± 106	411 ± 102	298 ± 62	<0.001
Minimum, mg.dL ⁻¹	90 (70–117)	90 (67–121)	94 (75–101)	0.500
Range, mg.dL ⁻¹ †	288.8 ± 125.0	310.1 ± 126.7	209.1 ± 77.3	<0.001
SD, mg.dL ⁻¹ #	74.2 ± 29.9	81.3 ± 29.3	48.3 ± 12.9	<0.001
CV, (%) §	33.9 ± 10.4	35.2 ± 10.7	29.2 ± 7.5	<0.001
TIR, (%) §	21.0 ± 14.3	16.9 ± 11.3	36.1 ± 14.4	<0.001

Annotations: † Range, difference between the maximum and minimum BG levels; # SD, standard deviation, square root of the total variance; § CV, coefficient of variation, percentage of the standard deviation relative to the mean; § TIR, time in range, percentage of time in the target range. Abbreviations: ALT, alanine aminotransferase; Anti-Xa, anti-factor Xa; AST, aspartate aminotransferase; BG, blood glucose; BMI, body mass index; bpm, beats per minute; CSS, cytokine storm syndrome; CKD, chronic kidney disease; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HFNC, high-flow nasal cannula; HR, heart rate; ICU, intensive care unit; IMV, invasive mechanical ventilation; NIV, non-invasive ventilation; NRB, non-rebreathing; PaO₂/FiO₂, partial pressure of arterial oxygen to fraction of inspired oxygen ratio; PCT, procalcitonin; RR, respiratory rate; SBP, systolic blood pressure; SIRS, systemic inflammatory response syndrome; SpO₂, peripheral oxygen saturation; T2DM, type 2 diabetes; WBC, white blood cell count.

Table 2 shows treatment differences between the well-controlled and poorly controlled groups. Patients in the well-controlled group tended to have a longer ICU stay. The poorly controlled group required significantly higher insulin exposure, including total dosage (median 324 vs. 97 IU), daily dosage (36 vs. 16 IU), and longer duration of therapy (8 vs. 4 days). They also had a longer ICU course under CST (64.9% vs. 47.6%, $p = 0.002$). Additionally, 56.8% of patients required IMV.

Table 2. Treatment characteristics of the study population.

Variables	Total (n = 338)	Poorly Controlled (n = 267)	Well-Controlled (n = 71)	p-Value
Corticosteroid therapy				
Total dose, mg †	78 (48–112)	73 (46–106)	92 (59–119)	0.105
Mean dose, mg.day ⁻¹ ‡	9.2 (6.6–11.4)	9.2 (6.6–11.4)	9.9 (6.6–11.3)	0.270
Days on CST, (%)	61.5 (38.9–83.3)	64.9 (42.9–85.7)	47.6 (25.7–67.9)	0.002
Pulse-dose CST use, n (%)	25 (7.4)	18 (6.7)	7 (9.9)	0.524
Insulin therapy				
Total dose, IU	254 (78–593)	324 (128–689)	97 (0–290)	<0.001
Mean dose, IU.day ⁻¹ ‡	30 (14–50)	36 (18–54)	16 (0–30)	<0.001
Use of mixtard, n (%)	127 (37.6)	113 (42.3)	14 (19.7)	<0.001
Use of glargine, n (%)	28 (8.3)	23 (8.6)	5 (7.0)	0.853
Days on insulin therapy, (%)	75.0 (28.6–91.7)	81.8 (45.3–93.3)	20.7 (0.0–71.1)	<0.001
Oxygen therapy #, n (%)				
- Cannula	50 (14.8)	43 (16.1)	7 (9.9)	0.306
- NRB mask	20 (5.9)	17 (6.4)	3 (4.2)	
- NIV or HFNC	76 (22.5)	62 (23.2)	14 (19.7)	
- IMV	192 (56.8)	145 (54.3)	47 (66.2)	

Table 2. Cont.

Variables	Total (n = 338)	Poorly Controlled (n = 267)	Well-Controlled (n = 71)	p-Value
Duration				
ICU stay, days	14.0 (9.0–21.0)	13.0 (9.0–19.0)	19.0 (12.5–26.5)	<0.001
IMV use, days	3.0 (0.0–9.0)	2.0 (0.0–8.0)	5.0 (0.0–14.5)	0.009
CST use, days	9.0 (6.0–10.0)	9.0 (6.0–10.0)	10.0 (6.0–11.0)	0.158
Insulin therapy use, days	8.0 (3.0–13.8)	8.0 (4.0–14.0)	4.0 (0.0–10.5)	<0.001

Annotations: † Corticosteroid doses are converted to an equivalent dose of dexamethasone. ‡ The average daily dose is calculated by dividing the total dose by the number of days used; # The highest level required. Abbreviations: CST, corticosteroid therapy; HFNC, high-flow nasal cannula; ICU, intensive care unit; IMV, invasive mechanical ventilation; NRB, non-rebreathing; NIV, non-invasive ventilation.

3.2. Prevalence

Nearly 15,000 capillary BG measurements were obtained during ICU stay (Figure 2A). The histogram for the well-controlled group, with its sharp peak, steep edges, and narrow base, reflects greater stability of BG levels. In contrast, poorly controlled hyperglycemia was observed in 79% of patients (Figure 2B). In both groups, BG levels were higher early after ICU admission and stabilized after the second week (Supplementary S2). Thereafter, mean glucose remained consistently higher in the poorly controlled group than in the well-controlled group (~ 200 mg.dL⁻¹ versus ~ 150 mg.dL⁻¹).

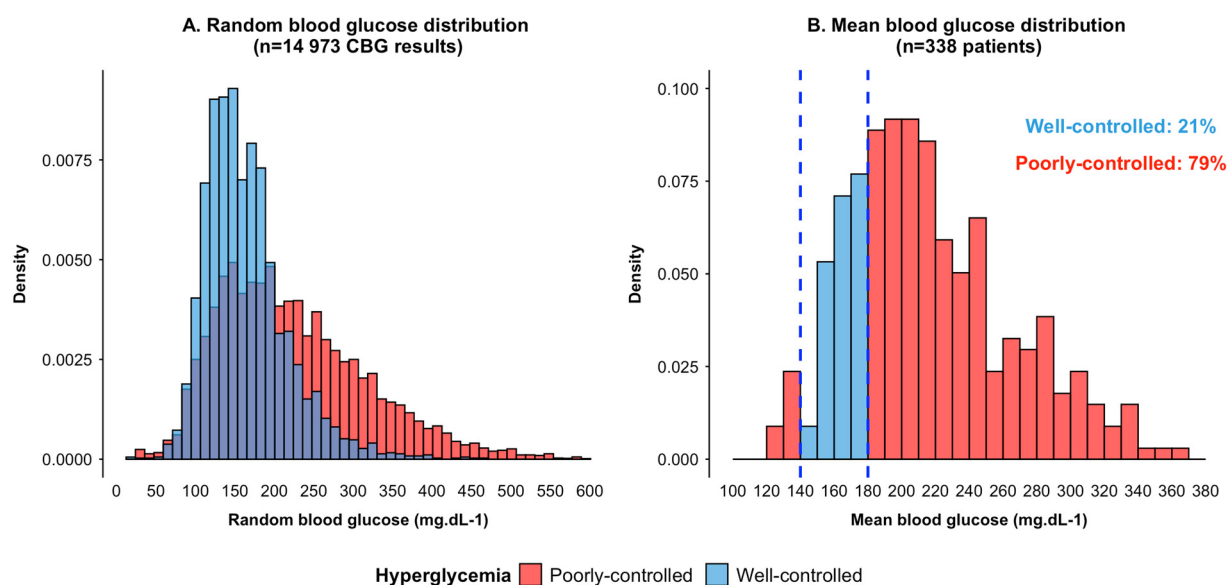


Figure 2. Histogram of capillary CBG monitoring during ICU stay. Panel (A) shows the distribution of 14,973 CBG measurements obtained from hyperglycemic patients during intensive care unit admission. Panel (B) summarizes mean CBG values for all 338 patients. The dashed lines represent the target range of mean blood glucose (140–180 mg.dL⁻¹), indicating well-controlled hyperglycemia. Abbreviations: CBG, capillary blood glucose.

3.3. Associated Factors of Glycemic Control

Multivariable logistic regression identified several independent predictors of poor glycemic control, and the final model demonstrated good calibration (Hosmer–Lemeshow $p = 0.992$) with acceptable overall performance (accuracy, 83.3%). These included pre-existing T2DM, elevated admission BG, HbA1c > 7.0% at ICU entry, and the need for IMV. Prolonged CST exposure was the only modifiable predictor, underscoring its critical role in worsening glycemic instability (Figure 3).

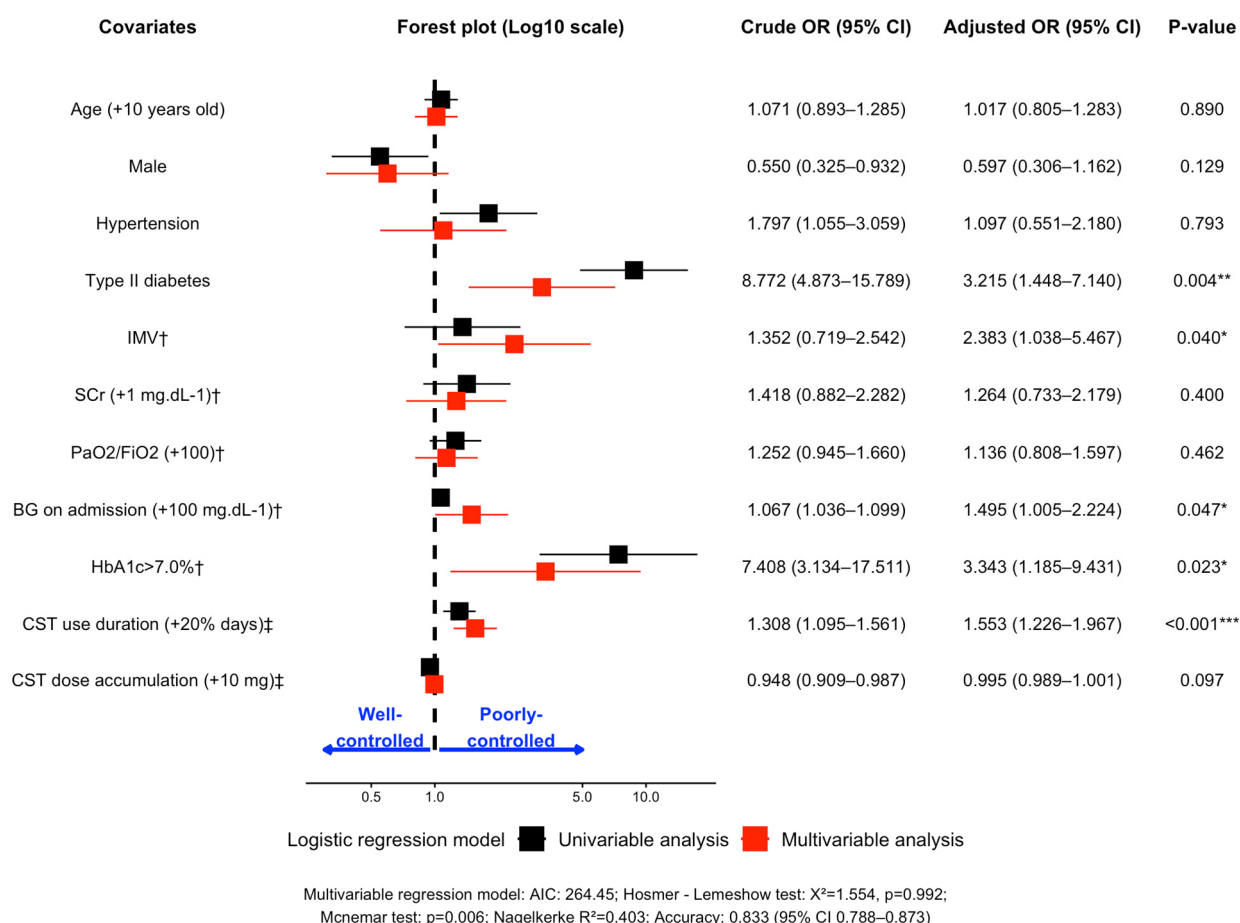


Figure 3. Forest plot of factors associated with glycemic control. Annotations: † Evaluated at the time of ICU admission; ‡ Evaluated continuously during the ICU stay; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. All variance inflation factors were <2 . Abbreviations: BG, blood glucose; CI, confidence interval; CST, corticosteroid therapy; HbA1c, hemoglobin A1c; IMV, invasive mechanical ventilation; OR, odds ratio; PaO₂/FiO₂, partial pressure of arterial oxygen to fraction of inspired oxygen ratio; SCr, serum creatinine.

3.4. Outcomes

Figure 4A demonstrates a 95% overlap in propensity scores between groups post-matching, indicating improved group comparability. Figure 4B shows that baseline imbalances were reduced after matching. Baseline characteristics, laboratory parameters, and treatments before and after PSM are presented in Supplementary S3.

In-hospital mortality was significantly higher in the poorly controlled group compared with the well-controlled group (54.8% vs. 35.5%, $p = 0.047$). This association remained robust in multivariable Cox regression of the unmatched cohort (adjusted HR 1.61, 95% CI 1.01–2.55, $p = 0.045$) and was confirmed by Kaplan–Meier survival analysis (log-rank $p = 0.041$).

Secondary outcomes, defined as composite ICU complications, did not differ significantly between groups. Rates of bacterial pneumonia, bacteremia, septic shock, acute kidney injury, and metabolic complications (hypoglycemia, diabetic ketoacidosis, hyperosmolar hyperglycemic state) were comparable between groups (Figure 5).

3.5. Sensitivity and Subgroup Analysis

Multivariable Cox regression identified six independent predictors of in-hospital mortality (Supplementary S4). Poor glycemic control was associated with a significantly increased risk of death, with an adjusted hazard ratio of 1.61 (95% CI 1.01–2.55, $p = 0.045$).

(Figure 6). Consistent with these findings, Kaplan–Meier survival analysis demonstrated significantly poorer survival among patients with poorly controlled hyperglycemia compared with those in the well-controlled group (log-rank $p = 0.006$). Other independent predictors of mortality were advanced age, procalcitonin, lower $\text{PaO}_2/\text{FiO}_2$, IMV requirement, and new-onset hyperglycemia. Subgroup analysis (Supplementary S5) showed improved survival with well-controlled hyperglycemia only in patients with T2DM or IMV requirement.

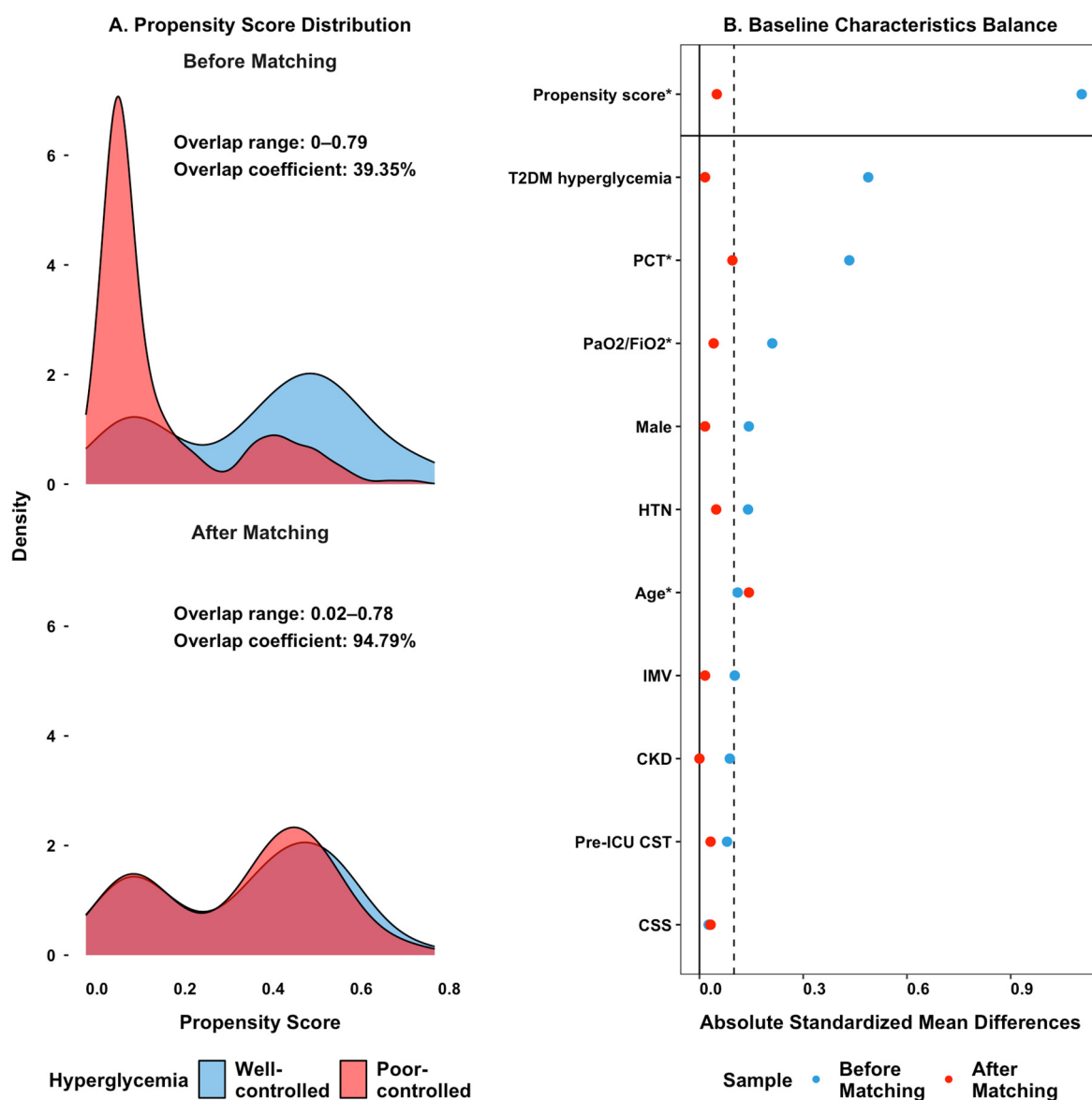


Figure 4. Propensity score matching model evaluation. (A) Distribution of propensity scores in the two groups before and after matching, demonstrating improved comparability after matching. (B) Balance of covariates before and after matching, assessed using absolute standardized mean differences. Annotations: * Variables treated as continuous in the propensity score model; the dashed vertical line indicates the threshold for acceptable covariate balance (aSMD = 0.1). Abbreviations: aSMD: absolute standardized mean difference; CKD, chronic kidney disease; CSS, cytokine storm syndrome; CST, corticosteroid therapy; HTN, hypertension; ICU, intensive care unit; IMV, invasive mechanical ventilation; PCT, procalcitonin levels; T2DM, type 2 diabetes mellitus.

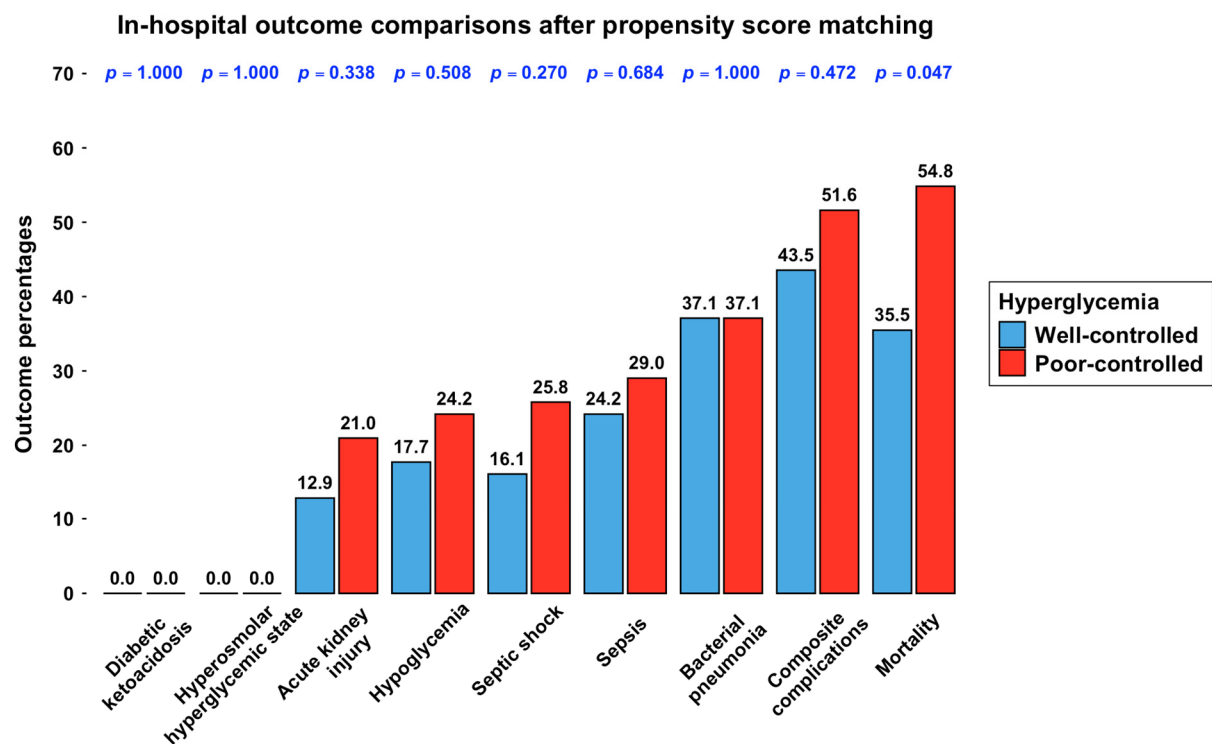


Figure 5. Post-matching outcome differences between well-controlled and poorly controlled hyperglycemia.

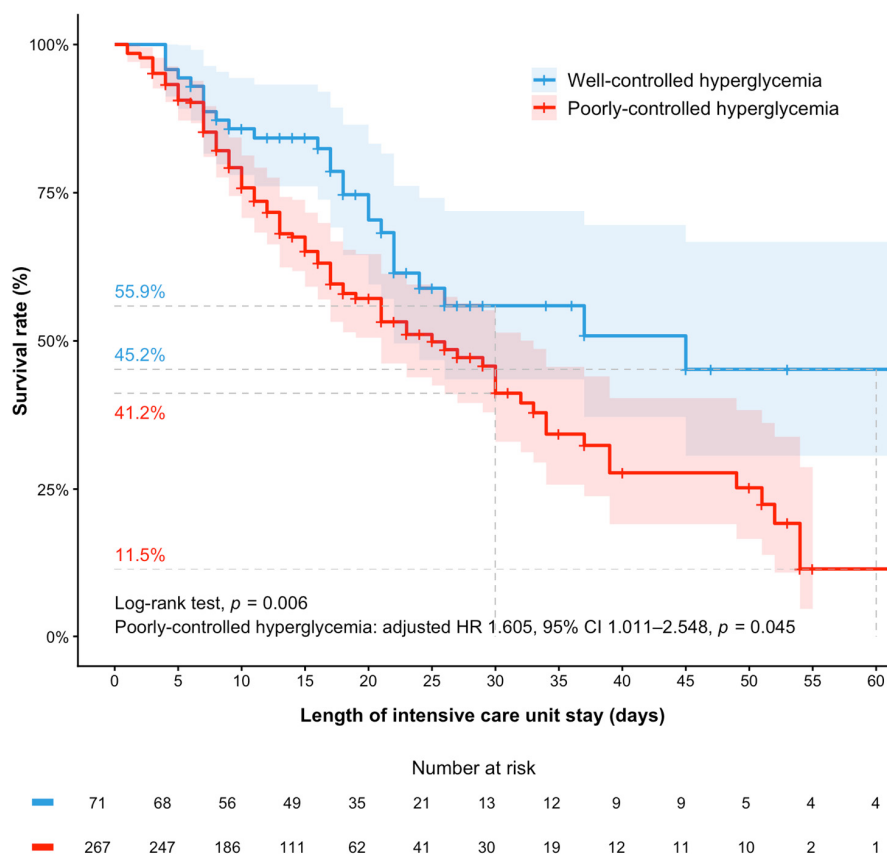


Figure 6. Kaplan–Meier survival analysis by glycemic control status. Annotations: Dashed horizontal and vertical lines indicate estimated cumulative survival rates at 30 and 60 days for each group; mortality was 43.8%, with 148 events among 338 patients. Abbreviations: CI, confidence interval; HR, hazard ratio.

4. Discussion

4.1. Burden and Clinical Impact of Poor Glycemic Control

In this retrospective ICU cohort, poorly controlled hyperglycemia was defined as mean ICU glucose outside 140–180 mg.dL⁻¹. The definition is supported by both randomized evidence and contemporary guidelines. The NICE-SUGAR trial demonstrated increased mortality and severe hypoglycemia with intensive glucose lowering, establishing moderate control as the safer strategy in critically ill patients [18]. Accordingly, current guidelines recommend a target range of 140–180 mg.dL⁻¹ for most ICU populations to balance harms from sustained hyperglycemia and hypoglycemia [26]. As these recommendations emphasize cumulative glycemic exposure rather than isolated measurements, mean ICU glucose provides a pragmatic and clinically meaningful indicator of failure to achieve guideline-concordant glycemic control. Our findings showed that this poorly controlled hyperglycemia was highly prevalent (79% of patients with hyperglycemia) and independently associated with higher in-hospital mortality after adjustment with propensity score matching and multivariable Cox regression (adjusted HR $\approx$ 1.61). These findings align with prior observations that hyperglycemia in severe COVID-19 is common and portends adverse outcomes [2–4]. They also converge with studies linking better inpatient glucose control to improved survival and fewer complications [12,13]. Our study adds weight to this evidence base by combining a relatively large sample ($n = 338$) with high-frequency capillary measurements ($\sim 15,000$ readings) and contemporary causal-inference methods (propensity score matching and time-to-event modeling), thereby improving internal validity while acknowledging the constraints of observational design [27,28]. Clinically, these data support approaching hyperglycemia in the ICU as both a marker of severity and a modifiable therapeutic target that warrants systematic, protocolized management.

4.2. Determinants of Poor Control: The Role of Corticosteroids

Multivariable analysis identified several non-modifiable predictors of poor control, including pre-existing type 2 diabetes, elevated admission glucose, higher HbA1c at ICU entry, and the need for invasive mechanical ventilation, consistent with prior reports in severe COVID-19 [3,4]. Importantly, the duration of corticosteroid therapy emerged as the only modifiable independent predictor. This observation is biologically plausible and concordant with the literature demonstrating dexamethasone-associated hyperglycemia and dose-response insulin resistance in COVID-19 [5], as well as the increased incidence of hyperglycemia reported with higher steroid dosing strategies [9]. Together, these data suggest that while corticosteroids remain a cornerstone of care for severe COVID-19 and ARDS, their metabolic liabilities can undermine glycemic stability unless proactively managed. In practice, this supports individualized steroid stewardship (dose, duration, taper) in parallel with anticipatory insulin protocols and close monitoring.

4.3. Implications for ICU Practice Beyond COVID-19

Although generated during the Delta wave in a largely unvaccinated population, the patterns observed here extend beyond COVID-19. Stress hyperglycemia and steroid-induced hyperglycemia are pervasive problems across critical illness, including ARDS and sepsis [11]. Current guidance generally targets 140–180 mg/dL for most ICU patients [10], which our data reinforce as a pragmatic range that remains difficult to sustain without structured protocols. The high variability and low time-in-range seen even among “well-controlled” patients underscore the need for high-frequency bedside monitoring, early insulin initiation in patients at risk (e.g., known diabetes, HbA1c $> 7\%$), and systematic review of steroid exposure as part of routine ICU quality improvement. Notably, while some meta-analyses have reported associations between insulin therapy and adverse

outcomes [10], these likely reflect confounding by indication; other studies observed lower mean glucose and improved survival when hyperglycemia was effectively treated [29]. Our finding of greater insulin requirements among poorly controlled patients is most consistent with severity-driven treatment needs rather than harm from insulin per se.

4.4. Secondary Outcomes and Interpretation

After matching, we observed higher mortality with poor glycemic control, whereas differences in other complications were not statistically significant. This pattern suggests that glycemic control may primarily capture global illness severity and resilience rather than specific organ complications in this population. It also emphasizes that mortality is the most sensitive endpoint for hyperglycemia-related risk in severe COVID-19 cohorts, a result consistent with prior work [4,12]. Future studies powered for specific complications and incorporating continuous glucose monitoring could clarify organ-specific effects.

4.5. Limitations

This study has limitations. First, the retrospective, single-center design and the temporal overlap between hyperglycemic control, related factors, and outcomes limit causal inference and generalizability. Second, the cohort reflects a particular phase of the pandemic (Delta variant; low vaccination coverage) and resource constraints, which may differ from current ICU contexts and non-COVID critical illness. Third, potential confounders such as nutritional strategy, vasopressor exposure, and fluid balance were not captured, and information bias, as well as residual confounding due to missing laboratory data, remain inherent limitations that could influence glycemic dynamics. Fourth, definitions of “well-controlled” glycemia vary across studies; we selected a 140–180 mg.dL⁻¹ target consistent with hospital standards and prior guidance [17], and supported its face validity using variability indices and time-in-range. However, reliance on mean BG rather than time-weighted or continuous measures may underestimate transient glycemic fluctuations. Finally, while propensity score matching and multivariable modeling reduce imbalance, residual confounding is possible [24,25].

5. Conclusions

In a large ICU cohort with high-frequency glucose monitoring, poor glycemic control was common and independently associated with increased in-hospital mortality. Prolonged corticosteroid exposure was associated with poorer glycemic control, suggesting a potentially modifiable contributor to hyperglycemia in critically ill patients. However, given the observational nature of this study, these findings should be considered hypothesis-generating rather than prescriptive with respect to corticosteroid dosing or duration. They underscore the need for future prospective studies to better define optimal steroid strategies that balance established clinical benefits with metabolic risks. Meanwhile, these findings support vigilant glucose monitoring, timely and protocolized insulin therapy, and careful steroid stewardship in critically ill patients, with relevance that extends beyond COVID-19 to broader ICU practice.

Supplementary Materials: The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/diabetology7020038/s1>: Supplementary S1. Protocol for glycemic control intensive care unit [18,30–38]. Supplementary S2. Line graph comparing mean blood glucose variability throughout ICU stay between poorly controlled and well-controlled groups. A total of 14,976 capillary blood glucose measurements were performed. Group comparisons were conducted using independent Student’s *t*-test or Mann–Whitney U test, depending on data distribution. Note: *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$. Abbreviation: ICU: intensive care unit. Supplementary S3. Baseline characteristics, laboratory parameters, and treatments of poor-controlled and well-

controlled hyperglycemia before and after propensity score matching. Abbreviations: Anti-Xa, anti-factor Xa; BG, blood glucose; CSS, cytokine storm syndrome; CKD, chronic kidney disease; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CST, corticosteroid therapy; CVD, cardiovascular disease; HTN, hypertension; ICU, intensive care unit; IMV, invasive mechanical ventilation; $\text{PaO}_2/\text{FiO}_2$, ratio of arterial oxygen partial pressure to fraction of inspired oxygen; PCT, procalcitonin; SIRS, systemic inflammatory response syndrome; T2DM, type 2 diabetes mellitus. Supplementary S4. Forest plot depicting the Cox regression model identifying factors associated with mortality rate. Annotations: † Evaluated at the time of ICU admission, ‡ Evaluated continuously during the ICU stay. Mortality was 43.8% in the total population (148/338), 39.4% in the well-controlled group (105/267), and 44.9% in the poorly controlled group (32/71). All variance inflation factors were <2. The proportional hazards assumption was assessed using Schoenfeld residuals, with no significant violations. Abbreviations: AST, aspartate aminotransferase; CCS, cytokine storm syndrome; CI, confidence interval; HR, hazard ratio; IMV, invasive mechanical ventilation; PCT, procalcitonin; $\text{PaO}_2/\text{FiO}_2$, partial pressure of arterial oxygen to fraction of inspired oxygen ratio; SCr, serum creatinine; SIRS, systemic inflammatory response syndrome; WBC, white blood cell. Supplementary S5. Subgroup analysis of all-cause mortality comparing well-controlled versus poorly controlled hyperglycemia using adjusted hazard ratios. Abbreviations: CI, confidence interval; CSS, cytokine storm syndrome; HR, hazard ratio; IMV, invasive mechanical ventilation; $\text{PaO}_2/\text{FiO}_2$, ratio of arterial oxygen partial pressure to fraction of inspired oxygen; PCT, procalcitonin; SCr, serum creatinine; SIRS, systemic inflammatory response syndrome; T2DM, type 2 diabetes mellitus; WBC, white blood cell count.

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Institutional Review Board Statement: The authors are accountable for all aspects of the work and ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This retrospective study did not influence the patients' diagnosis, treatment, or follow-up. This study adhered to the ethical guidelines established by the Declaration of Helsinki. The Ethics Council in Biomedical Research of University Medical Center Ho Chi Minh City granted the study's ethical approval on 28 September 2023 (Approval No. 854/HĐĐĐ-ĐHYD).

Informed Consent Statement: Individual consent for this retrospective analysis was waived.

Data Availability Statement: The datasets used in this study can be obtained from the corresponding author upon reasonable request.

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References

1. World Health Organization (WHO). COVID-19 Epidemiological Update—14 March 2025. Available online: <https://www.who.int/publications/m/item/covid-19-epidemiological-update-edition-177> (accessed on 9 November 2025).

2. Zahedi, M.; Kordrostami, S.; Kalantarhormozi, M.; Bagheri, M. A Review of Hyperglycemia in COVID-19. *Cureus* **2023**, *15*, e37487. [CrossRef]
3. Le, V.T.; Ha, Q.H.; Tran, M.T.; Le, N.T.; Le, V.T.; Le, M.K. Hyperglycemia in Severe and Critical COVID-19 Patients: Risk Factors and Outcomes. *Cureus* **2022**, *14*, e27611. [CrossRef]
4. Nguyen, T.L.; Le, N.H. The blood glucose disorders of severe and critical ill COVID-19 patients at COVID-19 patients treatment hospital Ha Noi Medical University Hospital. *VMJ* **2023**, *525*, 259–263. [CrossRef]
5. Rhou, Y.J.J.; Hor, A.; Wang, M.; Wu, Y.F.; Jose, S.; Chipps, D.R.; Cheung, N.W. Dexamethasone-induced hyperglycaemia in COVID-19: Glycaemic profile in patients without diabetes and factors associated with hyperglycaemia. *Diabetes Res. Clin. Pract.* **2022**, *194*, 110151. [CrossRef]
6. Liao, W.I.; Wang, J.C.; Chang, W.C.; Hsu, C.W.; Chu, C.M.; Tsai, S.H. Usefulness of Glycemic Gap to Predict ICU Mortality in Critically Ill Patients with Diabetes. *Medicine* **2015**, *94*, e1525. [CrossRef]
7. Egi, M.; Bellomo, R.; Stachowski, E.; French, C.J.; Hart, G.K.; Hegarty, C.; Bailey, M. Blood glucose concentration and outcome of critical illness: The impact of diabetes. *Crit. Care Med.* **2008**, *36*, 2249–2255. [CrossRef] [PubMed]
8. Huang, J.; Li, J.; Chen, X.; Gu, J. Stress-induced hyperglycemia and mortality of non-diabetic patients with sepsis: A meta-analysis. *Front. Endocrinol.* **2025**, *16*, 1688494. [CrossRef] [PubMed]
9. RECOVERY Collaborative Group. Higher dose corticosteroids in patients admitted to hospital with COVID-19 who are hypoxic but not requiring ventilatory support (RECOVERY): A randomised, controlled, open-label, platform trial. *Lancet* **2023**, *401*, 1499–1507. [CrossRef]
10. Yang, Y.; Cai, Z.; Zhang, J. Insulin Treatment May Increase Adverse Outcomes in Patients With COVID-19 and Diabetes: A Systematic Review and Meta-Analysis. *Front. Endocrinol.* **2021**, *12*, 696087. [CrossRef]
11. Chander, S.; Deepak, V.; Kumari, R.; Leys, L.; Wang, H.Y.; Mehta, P.; Sadarat, F. Glycemic Control in Critically Ill COVID-19 Patients: Systematic Review and Meta-Analysis. *J. Clin. Med.* **2023**, *12*, 2555. [CrossRef]
12. Zhu, L.; She, Z.G.; Cheng, X.; Qin, J.J.; Zhang, X.J.; Cai, J.; Lei, F.; Wang, H.; Xie, J.; Wang, W.; et al. Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes. *Cell Metab.* **2020**, *31*, 1068–1077.e3. [CrossRef]
13. Kapoor, R.; Timsina, L.R.; Gupta, N.; Kaur, H.; Vidger, A.J.; Pollander, A.M.; Jacobi, J.; Khare, S.; Rahman, O. Maintaining Blood Glucose Levels in Range (70–150 mg/dL) is Difficult in COVID-19 Compared to Non-COVID-19 ICU Patients-A Retrospective Analysis. *J. Clin. Med.* **2020**, *9*, 3635. [CrossRef] [PubMed]
14. Vandembroucke, J.P.; von Elm, E.; Altman, D.G.; Gotzsche, P.C.; Mulrow, C.D.; Pocock, S.J.; Poole, C.; Schlesselman, J.J.; Egger, M.; Initiative, S. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): Explanation and elaboration. *PLoS Med.* **2007**, *4*, e297. [CrossRef] [PubMed]
15. World Health Organization (WHO). Diagnostic Testing for SARS-CoV-2. Available online: <https://www.who.int/publications/i/item/diagnostic-testing-for-sars-cov-2> (accessed on 9 November 2025).
16. World Health Organization (WHO). *Clinical Management of COVID-19: Living Guideline, June 2025*; WHO: Geneva, Switzerland, 2025. [CrossRef]
17. American Diabetes Association Professional Practice Committee. 16. Diabetes Care in the Hospital: Standards of Care in Diabetes-2024. *Diabetes Care* **2024**, *47*, S295–S306. [CrossRef] [PubMed]
18. The NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N. Engl. J. Med.* **2009**, *360*, 1283–1297. [CrossRef]
19. Mehta, P.; McAuley, D.F.; Brown, M.; Sanchez, E.; Tattersall, R.S.; Manson, J.J.; HLH Across Speciality Collaboration, UK. COVID-19: Consider cytokine storm syndromes and immunosuppression. *Lancet* **2020**, *395*, 1033–1034. [CrossRef]
20. Bone, R.C.; Balk, R.A.; Cerra, F.B.; Dellinger, R.P.; Fein, A.M.; Knaus, W.A.; Schein, R.M.; Sibbald, W.J. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Chest* **1992**, *101*, 1644–1655. [CrossRef]
21. Singer, M.; Deutschman, C.S.; Seymour, C.W.; Shankar-Hari, M.; Annane, D.; Bauer, M.; Bellomo, R.; Bernard, G.R.; Chiche, J.D.; Cooper-Smith, C.M.; et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* **2016**, *315*, 801–810. [CrossRef]
22. Khwaja, A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin. Pract.* **2012**, *120*, c179–c184. [CrossRef]
23. American Diabetes Association Professional Practice Committee. 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes-2025. *Diabetes Care* **2025**, *48*, S128–S145. [CrossRef]
24. Austin, P.C. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. *Multivar. Behav. Res.* **2011**, *46*, 399–424. [CrossRef] [PubMed]
25. Stuart, E.A. Matching methods for causal inference: A review and a look forward. *Stat. Sci.* **2010**, *25*, 1–21. [CrossRef]
26. American Diabetes Association Professional Practice Committee. 16. Diabetes Care in the Hospital: Standards of Care in Diabetes-2025. *Diabetes Care* **2025**, *48*, S321–S334. [CrossRef]
27. Austin, P.C. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat. Med.* **2009**, *28*, 3083–3107. [CrossRef]

28. Heinz, P.; Wendel-Garcia, P.D.; Held, U. Impact of the matching algorithm on the treatment effect estimate: A neutral comparison study. *Biom. J.* **2024**, *66*, e2100292. [[CrossRef](#)]
29. Sardu, C.; D'Onofrio, N.; Balestrieri, M.L.; Barbieri, M.; Rizzo, M.R.; Messina, V.; Maggi, P.; Coppola, N.; Paolisso, G.; Marfella, R. Outcomes in Patients with Hyperglycemia Affected by COVID-19: Can We Do More on Glycemic Control? *Diabetes Care* **2020**, *43*, 1408–1415. [[CrossRef](#)] [[PubMed](#)]
30. Egi, M.; Finfer, S.; Bellomo, R. Glycemic control in the ICU. *Chest* **2011**, *140*, 212–220. [[CrossRef](#)] [[PubMed](#)]
31. Farrokhi, F.; Smiley, D.; Umpierrez, G.E. Glycemic control in non-diabetic critically ill patients. *Best. Pract. Res. Clin. Endocrinol. Metab.* **2011**, *25*, 813–824. [[CrossRef](#)]
32. Hassan, E. Hyperglycemia management in the hospital setting. *Am. J. Health Syst. Pharm.* **2007**, *64*, S9–S14. [[CrossRef](#)]
33. Inzucchi, S.E. Clinical practice. Management of hyperglycemia in the hospital setting. *N. Engl. J. Med.* **2006**, *355*, 1903–1911. [[CrossRef](#)]
34. Inzucchi, S.E.; Siegel, M.D. Glucose control in the ICU—how tight is too tight? *N. Engl. J. Med.* **2009**, *360*, 1346–1349. [[CrossRef](#)] [[PubMed](#)]
35. Kavanagh, B.P.; McCowen, K.C. Clinical practice. Glycemic control in the ICU. *N. Engl. J. Med.* **2010**, *363*, 2540–2546. [[CrossRef](#)]
36. Kollef, M.H. *The Washington Manual of Critical Care*, 1st ed.; Lippincott Williams & Wilkins: Philadelphia, PA, USA, 2008; Volume VI, pp. 209–215.
37. Maerz, L.L.; Akhtar, S. Perioperative glycemic management in 2011: Paradigm shifts. *Curr. Opin. Crit. Care* **2011**, *17*, 370–375. [[CrossRef](#)] [[PubMed](#)]
38. Marik, P.E.; Preiser, J.C. Toward understanding tight glycemic control in the ICU: A systematic review and metaanalysis. *Chest* **2009**, *137*, 544–551. [[CrossRef](#)] [[PubMed](#)]

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