VIA MEDICA
RESEARCH PAPER
ISSN 2450–7458
e-ISSN 2450–8187

Burhan Gunawan[1, 2], Raymond Sebastian Purwanta[1], Jennifer[1], Soesilowati Soerachmad[1], Liana Dewi Hendrawan[1, 2]
[1]Department of Internal Medicine, Sumber Waras Hospital, West Jakarta, Indonesia
[2]Diabetes Initiative Indonesia

Glycemic Variability as an Independent Predictor of 30-Day Mortality in Type 2 Diabetes Individuals with Sepsis in the Intensive Care Unit

ABSTRACT

Objective: Diabetes individuals are more likely to develop dysglycemia in 72 hours after intensive care admission and are associated with mortality. This retrospective study aimed to determine the role of glycemic variability (GV) in mortality in individuals with type 2 diabetes (T2D) with sepsis in the intensive care unit (ICU).

Materials and methods: Adult individuals diagnosed with sepsis or septic shock and T2D who were admitted to the ICU between January 2022 and June 2024 were include in the study. The GV parameters of mean amplitude of glucose excursion (MAGE) and the glucose coefficient of variation (GluCV) were used to determined survival at 30 days and length of stay (LoS). Acute Physiology and Chronic Health Evaluation-IV (APACHE-IV) and the Sequential Organ Failure Assessment (SOFA) score were used for comparison with the GV parameters for the survival outcome.

Results: A total 233 individuals were included for final analysis, divided into high GV (39.48%) and low GV (60.52%) based on a cut-off MAGE of 65 mg/dL. The low-GV group had a significantly lower mortality rate (1.4% vs. 97.8%, p = 0.000). The was no significant difference in LoS using MAGE (p = 0.14), but the difference became significant using GluCV < 25% (p = 0.029). Multivariate analysis with linear logistic regression showed that APACHE-IV, SOFA, hypoglycemic episode, MAGE, and GluCV were independently associated with survival at 30 days. Survival analysis showed a significant difference in the estimated survival time for patients with low MAGE (29.65 vs. 4.24 days, p = 0.000).

Conclusions: High glycemic variability was observed in 39% of individuals; it was associated with higher mortality in diabetic individuals with sepsis and was independently associated with high 30-day mortality. (Clin Diabetol 2025; 14, 1: 18–25)

Keywords: diabetes mellitus, sepsis, glycemic variability, APACHE-IV, SOFA

Address for correspondence:
Burhan Gunawan
Department of Internal Medicine, Sumber Waras Hospital
Kyai Tapa Street Number 1, West Jakarta, 11460, Indonesia
E-mail: burhangunawan99@gmail.com
Clinical Diabetology 2025, 14; 1: 18–25
DOI: 10.5603/cd.102762
Received: 24.09.2024 Accepted: 4.12.2024
Early publication date: 27.01.2025

Introduction

Sepsis is prevalent among critically ill individuals and results from a dysregulated immune response to infections and organ damage. This encompasses exaggerated

inflammatory, immunosuppressive, vascular leakage, and coagulative processes [1, 2]. Moreover, the incidence of sepsis remains high in high-risk individuals, such as those with diabetes mellitus (DM), cancer, the elderly, and the immunocompromised [1]. The prevalence of sepsis using the Sepsis-3 criteria is 22.4%, and it contributes to 11 million deaths annually or 20% of global deaths. The mortality remains high at 30–45% with more than one-third of individuals dying within 90 days, especially in low- and middle-income countries [2–4]. Respiratory, intra-abdominal, and urinary infections with gram-negative bacteria predominate in the etiology of sepsis [4].

Glucometabolic disorders are highly prevalent in critically ill individuals and adversely affect their prognosis. The activation of stress induces hyperglycemia and increases glycemic variability (GV). Although acute GV is closely associated with endothelial cell damage and leads to endothelial dysfunction [5], Magee et al. found that early fluctuation of blood glucose increased 30-day mortality and all-cause hospital mortality in sepsis individuals [6]. Lu et al. also stated that GV level during intensive care unit (ICU) hospitalization is relevant to septic prognosis [5]. However, there has been no standard consensus on a standard definition of glycemic variability until now. Available metrics of GV, such as coefficient variation (CV), mean amplitude of glucose excursion (MAGE), and glycemic lability index (GLI), are associated with increased mortality in sepsis, and the lower variability has a protective effect on sepsis [7, 8]. The exact targets for these parameters need to be established.

Individuals with diabetes are more likely to develop dysglycemia in 72 hours after intensive care admission. The event of hypoglycemia may be exaggerated in individuals with diabetes and is closely associated with worse outcomes and mortality [9, 10]. Moreover, the practical implication of MAGE and CV are still limited in sepsis patients in the ICU setting and need to be clarified. Therefore, we conducted a retrospective study to determine the role of glycemic variability (GV) in mortality in type 2 diabetes (T2D) individuals with sepsis in the ICU setting. We hypothesized that higher GV adversely affects the outcome in individuals with diabetes and sepsis.

Materials and methods

Subjects

Adult individuals diagnosed with sepsis or septic shock and T2D, admitted to the ICU between January 2022 and June 2024, were screened for eligibility according to the following criteria: 1) age 18–80 years; 2) quick sequential organ failure assessment (qSOFA) score ≥ 2 points within 24 h of admission; 3) history of diabetes treatment, and 4) minimum routine BG monitoring every 8 h in the ICU. The exclusion criteria were as follows: 1) discharge or death within 2 days of admission; 2) fewer than 3 records of BG per day in the ICU; 3) on high-dose corticosteroid therapy (dexamethasone > 6 mg daily or equivalent); and 4) concurrent major operative procedure, hemorrhagic stroke, tumors, pregnancy, blood diseases, and active bleeding.

Study design

This was a retrospective, exploratory study based on a review of the medical records of adult intensive care individuals at a secondary hospital (Sumber Waras Hospital, affiliated with the Faculty of Medicine, Tarumanagara University, Jakarta, Indonesia). This ICU has 7 critical beds. Individuals admitted to the ICU were treated based on the national intensive glucose regulation protocol, in which insulin is used for glucose control to maintain targets of 80–180 mg/dL (4.4–10 mmol/L). The initial dose of rapid-acting insulin drip was 0.5–1 U/h. The blood glucose (BG) target was 140–180 mg/dL with a decrement of 60 mg/dL per hour. If BG < 100 mg/dL, the insulin drip is stopped. The insulin dose reduces by 50% per hour and increases by 25% per hour if BG 100–140 mg/dL and > 180 mg/dL, respectively.

In the event of hypoglycemia, 50 mL of 25% dextrose solution (DS) was injected, followed by a 10% DS intravenous drip, and the BG was re-tested after one hour.

Data collection

Diabetes was diagnosed according to American Diabetes Association (ADA) 2023 [11]. Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction was defined as an increase in the quick Sequential (sepsis-related) Organ Failure Assessment (qSOFA) score by ≥ 2 points. Septic shock is a type of sepsis characterized by profound circulatory, cellular, and metabolic abnormalities associated with a greater risk of mortality than sepsis alone [12]. We quantify the sepsis-related critical score: APACHE-IV score (with online calculator: https://intensivecarenetwork.com/Calculators/Files/Apache4.html) and SOFA score.

The minimum routine BG level was measured applied every 8 h, depending on the individual's condition. All patients underwent 3 or more measurements on recording days. We used 2 parameters to assess glucose variation: mean amplitude of glucose excursion (MAGE) and glucose coefficient of variation (GluCV). Briefly, MAGE is a mean blood glucose value exceeding the standard deviation from the 24-h mean blood glucose level, whereas GluCv is the percentage ratio of

the standard deviation (SD) to the mean glucose level. According to scientific literature, the value of MAGE in patients without DM is nearly 30–40 mg/dL and nearly 60–70 mg/dL for cardiovascular events [13, 14]. In the studies from Furushima et al. [13] and Asakasa et al. [14], they found that MAGE > 65 mg/dL caused a significantly higher rate of cardiovascular events and mortality in ICU settings. The MAGE cut-off applied in this study was 65 mg/dL, based on the studies above. For the GluCV, Chao et al. [15] used a cut-off of 30% in their study and found that diabetic individuals with CV > 30% had worse outcomes which were independently associated with mortality. We decided to classify them into 3 groups: < 25%, 25–50%, and > 50%, to minimize the bias and increase the sensitivity [15].

Statistical analysis

The primary outcome was 30-day survival and length of stay (LoS) in low and high glucose variations based on MAGE and GluCV values. The secondary outcomes were 1) the significance of MAGE and GluCV in relation to 30-day mortality, 2) the sensitivity and specificity of MAGE and GluCV to predict 30-day mortality.

The minimum sample size calculated using G*Power software (power 0.80, alpha 0.05) for correlation analysis between the 2 groups was 201 participants.

Differences between the 2 groups were analyzed using Student's t test or the Mann-Whitney U test. The chi-squared test or Fisher's exact test was used for categorical variables. The correlation between MAGE and GluCV was analyzed using Pearson correlation. Kaplan-Meier analysis was used to test the association between 30-day mortality and acute GV using the cut-off MAGE and gluCV percentage. Variables were considered to be included in the multivariate analysis if the univariate p value was < 0.20. A linear regression model was constructed to identify independent variables that predicted 30-day mortality. The sensitivity and specificity of MAGE and GluCV for predicting mortality were analyzed using receiver operating characteristic (ROC) curves. Statistical significance was set at a two-sided p-value of < 0.05. All data were analyzed using SPSS software version 26.0 (SPSS Inc., Chicago, IL, USA).

Ethics statement

The present study protocol was reviewed and approved by the Institutional Review Board of the Sumber Waras Research Ethics Committee (approval No. 23/ /RSSW/KoM.EP/EC/V/2024)

Results

A total of 301 consecutive individuals were admitted to the medical ICU due to sepsis and T2D between January 2022 and June 2024; of these, 68 were excluded because lack of BG measurement, concurrent major operative procedure, and diagnosis of diabetic ketoacidosis/hyperosmolar hyperglycemia syndrome. The remaining 233 individuals were eligible for analysis and divided into high GV (n = 92, 39.48%) and low GV (n = 141, 60.52%) based on MAGE 65 mg/dL as a cut-off point. The Supplementary Figure 1 illustrates the subject flow in the study.

Table 1 summarizes the demographics, comorbidities, sepsis-related data, glycemic data, insulin prescriptions, and outcomes. The mean age was 60.49 ± 12.04 years, and 47.21% of subjects were female. The most common underlying comorbidity was cerebrovascular disease (50.21%), followed by congestive heart failure (36.91%). Septic shock was diagnosed in 34.76% of individuals, with a mean SOFA score of 10.43 ± 6.10. The mean MAGE and GluCV values were 58.18 ± ± 20.50 mg/dL and 28.04 ± 18.23%, respectively. The low-GV group had fewer comorbidities (1.62 vs. 1.98), a lower rate of septic shock (53.27% vs. 22.70%), lower APACHE-IV score (48.11 vs. 182.01), lower SOFA score (6.19 vs. 16.95), lower rate of mechanical ventilation (31.91% vs. 83.69%), and fewer hypoglycemic episodes (0.10 vs. 2.69). A full comparison of each variable in the 2 groups (low and high MAGE) is presented in Table 1.

The low-GV group showed significantly lower mortality rate [1.4% vs. 97.8%, p = 0.000, odds ratio (OR) = 68.49 (17.27–271.25)] compare to high GV. The GluCV < 25% showed a significantly lower mortality rate rather than 25–50% and > 50% groupw (0.8% vs. 83.6% vs. 100%, p = 0.000). There was no significant difference in ICU LoS using MAGE (p = 0.14), but it became significant using GluCV. A GluCV < 25% show significantly shorter LoS in ICU (p = 0.029). MAGE and GluCV also showed strong correlation (r = 0.930), where 92.1% low GV group had GluCV < 25%. A full description and analysis are presented in Table 2 and Figure 1.

Multivariate analysis with linear logistic regression was performed with variables that had a p-value < 0.20 (Suppl. Tab. 1). The APACHE-IV score (p = 0.001), SOFA score (0.000), number of hypoglycemic episodes (p = 0.000), MAGE (p = 0.000), and GluCV (p = 0.001) were significant independently associated with 30-day survival.

The mean estimated survival time of the low-MAGE group using Kaplan-Meier survival analysis in the 30-day observation was longer than in the high-MAGE group (29.65 vs. 4.24 days, respectively, p = 0.000). When using GluCV as a classifier, GluCV < 25% showed the longest survival time (29.79 vs. 8.37 vs. 3.16 days,

Table 1. Baseline Characteristics

	Low glucose variability (MAGE ≤ 65 mg/dL) (n = 141)	High glucose variability (MAGE > 65 mg/dL) (n = 92)	P-value
Age [years]	59.5 ± 12.0	61.9 ± 11.9	0.151
Female (%)	66 (46.8)	44 (47.8)	0.980
Comorbidities			
Cerebrovascular disease (%)	64 (45.4)	53 (57.6)	0.004*
Congestive heart failure (%)	34 (24.1)	52 (56.5)	0.003*
Kidney disease (%)	32 (22.7)	38 (41.3)	0.108
Myocardial infarct (%)	18 (12.8)	36 (39.1)	0.002*
Lung disease (%)	20 (14.2)	16 (17.4)	0.251
Hematological disease (%)	22 (15.6)	11 (12.0)	0.002*
Liver disease (%)	1 (0.7)	3 (3.3)	0.374
Malnutrition (%)	0 (0)	4 (4.33)	0.119
Individual comorbidity number (n)	1.6 ± 1.0	2.0 ± 1.0	0.009
Sepsis-related data			
Sepsis (%)	109 (77.3)	43 (46.7)	< 0.001*
Septic Shock (%)	32 (22.7)	49 (53.3)	< 0.001*
APACHE-IV Score	48.1 ± 31.6	182.0 ± 43.9	< 0.001**
SOFA Score	6.2 ± 2.7	17.0 ± 3.6	< 0.001**
Mechanical ventilation (%)	45 (31.9)	77 (83.7)	< 0.001*
Glycemic parameter			
Mean glucose at day-1 [mg/dL]	172.9 ± 12.5	147.5 ± 67.0	< 0.001**
Mean glucose during observation [mg/dL]	170.4 ± 9.3	154.0 ± 58.9	< 0.001**
MAGE [mg/dL]	24.1 ± 11.3	110.0 ± 35.4	< 0.001**
GluCV category			
Mean percentage (%)	14.4 ± 6.6	48.7 ± 7.4	< 0.001**
< 25% (n)	128 (90.8)	2 (2.2)	
25–50% (n)	13 (9.2)	40 (43.5)	
> 50% (n)	0 (0)	30 (32.6)	
Total hypoglycemic episodes (n)	0.1 ± 0.4	2.7 ± 0.9	< 0.001**
Outcome			
ICU LoS (days)	3.5 ± 2.0	3.9 ± 2.3	0.140
Mortality at D-30 (%)	3 (2.1)	90 (97.8)	< 0.001**

*p-value < 0.05 comparison using chi-square test; **p-value < 0.05 comparison using independent t-test

APACHE-IV — Acute Physiology and Chronic Health Evaluation-IV; GluCV — glucose coefficient of variation; ICU — intensive care unit; LoS — length of stay; MAGE — mean amplitude glucose excursion; SOFA — Sequential Organ Failure Assessment

p = 0.000) compared to GluCV 25–50% and > 50% (Fig. 2). MAGE and GluCV showed excellent sensitivity and specificity for predicting 30-day survival for sepsis individuals with T2D. The area under the curve (AUC) in the ROC analysis was 0.998 and 0.992 for MAGE and GluCV, respectively. The Supplementary Figure 2 shows the ROC curve.

Discussion

This study explored the association between GV and short-term mortality in T2D individuals with sepsis in an ICU setting. Based on the investigation of 233 medical records and 2559 glucose measurements, GV was prevalent in sepsis and T2D individuals. We found that 39% of individuals had high GV, reflected by MAGE > 65 mg/dL and GluCV > 25%. High MAGE and GluCV > 25% were independent variables for mortality in 30-day observation. The low-GV group also had a lower rate of critical related parameters, including the APACHE-IV and SOFA scores.

Glycemic variability, defined as the fluctuation of blood glucose levels that occurs throughout the day, includes hypoglycemic episodes and postprandial hyperglycemia [16]. Variability in blood glucose levels is

Table 2. Association between MAGE and GluCV with Survival and ICU LoS

	Mortality [n (%)]		ICU LoS (days)	
MAGE				
Low (≤ 65 mg/dL)	2 (1.4%)	p = 0.000*, OR = 68.5 (17.3-271.3)	3.5 ± 2.0	p = 0.140
High (> 65 mg/dL)	91 (97.8%)		3.9 ± 2.3	
GluCV				
< 25%	1 (0.8%)		3.5 ± 0.3	
25–50%	61 (83.6%)	p = 0.000*	3.2 ± 0.1	p = 0.029**
> 50%	31 (100%)		4.2 ± 0.1	

*p-value < 0.05 comparison using chi-square test; ** p-value < 0.05 comparison using independent t-test
GluCV — glucose coefficient of variation; ICU — intensive care unit; LoS — length of stay; MAGE — mean amplitude glucose excursion

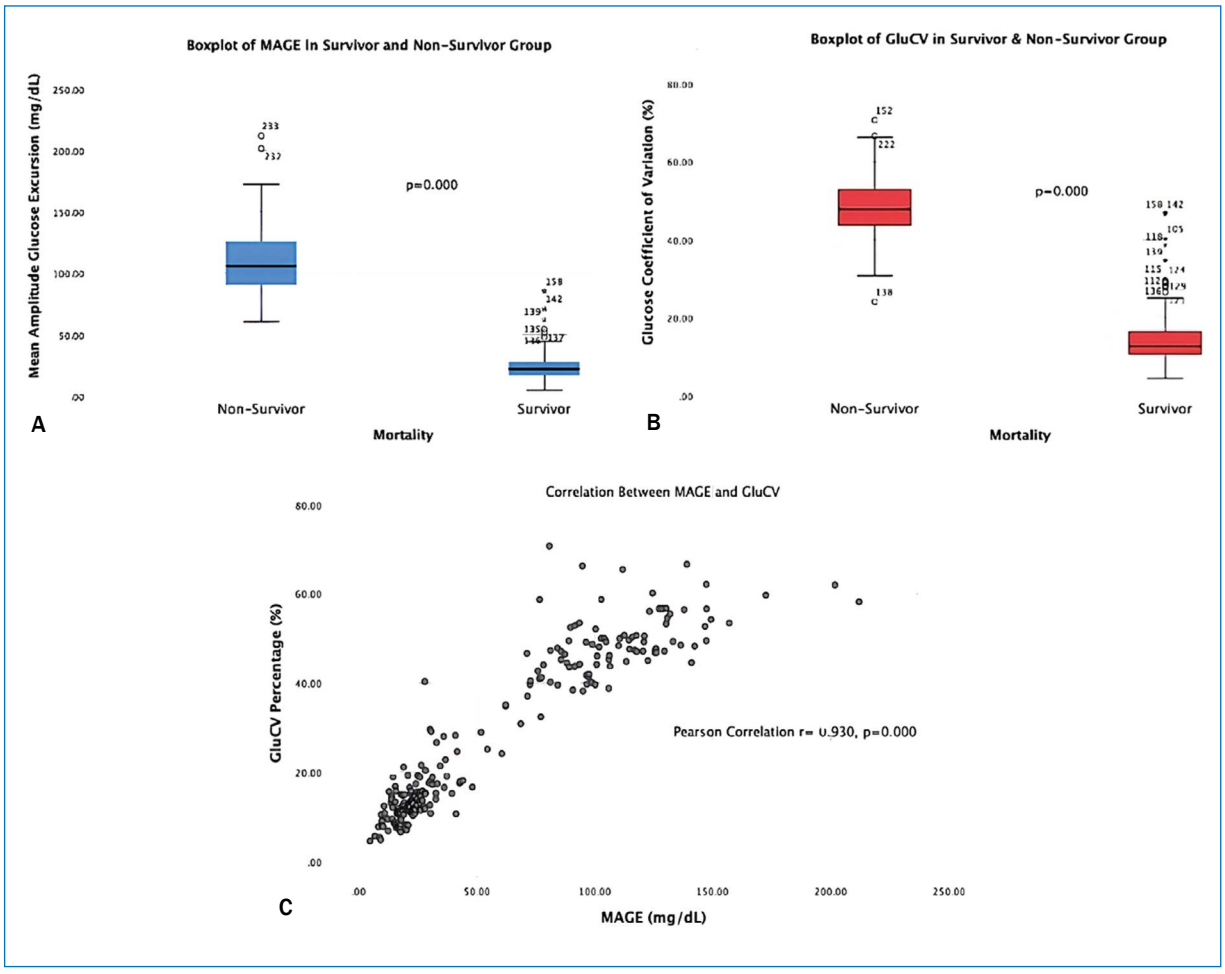

Figure 1. Chi-square analysis showing significantly lower rate of mortality in low GV using (**A**) MAGE and (**B**) GluCV. (**C**) Pearson correlation test showing strong and significant correlation between MAGE and GluCV score
GluCV — glucose coefficient of variation; MAGE — mean amplitude glucose excursion

independently associated with short-term mortality in individuals with sepsis. One strength of our study is that all enrolled individuals received intensive glucose monitoring (at least 3 times/day), which enabled us to investigate the prevalence of high GV and its association with 30-day mortality. In line with our findings, a retrospective study from Silveira et al. from 6730 glycemia measurements in the ICU showed a higher standard deviation of mean glycemia and MAGE associated with mortality in the ICU [17]. A study from

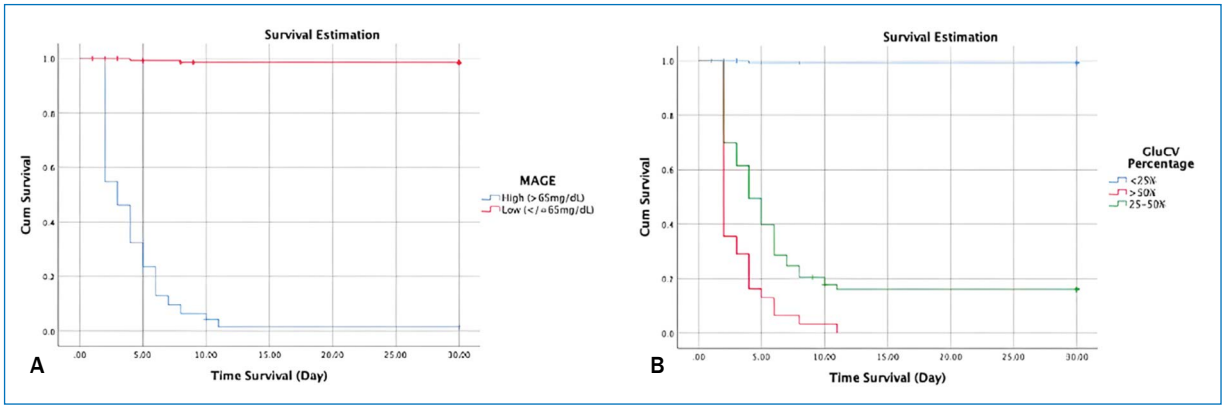

Figure 2. Kaplan-Meier survival analysis showing mean estimate survival time in low MAGE was 29.65 (29.16–30.13) days, and in high MAGE it was 4.24 (3.42–5.06) days. (**A**) The difference was 19.45 (17.78–21.12) days, SE = 0.85, p = 0.000. The mean estimate survival time in GluCV < 25% was 29.79 (29.39–30.20) days, GluCV 25–50% was 8.37 (6.13–10.61) days, and GluCV > 50% was 3.16 (2.42–3.91) days. (**B**) The difference was 19.45 (17.78–21.12), SE 0.85, p = 0.000
GluCV — glucose coefficient of variation; MAGE — mean amplitude glucose excursion; SE — standard error

Liu et al. found that T2D sepsis individuals with moderate maintenance blood glucose for 72 hours achieved better outcomes, including 90-day mortality [7]. In addition, a prospective study by Furushima et al. from 48 critically ill individuals with sepsis also found that higher MAGE (> 65 mg/dL) was independently inversely correlated with 90-day survival in the ICU [8].

There are several mechanism adverse effects of GV in sepsis individuals, including excessive protein glycation end products (AGE) and activation of oxidative stress, which cause endothelial dysfunction. GV induces overproduction of superoxide by the mitochondrial electron-transfer chain and causes a cascade of deleterious effect such as enhanced polyol activity, activation protein kinase C (PKC), nuclear factor-kß, and hexosamine pathway flux. Through these pathways, the increase of intracellular reactive oxygen species (ROS) causes vascular endothelial dysfunction by decreasing the of activity nitrite oxide synthase and activation of adhesion molecules [18, 19]. An observational study from Rodrigues et al. with 90 T1D individuals in the ICU showed that glycemic fluctuation correlated with oxidative stress and erythrocyte membrane stability parameters by interference with lipid peroxidation and cell membrane behavior [20].

We found a significant association between GV and increased incidence of hypoglycemia. Hypoglycemia induces the release of inflammatory cytokines and increases platelet and neutrophil activation and adrenaline secretion, which contribute to arrhythmia events and cardiovascular risk [21, 22]. In line with our study, we found that the high-GV group had more episodes of hypoglycemia, especially on the first day of admission, and hypoglycemia itself became an independent variable for mortality.

Our findings found that GluCV < 25% had better outcome for 30-day survival compared to GluCV 25–50% and > 50%. A study by Lanspa on 6106 critical ill individuals showed that GluCV was associated with mortality for the entire cohort, with OR1.25 for every 10% increase (p < 0.001) [23]. In the present study, GluCV > 25% had very strong association with mortality and excellent sensitivity to predict 30-day survival [0.992 (0.983–1.000), p = 0.000]. A recent study also showed that lower GV was associated with lower microvascular complications and decreased occurrence of hypoglycemia [16, 24]. Unlike glycated hemoglobin (HbA1c), GV can estimated hypoglycemic episode up to 40–50% in the future, and it is an independent predictor of hypoglycemia [25].

Our multivariate analysis showed that high MAGE and GluCV > 25% were significantly associated with short-term mortality, the same as with validated critically ill parameters, such as APACHE-IV and SOFA. The GluCV < 25% group also had shorter duration of ICU LoS significantly. This is in line with a retrospective study by Guo et al. on a total 6777 individuals, in which they found that the hazard ratio (HR) of CV > 25% was 1.37 (1.21–1.56), p < 0.001, after adjustment for SOFA score and multiple comorbidities [26]. A meta-analysis from Brett et al. from 41 studies (162,259 individuals) also showed a consistent association between increased measure of glycemic variability and higher short-term mortality in individuals with critical illness [24]. A study from Asakasa et al. suggested that large glycemic excursion parameter (MAGE, CV) was closely linked with

vascular endothelial dysfunction and deterioration of vascular endothelium. They found that MAGE was associated with higher risk of cardiovascular events and was a risk factor for coronary stenosis [14].

In consideration of easier measurement and modality, GV itself could become a good prognostic marker to predict the mortality and length of hospital stay in T2D individuals with sepsis. Furthermore, monitoring GV fluctuations could provide early clues for anticipating potential deterioration and aiding therapeutic adjustment [27].

There are several limitations to this study. First, it was a retrospective study in a single-center, which limited the robustness. Second, we excluded 30 subjects who died after < 24 h in the ICU, and this group may have greater fluctuations in BG levels. Third, despite highlighting the role of GV in T2D individuals with sepsis, the study only used periodic blood glucose monitoring (every 8 hours), not continuous glucose monitoring (CGM), which could offer more precise data on glucose fluctuations. Fourth, the generalizability of the findings should be applied with caution because of the high frequency of comorbidities that may influence BG fluctuations. Finally, we did not consider a variety of treatments that may influence BG.

Despite these limitations, the present study highlights the critical role of intensive GV monitoring in diabetic individuals with sepsis, which is feasible and can be incorporated into standard ICU procedures. CGM technology provides enhanced capabilities for closely tracking and identifying rapid fluctuations in BG levels. The reported CGM measurements significantly correlated with oxidative stress and endothelial dysfunction markers (urinary 8-iso-prostaglandin F2a, Gensini score, reactive hyperemia index) [14]. CGM has been associated with better control of short-term fluctuations in BG levels, reduced HbA1c values, reduced risk of severe hyperglycemia, and improved glycemic control [27]. Further studies are needed to investigate the optimal control strategy for individuals with high BG fluctuation with CGM.

Conclusions

High glycemic variability was observed in 39% of individuals; it was associated with higher mortality in diabetic individuals with sepsis, and was independently associated with high 30-day mortality. These findings emphasize the critical importance of early monitoring and detection of blood glucose fluctuations, especially to prevent large excursions and hypoglycemia episodes. Additional studies are required to explore the mechanism underlying GV and to optimize glucose control.

Article information

Supplementary material

Supplementary materials for this article can be found at https://journals.viamedica.pl/clinical_diabetology/article/view/102762.

Data availability

Original contributions presented in the study are included in the article. Further inquiries can be directed to the corresponding author.

Ethical approval

The present study protocol was reviewed and approved by the Institutional Review Board of the Sumber Waras Research Ethics Committee (approval No. 23/ /RSSW/KoM.EP/EC/V/2024). Written informed consent was not applicable due to the retrospective design of the study from medical records.

Authors' contributions

Conception or design: BG, J, RS, SS, LD; acquisition, analysis, or interpretation of data: BG, J; drafting the work or revising: BG, J, RS; final approval of the manuscript: J, RS, SS, LD.

Funding

No funding was granted for this study.

Acknowledgments

None.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016; 315(8): 801–810, doi: 10.1001/jama.2016.0287, indexed in Pubmed: 26903338.
2. Li X, Zhang D, Chen Y, et al. Acute Glycaemic Variability and risk of mortality in individuals with sepsis : a meta-analysis. Diabetol Metab Syndr. 2022; 14(1): 59, doi: 10.1186/s13098-022-00819-8, indexed in Pubmed: 35461267.
3. Vijayaraghavan BT, Adhikari N. Sepsis Epidemiology and Outcomes in Asia: Advancing the Needle. American Journal of Respiratory and Critical Care Medicine. 2022; 206(9): 1059–1060, doi: 10.1164/rccm.202207-1257ed.
4. Li A, Ling L, Qin H, et al. Epidemiology, Management, and Outcomes of Sepsis in ICUs among Countries of Differing National Wealth across Asia. Am J Respir Crit Care Med. 2022; 206(9): 1107–1116, doi: 10.1164/rccm.202112-2743OC, indexed in Pubmed: 35763381.
5. Lu Z, Tao G, Sun X, et al. Association of Blood Glucose Level and Glycemic Variability With Mortality in Sepsis Patients During ICU Hospitalization. Frontiers in Public Health. 2022; 10, doi: 10.3389/fpubh.2022.857368.

6. Magee F, Bailey M, Pilcher DV, et al. Early glycemia and mortality in critically ill septic patients: Interaction with insulin-treated diabetes. J Crit Care. 2018; 45: 170–177, doi: 10.1016/j.jcrc.2018.03.012, indexed in Pubmed: 29544173.
7. Liu D, Fan Y, Zhuang Y, et al. Association of Blood Glucose Variability with Sepsis-Related Disseminated Intravascular Coagulation Morbidity and Mortality. J Inflamm Res. 2022; 15: 6505–6516, doi: 10.2147/JIR.S383053, indexed in Pubmed: 36474519.
8. Almagthali A, Alsohimi S, Alkhalaf A, et al. Assessing glycemic variability in critically ill patients: A prospective cohort study comparing insulin infusion therapy with insulin sliding scale. Sci Rep. 2024; 14(1): 10128, doi: 10.1038/s41598-024-57403-5, indexed in Pubmed: 38698018.
9. Umpierrez G, Cardona S, Pasquel F, et al. Randomized Controlled Trial of Intensive Versus Conservative Glucose Control in Patients Undergoing Coronary Artery Bypass Graft Surgery: GLUCO-CABG Trial. Diabetes Care. 2015; 38(9): 1665–1672, doi: 10.2337/dc15-0303, indexed in Pubmed: 26180108.
10. See KC. Glycemic targets in critically ill adults: A mini-review. World J Diabetes. 2021; 12(10): 1719–1730, doi: 10.4239/wjd.v12.i10.1719, indexed in Pubmed: 34754373.
11. American Diabetes Association. American Diabetes Association Releases 2023 Standard of Care in Diabetes to Guide Prevention, Diagnosis, and Treatment for People Living with Diabetes 2022. https://diabetes.org/newsroom/american-diabetes-association-2023-standards-care-diabetes-guide-for-prevention-diagnosis-treatment-people-living-with-diabetes (23.09.2024).
12. Society of Critical Care Medicine. Surviving Sepsis Campaign 2021. https://www.sccm.org/sccm/media/PDFs/Surviving-Sepsis-Campaign-2021-Adult-Guidelines-Learning-Slides.pdf?lang=en-US (23.09.2024).
13. Furushima N, Egi M, Obata N, et al. Mean amplitude of glycemic excursions in septic patients and its association with outcomes: A prospective observational study using continuous glucose monitoring. J Crit Care. 2021; 63: 218–222, doi: 10.1016/j.jcrc.2020.08.021, indexed in Pubmed: 32958351.
14. Akasaka T, Sueta D, Tabata N, et al. Effects of the Mean Amplitude of Glycemic Excursions and Vascular Endothelial Dysfunction on Cardiovascular Events in Nondiabetic Patients With Coronary Artery Disease. J Am Heart Assoc. 2017; 6(5), doi: 10.1161/JAHA.116.004841, indexed in Pubmed: 28446494.
15. Chao HY, Liu PH, Lin SC, et al. Association of In-Hospital Mortality and Dysglycemia in Septic Patients. PLoS One. 2017; 12(1): e0170408, doi: 10.1371/journal.pone.0170408, indexed in Pubmed: 28107491.
16. Suh S, Kim JH. Glycemic Variability: How Do We Measure It and Why Is It Important? Diabetes Metab J. 2015; 39(4): 273–282, doi: 10.4093/dmj.2015.39.4.273, indexed in Pubmed: 26301188.
17. Silveira LM, Basile-Filho A, Nicolini EA, et al. Glycaemic variability in patients with severe sepsis or septic shock admitted to an Intensive Care Unit. Intensive Crit Care Nurs. 2017; 41: 98–103, doi: 10.1016/j.iccn.2017.01.004, indexed in Pubmed: 28318952.
18. Zhou Z, Sun B, Huang S, et al. Glycemic variability: adverse clinical outcomes and how to improve it? Cardiovasc Diabetol. 2020; 19(1): 102, doi: 10.1186/s12933-020-01085-6, indexed in Pubmed: 32622354.
19. Kusunoki Y, Konishi K, Tsunoda T, et al. Significance of Glycemic Variability in Diabetes Mellitus. Intern Med. 2022; 61(3): 281–290, doi: 10.2169/internalmedicine.8424-21, indexed in Pubmed: 34544956.
20. Rodrigues R, de Medeiros LA, Cunha LM, et al. Correlations of the glycemic variability with oxidative stress and erythrocytes membrane stability in patients with type 1 diabetes under intensive treatment. Diabetes Res Clin Pract. 2018; 144: 153–160, doi: 10.1016/j.diabres.2018.01.031, indexed in Pubmed: 29427698.
21. Smith-Pamer J, Brandle M, Trevisan R, et al. Assessment of the association between glycaemic variability and diabetes-related complication in type 1 and type 2 diabetes. Diabetes Res Clin Pract. 2014; 105(3): 273–284, doi: 10.1016/j.diabres.2014.06.007, indexed in Pubmed: 25023992.
22. Chao WC, Tseng CH, Wu CL, et al. Higher glycemic variability within the first day of ICU admission is associated with increased 30-day mortality in ICU patients with sepsis. Ann Intensive Care. 2020; 10(1): 17, doi: 10.1186/s13613-020-0635-3, indexed in Pubmed: 32034567.
23. Lanspa MJ, Dickerson J, Morris AH, et al. Coefficient of glucose variation is independently associated with mortality in critically ill patients receiving intravenous insulin. Crit Care. 2014; 18(2): R86, doi: 10.1186/cc13851, indexed in Pubmed: 24886864.
24. Issarawattana T, Bhurayanontachai R. Maximal Glycemic Difference, the Possible Strongest Glycemic Variability Parameter to Predict Mortality in ICU Patients. Crit Care Res Pract. 2020; 2020: 5071509, doi: 10.1155/2020/5071509, indexed in Pubmed: 32908696.
25. Guo Y, Qiu Y, Xue T, et al. Association between glycemic variability and short-term mortality in patients with acute kidney injury: a retrospective cohort study of the MIMIC-IV database. Sci Rep. 2024; 14(1): 5945, doi: 10.1038/s41598-024-56564-7, indexed in Pubmed: 38467770.
26. Hryciw B, Ghossein J, Rochwerg B, et al. Glycemic Variability As a Prognostic Factor for Mortality in Patients With Critical Illness: A Systematic Review and Meta-Analysis. Crit Care Exp. 2024; 6(1): e1025, doi: 10.1097/cce.0000000000001025.
27. Juneja D, Deepak D, Nasa P. What, why and how to monitor blood glucose in critically ill patients. World J Diabetes. 2023; 14(5): 528–538, doi: 10.4239/wjd.v14.i5.528, indexed in Pubmed: 37273246.