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Optimal Glycemic Control for Patients with Pancreatitis in the Intensive Care Unit: A Retrospective Study Based on a Large Intensive Care Unit Database

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Abstract

Objectives: Stress hyperglycemia is a common complication of pancreatitis. This study aimed to determine optimal blood glucose control goals for patients with pancreatitis. Methods: We conducted a screening of adult patients diagnosed with pancreatitis who were admitted to the ICU using data from the Medical Information Marketplace for Intensive Care IV (MIMIC-IV) database. In total, 574 cases were enrolled in this study and were divided into four groups based on blood glucose levels. We investigated the effects of four groups on the prognosis of patients with pancreatitis. Results: The survival group exhibited lower Glu_mean and Glu_cv values, but there was no significant effect on mortality. Glu_cv and frequency of daily blood glucose monitoring were significantly correlated with length of hospital stay, but had no significant effect on length of ICU stay. Subgroup analysis showed that the mortality rate was the highest when the mean blood glucose was 7.8 - 10.0 mmol/L, and the lowest when Glu_mean was 6.1 - 7.8 mmol/L.

Keywords

Blood Glucose, Pancreatitis, ICU

1. Introduction

Stress hyperglycemia has been identified as a common complication of pancreatitis, especially in severe acute pancreatitis (SAP), with a prevalence of approximately 35% - 80% among SAP patients [1]. According to a retrospective cohort

study, hyperglycemia in intensive care unit patients has been associated with increased incidence of complications and mortality [2]. Relevant guideline recommended the target blood glucose level for SAP patients is 7.8 - 10.0 mmol/L [3]. Hyperglycemia is an independent risk factor for increased mortality among critically ill patients [4]. Hyperglycemia also increases the risk of infection, length of stay, and even mortality in critically ill patients in the intensive care unit [5]. According to the findings of a previous study, patients who develop hypoglycaemia may have even worse prognosis than those who develop hyperglycaemia during the period of critical illness [6]. Furthermore, hypoglycemia also increases the risk of death in critically ill patients [7]. At present, there is no uniform standard for blood glucose control in patients with pancreatitis. The current study examined Blood glucose control goals in patients with pancreatitis, intending to provide clinicians with correlative therapeutic strategies for pancreatitis management.

2. Methods

2.1. Data Sources and Screening Patients

Data were collected from the updated Medical Information Mart for Intensive Care IV (MIMIC-IV) database with institutional review board approval. MIMIC-IV data from 2008 to 2019 were sourced from respective hospital databases of Beth Israel Deaconess Medical Center emergency department and ICUs. One author acquired database access and was responsible for data fetch.

Patients admitted to the ICU with pancreatitis as their primary diagnosis were included. Exclusion criteria were as follows: 1) Patients aged <18 years or >80 years; 2) The length of ICU stay was less than 48 hours; 3) Blood glucose was monitored less than once daily. For patients with repeated ICU admissions, we only extracted the information from the first admission (**Figure 1**).

Following variables were extracted or calculated, including the baseline characteristics (age, gender, ethnicity), comorbidities (diabetes, hypertension, infection, hypoglycemia), the severity of organ dysfunction (Acute Physiology Score, APS III), Sequential Organ Failure Assessment (SOFA) score, the duration of antibiotic use. Primary outcome variable: mortality in hospital. Secondary outcome variable: length of hospital and ICU stay, duration of antibiotic use.

2.2. Statistical Analysis

Continuous variables are represented by median and interquartile spacing (IQR), and categorical variables are represented by frequency and percentage. We compared categorical variables by Fisher test. Continuous variables were compared with the Mann-Whitney U test.

Firstly, we analyzed the relationship between the baseline characteristics and mortality in pancreatitis patients. Then we divided patients with different mean blood glucose levels into four groups (6.1 - 7.8 mmol/L, 6.1 - 11.1 mmol/L, 7.8 - 10.0 mmol/L or 3.9 - 11.1 mmol/L) based on the glycemic targets recommended

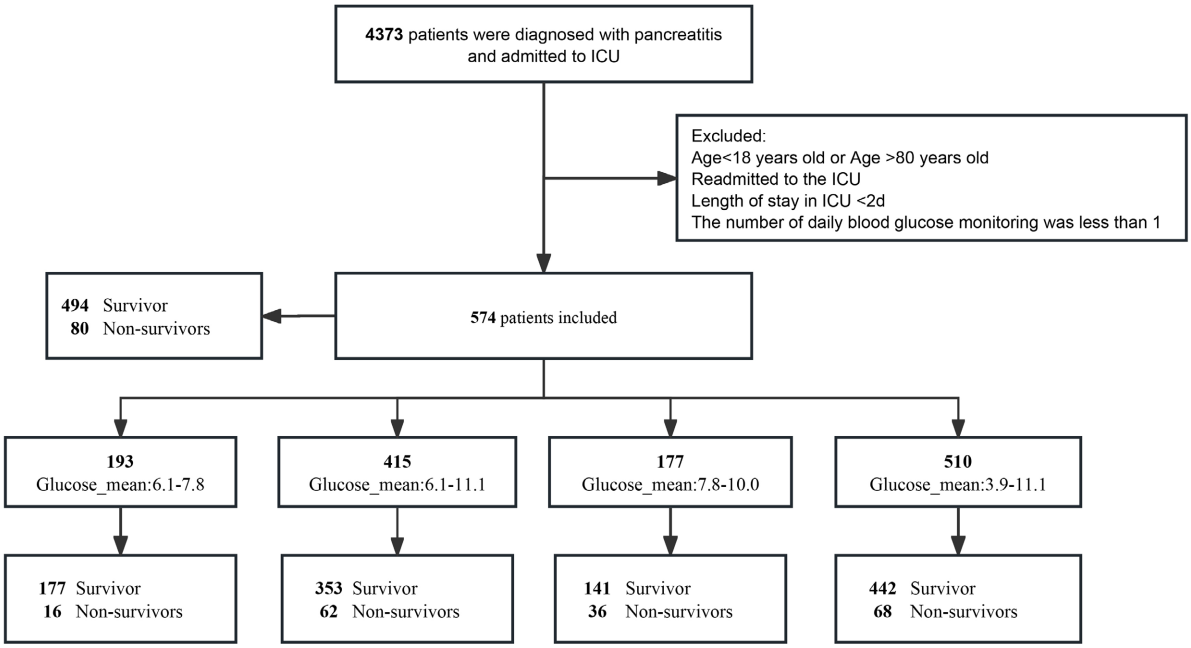

Figure 1. Flow chart of the study.

by existing studies and consensus.

Then we explored the relationship between variables and primary outcome variables in univariate analyses. Variables that present significant correlations in univariate analyses were included in Multiple logistic regression analysis and significance was set at 0.10. When outcome variables are continuous variables, we choose to analyze the correlation between relevant variables and outcome variables through multiple linear regression.

All data were filtered and collated by Stata (version 16) software and analyzed by R (version 4.2.3) software.

3. Results

We included 574 patients. Table 1 shows the baseline characteristics. Univariate analysis showed that the variables significantly related to mortality were age, APS III, SOFA score, mean and coefficient of variation of blood glucose (Glu_mean, Glu_cv), frequency of daily glucose monitoring and infection occurrence (Table 1). Ethnic variables were excluded temporarily because of incomplete data. Glu_mean and Glu_cv were lower in the survival group, but there was no significant effect on mortality (Figure 2). Subgroup analysis showed that the mortality rate was the highest when the mean blood glucose was 7.8 - 10.0 mmol/L, and the lowest when Glu_mean was 6.1 - 7.8 mmol/L. After multiple regression analysis, there was no significant difference in mortality between the two groups (Table 2). Subgroup analysis also found that Glu_cv and the frequency of daily blood glucose monitoring were higher in patients with diabetes (Table 2). Glu_cv and frequency of daily blood glucose monitoring were significantly correlated with length of hospital stay, but had no significant effect on

Table 1. Baseline characteristics.

	Died	Alive	P	logistics
n	80	494		
Age, median [Q1, Q3]	63.0 [54.00, 71.25]	53.00 [42.00, 64.00]	<0.001	<0.001
Male, n	48	304	0.805	
Male, (%)	60.00%	61.54%		
ethnicity				
white, n	48	297		
white, (%)	60.00%	60.12%		
BLACK/AFRICAN AMERICAN, n	6	63		
BLACK/AFRICAN AMERICAN, (%)	7.50%	12.75%		
AMERICAN INDIAN/ALASKA NATIVE, n	0	2		
AMERICAN INDIAN/ALASKA NATIVE, (%)	0.00%	0.40%		
PORTUGUESE, n	0	5		
PORTUGUESE, (%)	0.00%	1.01%		
UNKNOWN, n	12	58		
UNKNOWN, (%)	15.00%	11.74%		
ASIAN, n	6	14		
ASIAN, (%)	7.50%	2.83%		
OTHER, n	2	21		
OTHER, (%)	2.50%	4.25%		
HISPANIC/LATINO, n	0	25		
HISPANIC/LATINO, (%)	0.00%	5.06%		
UNABLE TO OBTAIN, n	6	9		
UNABLE TO OBTAIN, (%)	7.50%	1.82%		
ApsⅢ, median [Q1, Q3]	95.50 [71.75, 112.25]	55.00 [39.00, 76.00]	<0.001	<0.001
inSOFA, median [Q1, Q3]	4.00 [1.00, 7.00]	1.00 [0, 3.00]	<0.001	<0.001
▲SOFA, median [Q1, Q3]	4.00 [2.00, 9.25]	0 [−1.00, 2.00]	<0.001	
Glu_mean[a] (mmol/L), median [Q1, Q3]	8.88 [7.69, 10.31]	7.63 [6.47, 9.11]	<0.001	0.104
Glu_cv[b], median [Q1, Q3]	0.34 [0.24, 0.41]	0.22 [0.16, 0.31]	<0.001	0.151
Glu_frequency[*] (n/day), median [Q1, Q3]	5.50 [4.32, 7.34]	4.52 [3.24, 6.22]	<0.001	0.652
LOS in ICU[c], median [Q1, Q3]	8.58 [4.48, 19.09]	4.43 [2.92, 9.97]	<0.001	
LOS in hospital[d], median [Q1, Q3]	17.16 [8.44, 29.01]	15.57 [8.81, 25.59]	0.536	
infection, n	52	213	<0.001	0.221
infection, (%)	65.00%	43.12%		

Continued

blood-infection, n	33	124	
blood-infection, (%)	41.25%	25.10%	
Abdominal-infection, n	21	54	
Abdominal-infection, (%)	26.25%	10.93%	
urinary-infection, n	11	53	
urinary-infection, (%)	13.75%	10.73%	
respiratory-infection, n	20	65	
respiratory-infection, (%)	25.00%	13.16%	
diabetes, n	30	169	0.613
diabetes, (%)	37.50%	34.21%	
hypoglycemia, n	2	9	0.657
hypoglycemia, (%)	4.17%	2.96%	
hyperlipidemia, n	18	97	0.5488
hyperlipidemia, (%)	22.50%	19.64%	

[a]: Mean of blood glucose; [b]: Coefficient of variation of blood glucose = Mean of blood glucose/standard deviation of blood glucose; [c]: Length of ICU stay; [d]: The total length of hospital stay.

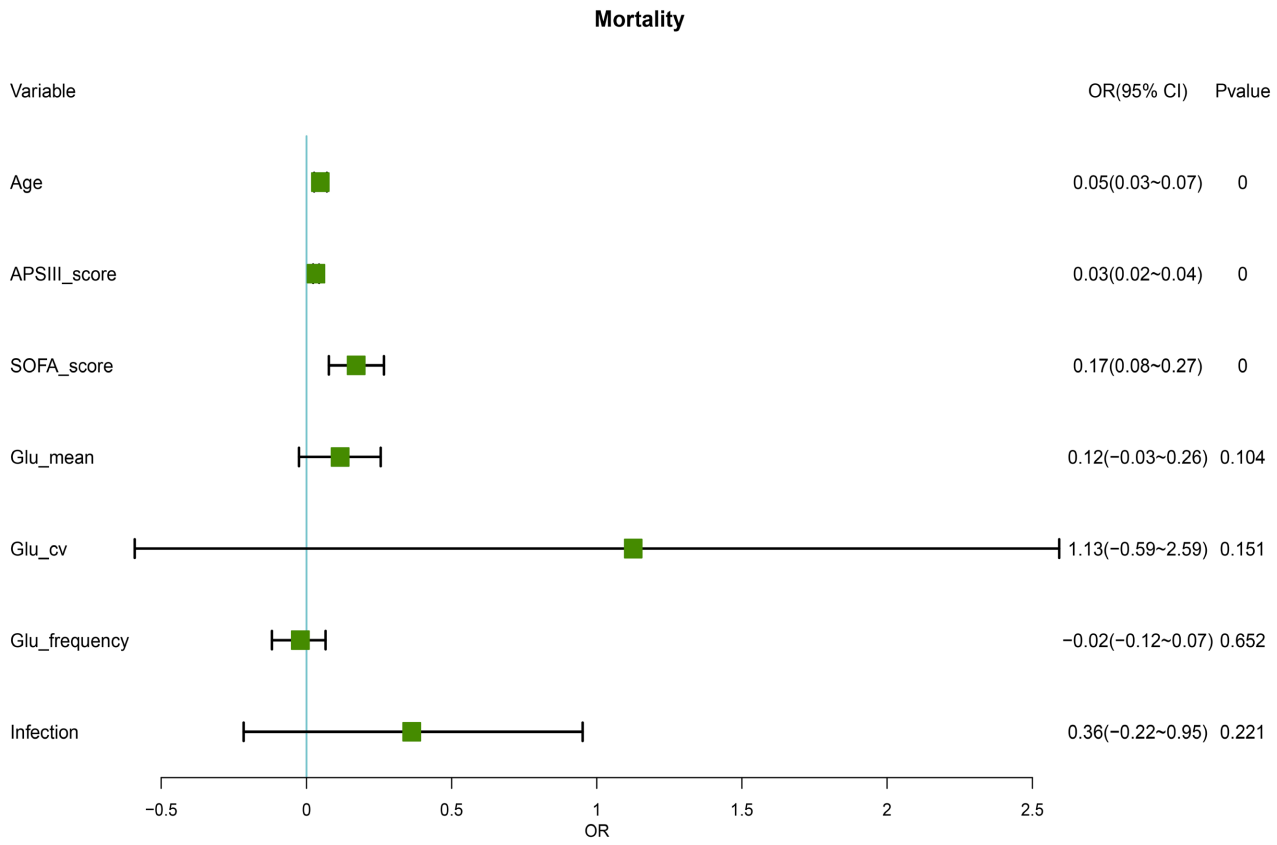

Figure 2. Multiple regression analysis of factors affecting mortality.

Table 2. Subgroup analysis was performed according to history of diabetes and mean blood glucose level.

	diabetes	no-diabetes	P	logistics
n	199	375		
Age, median [Q1, Q3]	59.00 [47.50, 66.50]	52.00 [41.00, 64.00]	<0.001*	0.006
Male, n	140	212	0.001	0.007
Male, (%)	70.35%	56.53%		
ethnicity				
white, n	115	230		
white, (%)	57.79%	61.33%		
BLACK/AFRICAN AMERICAN, n	32	37		
BLACK/AFRICAN AMERICAN, (%)	16.08%	9.87%		
AMERICAN INDIAN/ALASKA NATIVE, n	2	0		
AMERICAN INDIAN/ALASKA NATIVE, (%)	1.01%	0.00%		
PORTUGUESE, n	1	4		
PORTUGUESE, (%)	0.50%	1.07%		
UNKNOWN, n	20	50		
UNKNOWN, (%)	10.05%	13.33%		
ASIAN, n	8	12		
ASIAN, (%)	4.02%	3.20%		
OTHER, n	6	17		
OTHER, (%)	3.02%	4.53%		
HISPANIC/LATINO, n	8	17		
HISPANIC/LATINO, (%)	4.02%	4.53%		
UNABLE TO OBTAIN, n	7	8		
UNABLE TO OBTAIN, (%)	3.52%	2.13%		
Aps III, median [Q1, Q3]	60.00 [41.00, 85.00]	59.00 [41.00, 84.00]	0.517	/
inSOFA, median [Q1, Q3]	1.00 [0, 4.00]	1.00 [0, 4.00]	0.787	/
▲SOFA, median [Q1, Q3]	1.00 [0, 3.00]	1.00 [−1.00, 3.00]	0.444	/
Glu_mean[a] (mmol/L), median [Q1, Q3]	9.43 [8.12, 11.12]	7.15 [6.25, 8.22]	<0.001*	<0.001*
Glu_cv[b], median [Q1, Q3]	0.30 [0.21, 0.41]	0.21 [0.16, 0.27]	<0.001*	0.835
Glu_frequency* (n/day), median [Q1, Q3]	6.30 [4.81, 10.65]	4.13 [2.61, 5.16]	<0.001*	<0.001*
LOS in ICU[c], median [Q1, Q3]	4.10 [2.91, 8.82]	5.22 [2.99, 12.77]	0.052	/
LOS in hospital[d], median [Q1, Q3]	1.00 [0, 3.00]	1.00 [0, 3.50]	0.002	/
antibiotic day, median [Q1, Q3]	1.00 [0, 3.00]	1.00 [0, 3.50]	0.030	/
infection, n	80	185	0.030	/

Continued

infection, (%)	40.20%	49.33%	0.043	0.094
blood-infection, n	53	104		
blood-infection, (%)	26.63%	27.73%	0.844	/
Abdominal-infection, n	18	57		
Abdominal-infection, (%)	9.05%	15.20%	0.038	/
urinary-infection, n	18	46		
urinary-infection, (%)	9.05%	12.27%	0.267	/
respiratory-infection, n	20	65		
respiratory-infection, (%)	10.05%	17.33%	0.019	/
die, n	30	50		
die, (%)	15.08%	13.33%	0.613	/
hypoglycemia, n	4	7		
hypoglycemia, (%)	2.86%	3.30%	1.000	/
hyperlipidemia, n	58	57		
hyperlipidemia, (%)	29.15%	15.20%	<0.001*	0.123

	infection	no-infection	P	logistics
n	265	309		
Age, median [Q1, Q3]	56.00 [47.00, 66.00]	53.00 [41.00, 64.00]	0.006	0.083
Male, n	164	188	0.864	/
Male, (%)	61.89%	60.84%		
ethnicity				
white, n	163	182		
white, (%)	61.51%	58.90%		
BLACK/AFRICAN AMERICAN, n	27	42		
BLACK/AFRICAN AMERICAN, (%)	10.19%	13.59%		
AMERICAN INDIAN/ALASKA NATIVE, n	1	1		
AMERICAN INDIAN/ALASKA NATIVE, (%)	0.38%	0.32%		
PORTUGUESE, n	4	1		
PORTUGUESE, (%)	1.51%	0.32%		
UNKNOWN, n	31	39		
UNKNOWN, (%)	11.70%	12.62%		
ASIAN, n	8	12		
ASIAN, (%)	3.02%	3.88%		
OTHER, n	12	11		

Continued

OTHER, (%)	4.53%	3.56%		
HISPANIC/LATINO, n	9	16		
HISPANIC/LATINO, (%)	3.40%	5.18%		
UNABLE TO OBTAIN, n	10	5		
UNABLE TO OBTAIN, (%)	3.77%	1.62%		
Aps III, median [Q1, Q3]	67.00 [52.00, 93.00]	50.00 [36.00, 72.00]	<0.001*	<0.001*
inSOFA, median [Q1, Q3]	2.00 [0, 4.00]	1.00 [0, 3.00]	0.008	0.289
▲SOFA, median [Q1, Q3]	1.00 [−1.00, 3.00]	1.00 [−1.00, 2.00]	0.120	/
Glu_mean[a] (mmol/L), median [Q1, Q3]	7.80 [6.63, 9.23]	7.70 [6.52, 9.46]	0.983	/
Glu_cv[b], median [Q1, Q3]	0.25 [0.19, 0.35]	0.22 [0.16, 0.32]	0.013	0.198
Glu_frequency* (n/day), median [Q1, Q3]	4.49 [3.60, 5.74]	4.75 [3.45, 6.97]	0.098	0.003
LOS in ICU[c], median [Q1, Q3]	7.15 [3.35, 16.87]	3.95 [2.77, 7.00]	<0.001*	/
LOS in hospital[d], median [Q1, Q3]	20.74 [11.81, 33.23]	12.73 [7.69, 19.89]	<0.001*	/
antibiotic day, median [Q1, Q3]	2.00 [0, 4.00]	1.00 [0, 3.00]	<0.001*	/
die, n	52	28	<0.001*	0.520
die, (%)	19.62%	9.06%		
blood-infection, n	157	0	/	/
blood-infection, (%)	59.25%	0.00%		
Abdominal-infection, n	75	0	/	/
Abdominal-infection, (%)	28.30%	0.00%		
urinary-infection, n	64	0	/	/
urinary-infection, (%)	24.15%	0.00%		
respiratory-infection, n	85	0	/	/
respiratory-infection, (%)	32.08%	0.00%		
diabetes, n	80	119	0.043	0.176
diabetes, (%)	30.19%	38.51%		
hypoglycemia, n	6	5	0.762	/
hypoglycemia, (%)	3.66%	2.66%		
hyperlipidemia, n	64	51	0.028	0.033
hyperlipidemia, (%)	24.15%	16.50%		

	antibiotic	no-antibiotic	P	logistics
n	360	214		
Age, median [Q1, Q3]	55.00 [43.00, 65.00]	54.00 [43.00, 64.00]	0.279	/
Male, n	220	132	0.930	/
Male, (%)	61.11%	61.68%		

Continued

ethnicity				
white, n	210	135		
white, (%)	58.33%	63.08%		
BLACK/AFRICAN AMERICAN, n	39	30		
BLACK/AFRICAN AMERICAN, (%)	10.83%	14.02%		
AMERICAN INDIAN/ALASKA NATIVE, n	1	1		
AMERICAN INDIAN/ALASKA NATIVE, (%)	0.28%	0.47%		
PORTUGUESE, n	4	1		
PORTUGUESE, (%)	1.11%	0.47%		
UNKNOWN, n	57	13		
UNKNOWN, (%)	15.83%	6.07%		
ASIAN, n	7	13		
ASIAN, (%)	1.94%	6.07%		
OTHER, n	14	9		
OTHER, (%)	3.89%	4.21%		
HISPANIC/LATINO, n	16	9		
HISPANIC/LATINO, (%)	4.44%	4.21%		
UNABLE TO OBTAIN, n	12	3		
UNABLE TO OBTAIN, (%)	3.33%	1.40%		
Aps III, median [Q1, Q3]	63.00 [44.75, 87.25]	50.50 [37.25, 76.75]	<0.001*	0.170
inSOFA, median [Q1, Q3]	1.00 [0, 4.00]	1.00 [0, 3.00]	0.010	0.174
▲SOFA, median [Q1, Q3]	1.00 [−1.00, 3.00]	0 [−1.00, 2.00]	0.062	/
Glu_mean[a] (mmol/L), median [Q1, Q3]	7.76 [6.60, 9.43]	7.82 [6.42, 9.15]	0.951	/
Glu_cv[b], median [Q1, Q3]	0.24 [0.17, 0.35]	0.23 [0.16, 0.31]	0.287	/
Glu_frequency* (n/day), median [Q1, Q3]	4.66 [3.58, 6.22]	4.50 [3.39, 6.81]	0.969	/
LOS in ICU[c], median [Q1, Q3]	5.81 [3.16, 13.26]	3.93 [2.79, 7.62]	<0.001*	/
LOS in hospital[d], median [Q1, Q3]	16.86 [9.60, 27.12]	13.06 [7.70, 22.70]	0.002	/
antibiotic day, median [Q1, Q3]	3.00 [1.00, 5.00]	0 [0, 0]	-	/
die, n	186	79	<0.001*	0.033
die, (%)	51.67%	36.92%		
blood-infection, n	110	47	0.026	/
blood-infection, (%)	30.56%	21.96%		
Abdominal-infection, n	50	25	0.522	/
Abdominal-infection, (%)	13.89%	11.68%		

Continued

urinary-infection, n	46	18	0.131	/
urinary-infection, (%)	12.78%	8.41%		
respiratory-infection, n	61	24	0.069	/
respiratory-infection, (%)	16.94%	11.21%		
diabetes, n	114	85	0.057	0.040
diabetes, (%)	31.67%	39.72%		
hypoglycemia, n	4	7	0.111	/
hypoglycemia, (%)	1.82%	5.30%		
die, n	63	17	0.001	0.090
die, (%)	17.50%	7.94%		
hyperlipidemia, n	79	36	0.161	0.122
hyperlipidemia, (%)	35.91%	27.27%		

	6.1 - 7.8	6.1 - 11.1	7.8 - 10.0	3.9 - 11.1
n	193	415	177	510
Age, median [Q1, Q3]	51.00 [40.00, 65.00]	55.00 [44.00, 65.00]	57.00 [47.00, 66.00]	54.00 [43.00, 65.00]
Male, n	114	249	105	307
Male, (%)	59.07%	60.00%	59.32%	60.20%
ethnicity				
white, n	126	256	109	312
white, (%)	65.28%	61.69%	61.58%	61.18%
BLACK/AFRICAN AMERICAN, n	21	51	25	59
BLACK/AFRICAN AMERICAN, (%)	10.88%	12.29%	14.12%	11.57%
AMERICAN INDIAN/ALASKA NATIVE, n	0	2	0	2
AMERICAN INDIAN/ALASKA NATIVE, (%)	0.00%	0.48%	0.00%	0.39%
PORTUGUESE, n	2	4	0	4
PORTUGUESE, (%)	1.04%	0.96%	0.00%	0.78%
UNKNOWN, n	24	50	20	63
UNKNOWN, (%)	12.44%	12.05%	11.30%	12.35%
ASIAN, n	5	12	4	14
ASIAN, (%)	2.59%	2.89%	2.26%	2.75%
OTHER, n	7	16	7	21
OTHER, (%)	3.63%	3.86%	3.95%	4.12%
HISPANIC/LATINO, n	5	13	5	21
HISPANIC/LATINO, (%)	2.59%	3.13%	2.82%	4.12%
UNABLE TO OBTAIN, n	3	11	7	14
UNABLE TO OBTAIN, (%)	1.55%	2.65%	3.95%	2.75%

Continued

Aps III, median [Q1, Q3]	56.00 [40.00, 79.00]	62.00 [43.00, 87.50]	64.00 [47.00, 89.00]	59.00 [41.00, 84.00]
inSOFA, median [Q1, Q3]	1.00 [0, 3.00]	1.00 [0, 4.00]	1.00 [0, 4.00]	1.00 [0, 4.00]
▲SOFA, median [Q1, Q3]	1.00 [−1.00, 3.00]	1.00 [−1.00, 3.00]	1.00 [0, 3.00]	1.00 [−1.00, 3.00]
Glu_mean[a] (mmol/L), median [Q1, Q3]	6.90 [6.55, 7.38]	7.88 [7.00, 8.92]	8.56 [8.18, 9.18]	7.55 [6.42, 8.61]
Glu_cv[b], median [Q1, Q3]	0.21 [0.16, 0.25]	0.23 [0.17, 0.33]	0.26 [0.20, 0.37]	0.22 [0.16, 0.31]
Glu_frequency[*] (n/day), median [Q1, Q3]	3.97 [2.58, 4.78]	4.59 [3.63, 6.34]	5.14 [4.19, 7.35]	4.43 [3.24, 6.10]
LOS in ICU[c], median [Q1, Q3]	4.99 [3.09, 12.61]	5.83 [3.14, 13.74]	5.96 [3.11, 14.05]	4.95 [2.96, 11.67]
LOS in hospital[d], median [Q1, Q3]	16.85 [10.62, 27.52]	17.76 [9.99, 28.95]	18.13 [8.83, 28.88]	16.62 [9.03, 26.71]
antibiotic day, median [Q1, Q3]	1.00 [0, 3.00]	1.00 [0, 3.00]	1.00 [0, 3.00]	1.00 [0, 3.00]
die, n	94	204	89	241
die, (%)	48.70%	49.16%	50.28%	47.25%
blood-infection, n	59	123	55	142
blood-infection, (%)	30.57%	29.64%	31.07%	27.84%
Abdominal-infection, n	24	60	24	71
Abdominal-infection, (%)	12.44%	14.46%	13.56%	13.92%
urinary-infection, n	20	45	22	57
urinary-infection, (%)	10.36%	10.84%	12.43%	11.18%
respiratory-infection, n	38	71	29	78
respiratory-infection, (%)	19.69%	17.11%	16.38%	15.29%
diabetes, n	25	135	82	148
diabetes, (%)	12.95%	32.53%	46.33%	29.02%
hypoglycemia, n	3	7	2	11
hypoglycemia, (%)	2.63%	2.81%	1.90%	3.58%
die, n	16	62	36	68
die, (%)	8.29%	14.94%	20.34%	13.33%
hyperlipidemia, n	29	85	47	96
hyperlipidemia, (%)	25.44%	34.14%	44.76%	31.27%

	6.1 - 7.8	3.9 - 11.1	P	logistics
n	193	510		
Age, median [Q1, Q3]	51.00 [40.00, 65.00]	54.00 [43.00, 65.00]	0.255	/
Male, n	114	307	0.796	/
Male, (%)	59.07%	60.20%		
ethnicity				
white, n	126	312		
white, (%)	65.28%	61.18%		
BLACK/AFRICAN AMERICAN, n	21	59		

Continued

BLACK/AFRICAN AMERICAN, (%)	10.88%	11.57%		
AMERICAN INDIAN/ALASKA NATIVE, n	0	2		
AMERICAN INDIAN/ALASKA NATIVE, (%)	0.00%	0.39%		
PORTUGUESE, n	2	4		
PORTUGUESE, (%)	1.04%	0.78%		
UNKNOWN, n	24	63		
UNKNOWN, (%)	12.44%	12.35%		
ASIAN, n	5	14		
ASIAN, (%)	2.59%	2.75%		
OTHER, n	7	21		
OTHER, (%)	3.63%	4.12%		
HISPANIC/LATINO, n	5	21		
HISPANIC/LATINO, (%)	2.59%	4.12%		
UNABLE TO OBTAIN, n	3	14		
UNABLE TO OBTAIN, (%)	1.55%	2.75%		
Aps III, median [Q1, Q3]	56.00 [40.00, 79.00]	59.00 [41.00, 84.00]	0.307	/
inSOFA, median [Q1, Q3]	1.00 [0, 3.00]	1.00 [0, 4.00]	0.410	/
▲SOFA, median [Q1, Q3]	1.00 [−1.00, 3.00]	1.00 [−1.00, 3.00]	0.769	/
Glu_mean[a] (mmol/L), median [Q1, Q3]	6.90 [6.55, 7.38]	7.55 [6.42, 8.61]	＜0.001*	/
Glu_cv[b], median [Q1, Q3]	0.21 [0.16, 0.25]	0.22 [0.16, 0.31]	0.003	0.137
Glu_frequency* (n/day), median [Q1, Q3]	3.97 [2.58, 4.78]	4.43 [3.24, 6.10]	＜0.001*	0.142
LOS in ICU[c], median [Q1, Q3]	4.99 [3.09, 12.61]	4.95 [2.96, 11.67]	0.579	/
LOS in hospital[d], median [Q1, Q3]	16.85 [10.62, 27.52]	16.62 [9.03, 26.71]	0.265	/
antibiotic day, median [Q1, Q3]	1.00 [0, 3.00]	1.00 [0, 3.00]	0.582	/
die, n	94	241	0.736	/
die, (%)	48.70%	47.25%		
blood-infection, n	59	142	0.513	/
blood-infection, (%)	30.57%	27.84%		
Abdominal-infection, n	24	71	0.711	/
Abdominal-infection, (%)	12.44%	13.92%		
urinary-infection, n	20	57	0.892	/
urinary-infection, (%)	10.36%	11.18%		
respiratory-infection, n	38	78	0.172	/
respiratory-infection, (%)	19.69%	15.29%		
diabetes, n	25	148	<0.001*	0.002

Continued

diabetes, (%)	12.95%	29.02%		
hypoglycemia, n	3	11	0.768	/
hypoglycemia, (%)	2.63%	3.58%		
die, n	16	68	0.069	0.275
die, (%)	8.29%	13.33%		
hyperlipidemia, n	29	96	0.2697	/
hyperlipidemia, (%)	25.44%	31.27%		

	6.1 - 11.1	3.9 - 11.1	P	logistics
n	415	510		
Age, median [Q1, Q3]	55.00 [44.00, 65.00]	54.00 [43.00, 65.00]	<0.001*	0.407
Male, n	249	307	1.000	/
Male, (%)	60.00%	60.20%		
ethnicity				
white, n	256	312		
white, (%)	61.69%	61.18%		
BLACK/AFRICAN AMERICAN, n	51	59		
BLACK/AFRICAN AMERICAN, (%)	12.29%	11.57%		
AMERICAN INDIAN/ALASKA NATIVE, n	2	2		
AMERICAN INDIAN/ALASKA NATIVE, (%)	0.48%	0.39%		
PORTUGUESE, n	4	4		
PORTUGUESE, (%)	0.96%	0.78%		
UNKNOWN, n	50	63		
UNKNOWN, (%)	12.05%	12.35%		
ASIAN, n	12	14		
ASIAN, (%)	2.89%	2.75%		
OTHER, n	16	21		
OTHER, (%)	3.86%	4.12%		
HISPANIC/LATINO, n	13	21		
HISPANIC/LATINO, (%)	3.13%	4.12%		
UNABLE TO OBTAIN, n	11	14		
UNABLE TO OBTAIN, (%)	2.65%	2.75%		
Aps III, median [Q1, Q3]	62.00 [43.00, 87.50]	59.00 [41.00, 84.00]	0.134	/
inSOFA, median [Q1, Q3]	1.00 [0, 4.00]	1.00 [0, 4.00]	0.986	/
▲SOFA, median [Q1, Q3]	1.00 [−1.00, 3.00]	1.00 [−1.00, 3.00]	0.992	/
Glu_mean[a] (mmol/L), median [Q1, Q3]	7.88 [7.00, 8.92]	7.55 [6.42, 8.61]	<0.001*	/
Glu_cv[b], median [Q1, Q3]	0.23 [0.17, 0.33]	0.22 [0.16, 0.31]	0.126	/

Continued

Glu_frequency* (n/day), median [Q1, Q3]	4.59 [3.63, 6.34]	4.43 [3.24, 6.10]	0.088	0.243
LOS in ICU[c], median [Q1, Q3]	5.83 [3.14, 13.74]	4.95 [2.96, 11.67]	0.072	/
LOS in hospital[d], median [Q1, Q3]	17.76 [9.99, 28.95]	16.62 [9.03, 26.71]	0.091	/
antibiotic day, median [Q1, Q3]	1.00 [0, 3.00]	1.00 [0, 3.00]	0.610	/
die, n	204	241	0.597	/
die, (%)	49.16%	47.25%		
blood-infection, n	123	142	0.004	/
blood-infection, (%)	29.64%	27.84%		
Abdominal-infection, n	60	71	0.850	/
Abdominal-infection, (%)	14.46%	13.92%		
urinary-infection, n	45	57	0.916	/
urinary-infection, (%)	10.84%	11.18%		
respiratory-infection, n	71	78	0.473	/
respiratory-infection, (%)	17.11%	15.29%		
diabetes, n	135	148	0.252	/
diabetes, (%)	32.53%	29.02%		
hypoglycemia, n	7	11	0.642	/
hypoglycemia, (%)	2.81%	3.58%		
die, n	62	68	0.5063	/
die, (%)	14.94%	13.33%		
hyperlipidemia, n	85	96	0.56	/
hyperlipidemia, (%)	34.14%	31.27%		

	6.1 - 11.1	7.8 - 10.0	P	logistics
n	415	177		
Age, median [Q1, Q3]	55.00 [44.00, 65.00]	57.00 [47.00, 66.00]	0.100	0.122
Male, n	249	105	0.927	/
Male, (%)	60.00%	59.32%		
ethnicity				
white, n	256	109		
white, (%)	61.69%	61.58%		
BLACK/AFRICAN AMERICAN, n	51	25		
BLACK/AFRICAN AMERICAN, (%)	12.29%	14.12%		
AMERICAN INDIAN/ALASKA NATIVE, n	2	0		
AMERICAN INDIAN/ALASKA NATIVE, (%)	0.48%	0.00%		
PORTUGUESE, n	4	0		
PORTUGUESE, (%)	0.96%	0.00%		
UNKNOWN, n	50	20		

Continued

UNKNOWN, (%)	12.05%	11.30%		
ASIAN, n	12	4		
ASIAN, (%)	2.89%	2.26%		
OTHER, n	16	7		
OTHER, (%)	3.86%	3.95%		
HISPANIC/LATINO, n	13	5		
HISPANIC/LATINO, (%)	3.13%	2.82%		
UNABLE TO OBTAIN, n	11	7		
UNABLE TO OBTAIN, (%)	2.65%	3.95%		
Aps III, median [Q1, Q3]	62.00 [43.00, 87.50]	64.00 [47.00, 89.00]	0.228	/
inSOFA, median [Q1, Q3]	1.00 [0, 4.00]	1.00 [0, 4.00]	0.680	/
▲SOFA, median [Q1, Q3]	1.00 [−1.00, 3.00]	1.00 [0, 3.00]	0.600	/
Glu_mean[a] (mmol/L), median [Q1, Q3]	7.88 [7.00, 8.92]	8.56 [8.18, 9.18]	<0.001*	/
Glu_cv[b], median [Q1, Q3]	0.23 [0.17, 0.33]	0.26 [0.20, 0.37]	0.005	0.254
Glu_frequency* (n/day), median [Q1, Q3]	4.59 [3.63, 6.34]	5.14 [4.19, 7.35]	0.002	0.222
LOS in ICU[c], median [Q1, Q3]	5.83 [3.14, 13.74]	5.96 [3.11, 14.05]	0.944	/
LOS in hospital[d], median [Q1, Q3]	17.76 [9.99, 28.95]	18.13 [8.83, 28.88]	0.792	/
antibiotic day, median [Q1, Q3]	1.00 [0, 3.00]	1.00 [0, 3.00]	0.407	/
die, n	204	89	0.858	/
die, (%)	49.16%	50.28%		
blood-infection, n	123	55	0.769	/
blood-infection, (%)	29.64%	31.07%		
Abdominal-infection, n	60	24	0.898	/
Abdominal-infection, (%)	14.46%	13.56%		
urinary-infection, n	45	22	0.573	/
urinary-infection, (%)	10.84%	12.43%		
respiratory-infection, n	71	29	0.905	/
respiratory-infection, (%)	17.11%	16.38%		
diabetes, n	135	82	0.002	0.043
diabetes, (%)	32.53%	46.33%		
hypoglycemia, n	7	2	1.000	/
hypoglycemia, (%)	2.81%	1.90%		
die, n	62	36	0.1167	/
die, (%)	14.94%	20.34%		
hyperlipidemia, n	85	47	0.107	/
hyperlipidemia, (%)	34.14%	44.76%		

	6.1 - 7.8	7.8 - 10.0	P	logistics
n	193	177		
Age, median [Q1, Q3]	51.00 [40.00, 65.00]	57.00 [47.00, 66.00]	0.005	0.120
Male, n	114	105	1.000	/
Male, (%)	59.07%	59.32%		
ethnicity				
white, n	126	109		
white, (%)	65.28%	61.58%		
BLACK/AFRICAN AMERICAN, n	21	25		
BLACK/AFRICAN AMERICAN, (%)	10.88%	14.12%		
AMERICAN INDIAN/ALASKA NATIVE, n	0	0		
AMERICAN INDIAN/ALASKA NATIVE, (%)	0.00%	0.00%		
PORTUGUESE, n	2	0		
PORTUGUESE, (%)	1.04%	0.00%		
UNKNOWN, n	24	20		
UNKNOWN, (%)	12.44%	11.30%		
ASIAN, n	5	4		
ASIAN, (%)	2.59%	2.26%		
OTHER, n	7	7		
OTHER, (%)	3.63%	3.95%		
HISPANIC/LATINO, n	5	5		
HISPANIC/LATINO, (%)	2.59%	2.82%		
UNABLE TO OBTAIN, n	3	7		
UNABLE TO OBTAIN, (%)	1.55%	3.95%		
Aps III, median [Q1, Q3]	56.00 [40.00, 79.00]	64.00 [47.00, 89.00]	0.004	0.397
inSOFA, median [Q1, Q3]	1.00 [0, 3.00]	1.00 [0, 4.00]	0.319	/
▲SOFA, median [Q1, Q3]	1.00 [−1.00, 3.00]	1.00 [0, 3.00]	0.483	/
Glu_mean[a] (mmol/L), median [Q1, Q3]	6.90 [6.55, 7.38]	8.56 [8.18, 9.18]	<0.001*	/
Glu_cv[b], median [Q1, Q3]	0.21 [0.16, 0.25]	0.26 [0.20, 0.37]	<0.001*	0.017
Glu_frequency* (n/day), median [Q1, Q3]	3.97 [2.58, 4.78]	5.14 [4.19, 7.35]	<0.001*	0.011
LOS in ICU[c], median [Q1, Q3]	4.99 [3.09, 12.61]	5.96 [3.11, 14.05]	0.514	/
LOS in hospital[d], median [Q1, Q3]	16.85 [10.62, 27.52]	18.13 [8.83, 28.88]	0.998	/
antibiotic day, median [Q1, Q3]	1.00 [0, 3.00]	1.00 [0, 3.00]	0.388	/
die, n	94	89	0.835	/
die, (%)	48.70%	50.28%		
blood-infection, n	59	55	1.000	/
blood-infection, (%)	30.57%	31.07%		

Continued

Abdominal-infection, n	24	24	0.759	/
Abdominal-infection, (%)	12.44%	13.56%		
urinary-infection, n	20	22	0.623	/
urinary-infection, (%)	10.36%	12.43%		
respiratory-infection, n	38	29	0.421	/
respiratory-infection, (%)	19.69%	16.38%		
diabetes, n	25	82	<0.001*	<0.001*
diabetes, (%)	12.95%	46.33%		
hypoglycemia, n	3	2	1.000	/
hypoglycemia, (%)	2.63%	1.90%		
die, n	16	36	0.001	0.102
die, (%)	8.29%	20.34%		
hyperlipidemia, n	29	47	0.007	/
hyperlipidemia, (%)	25.44%	44.76%		

Table 3. Influencing factors of hospitalization time of patients in different groups, influencing factors of ICU length of stay in different groups of patients.

(los_hospital)				
ALL				
term	estimate	std. error	statistic	p. value
(Intercept)	9.195	3.712	2.477	0.014
Age	−0.068	0.050	−1.356	0.176
Aps III	0.154	0.029	5.360	<0.001
inSOFA	−0.297	0.294	−1.010	0.313
Glu_mean	0.400	0.376	1.064	0.288
Glu_cv	12.681	4.822	2.630	0.009
Glu_frequency	−0.637	0.205	−3.105	0.002
infection	6.819	1.531	4.456	<0.001
Glu_mean: 3.9 mmol/L - 11.1 mmol/L				
term	estimate	std. error	statistic	p. value
(Intercept)	−0.854	4.527	−0.189	0.850
Age	−0.072	0.053	−1.356	0.176
Aps III	0.144	0.031	4.662	<0.001
inSOFA	−0.284	0.306	−0.928	0.354
Glu_mean	2.021	0.572	3.535	<0.001
Glu_cv	12.444	5.312	2.343	0.020
Glu_frequency	−0.742	0.226	−3.276	0.001
infection	6.488	1.638	3.962	<0.001

Continued

Glu_mean: 6.1 mmol/L - 7.8 mmol/L				
term	estimate	std. error	statistic	p. value
(Intercept)	−31.441	17.935	−1.753	0.081
Age	−0.003	0.080	−0.036	0.971
Aps III	0.194	0.047	4.117	<0.001
inSOFA	−0.316	0.543	−0.582	0.562
Glu_mean	6.118	2.513	2.434	0.016
Glu_cv	−8.698	12.519	−0.695	0.488
Glu_frequency	−0.122	0.482	−0.254	0.800
infection	4.928	2.445	2.015	0.045
Glu_mean: 6.1 mmol/L - 11.1 mmol/L				
term	estimate	std. error	statistic	p. value
(Intercept)	4.728	6.561	0.721	0.472
Age	−0.082	0.064	−1.284	0.200
Aps III	0.136	0.035	3.896	<0.001
inSOFA	−0.326	0.360	−0.905	0.366
Glu_mean	1.429	0.798	1.791	0.074
Glu_cv	14.673	6.010	2.442	0.015
Glu_frequency	−0.811	0.268	−3.026	0.003
infection	7.592	1.931	3.931	<0.001
Glu_mean: 7.8 mmol/L - 10.0 mmol/L				
term	estimate	std. error	statistic	p. value
(Intercept)	−1.428	22.596	−0.063	0.950
Age	−0.017	0.120	−0.139	0.890
Aps III	0.073	0.062	1.170	0.244
inSOFA	0.030	0.555	0.054	0.957
Glu_mean	2.364	2.549	0.927	0.355
Glu_cv	6.973	10.029	0.695	0.488
Glu_frequency	−0.944	0.387	−2.438	0.016
infection	7.881	3.353	2.350	0.020
diabetes				
term	estimate	std. error	statistic	p. value
(Intercept)	21.840	7.749	2.818	0.005
Age	−0.087	0.090	−0.965	0.336
Aps III	0.142	0.047	3.042	0.003
inSOFA	−0.555	0.495	−1.122	0.263
Glu_mean	−0.439	0.520	−0.845	0.399
Glu_cv	−0.904	9.684	−0.093	0.926
Glu_frequency	−0.637	0.268	−2.383	0.018
infection	7.845	2.440	3.215	0.002

Continued

no-diabetes				
term	estimate	std. error	statistic	p. value
(Intercept)	−2.514	4.892	−0.514	0.608
Age	−0.079	0.061	−1.292	0.197
ApsⅢ	0.142	0.037	3.887	<0.001
inSOFA	−0.210	0.359	−0.584	0.560
Glu_mean	1.817	0.593	3.065	0.002
Glu_cv	15.269	5.563	2.745	0.006
Glu_frequency	0.044	0.396	0.110	0.912
infection	6.216	1.916	3.244	0.001
(los_icu)				
ALL				
term	estimate	std. error	statistic	p. value
(Intercept)	0.603	1.886	0.320	0.749
Age	−0.053	0.025	−2.087	0.037
Aps III	0.166	0.015	11.380	<0.001
inSOFA	−0.382	0.149	−2.559	0.011
Glu_mean	−0.007	0.191	−0.039	0.969
Glu_cv	4.128	2.450	1.685	0.092
Glu_frequency	−0.165	0.104	−1.580	0.115
infection	2.957	0.778	3.803	<0.001
Glu_mean: 3.9 mmol/L - 11.1 mmol/L				
term	estimate	std. error	statistic	p. value
(Intercept)	−4.168	2.342	−1.779	0.076
Age	−0.056	0.027	−2.037	0.042
Aps III	0.165	0.016	10.346	<0.001
inSOFA	−0.381	0.158	−2.404	0.017
Glu_mean	0.721	0.296	2.439	0.015
Glu_cv	4.338	2.748	1.578	0.115
Glu_frequency	−0.221	0.117	−1.888	0.060
infection	2.847	0.847	3.360	0.001
Glu_mean: 6.1 mmol/L - 7.8 mmol/L				
term	estimate	std. error	statistic	p. value
(Intercept)	−19.770	10.672	−1.853	0.066
Age	−0.036	0.048	−0.745	0.457
Aps III	0.173	0.028	6.153	<0.001
inSOFA	−0.750	0.323	−2.320	0.021

Continued

Glu_mean	2.688	1.496	1.797	0.074
Glu_cv	9.810	7.449	1.317	0.190
Glu_frequency	−0.039	0.287	−0.136	0.892
infection	3.326	1.455	2.286	0.023
Glu_mean: 6.1 mmol/L - 11.1 mmol/L				
term	estimate	std. error	statistic	p. value
(Intercept)	−1.390	3.448	−0.403	0.687
Age	−0.061	0.034	−1.824	0.069
Aps III	0.173	0.018	9.410	<0.001
inSOFA	−0.401	0.189	−2.123	0.034
Glu_mean	0.309	0.419	0.737	0.461
Glu_cv	5.019	3.158	1.589	0.113
Glu_frequency	−0.203	0.141	−1.439	0.151
infection	3.506	1.015	3.455	0.001
Glu_mean: 7.8 mmol/L - 10.0 mmol/L				
term	estimate	std. error	statistic	p. value
(Intercept)	−5.048	11.049	−0.457	0.648
Age	−0.047	0.058	−0.803	0.423
Aps III	0.149	0.031	4.876	<0.001
inSOFA	−0.245	0.271	−0.902	0.369
Glu_mean	0.603	1.247	0.484	0.629
Glu_cv	9.085	4.904	1.853	0.066
Glu_frequency	−0.249	0.189	−1.316	0.190
infection	3.307	1.640	2.017	0.045
diabetes				
term	estimate	std. error	statistic	p. value
(Intercept)	2.915	3.382	0.862	0.390
Age	−0.054	0.039	−1.368	0.173
Aps III	0.154	0.020	7.538	<0.001
inSOFA	−0.536	0.216	−2.482	0.014
Glu_mean	0.025	0.227	0.110	0.913
Glu_cv	−2.522	4.227	−0.597	0.551
Glu_frequency	−0.148	0.117	−1.270	0.206
infection	2.298	1.065	2.157	0.032

Continued

no-diabetes				
term	estimate	std. error	statistic	p. value
(Intercept)	−2.545	2.657	−0.958	0.339
Age	−0.053	0.033	−1.601	0.110
Aps III	0.170	0.020	8.550	<0.001
inSOFA	−0.304	0.195	−1.558	0.120
Glu_mean	0.194	0.322	0.603	0.547
Glu_cv	6.057	3.021	2.005	0.046
Glu_frequency	0.078	0.215	0.360	0.719
infection	3.189	1.041	3.064	0.002

length of ICU stay, the length of hospital stay and ICU stay were not significantly associated with the four glycemic control regimens in this study (**Table 3**).

4. Discussion

A large number of studies have confirmed that stress hyperglycemia in critically ill patients can lead to related complications and increase the risk of in-hospital death, especially in non-diabetic patients [2] [8] [9]. In addition to excessive blood glucose level or hypoglycemia affecting the prognosis of critically ill patients, blood glucose variability also affects the mortality of patients [10]. Hyperglycemia is a common complication in patients with pancreatitis, and studies have found that reasonable blood glucose levels help to improve the prognosis of patients with pancreatitis [11] [12]. However, the pathophysiological state of ICU patients with pancreatitis is more complex, and there is still no universally accepted appropriate blood glucose level. Therefore, our study focused on the comparison of glycemic targets that are commonly used in critically ill patients.

In our study, Glu_mean and Glu_cv were significantly lower in the survival group than in the death group, although patients who died had closer glucose monitoring. This result support previous findings that blood glucose level can be used as a prognostic indicator, effective control of the level and variability of blood glucose in patients may help to improve their prognosis. Logistic regression analysis showed that these differences were no longer significant after adjustment for patient age, disease severity and organ dysfunction. The retrospective study by Zuo Y *et al.* showed similar results to ours [13]. The possible reasons why we all get this result are as follows: First, there is a U-shaped relationship between blood glucose and mortality in critically ill patients, Glu_mean in our study was just between 4.50 and 11.05 mmol/L, mortality fluctuates only slightly within this range [13] [14] [15] [16]. Second, a retrospective analysis using the MIMIC-III database was also conducted in patients with pancreatitis [17]. We observed higher Glu_mean levels in our patients. This could be attri-

buted to the fact that our study includes more recent cases, as accepted glycemic targets for physicians may have changed in recent years. Additionally, our results were derived from blood glucose monitoring in the ward rather than biochemical tests. This choice was made because bedside glucose monitoring offers more frequent and accurate assessments of glycemic control. Third, we discovered that physicians in the death group had to employ more frequent blood glucose monitoring to maintain Glu_mean and Glu_cv in patients, which was more costly. This heightened frequency indicates that achieving blood glucose control was more challenging in this group. Finally, we found that patients with lower Glu_mean and Glu_cv had shorter total hospital stay, this may also be regarded as an important indicator of patient prognosis.

Subgroup analysis showed that patients with diabetes had higher Glu_mean and more frequent glucose monitoring during hospitalization. However, after multiple regression analysis, there was no significant difference in blood glucose variability between diabetic patients and non-diabetic patients. In addition, we found that pancreatitis patients with diabetes had a lower incidence of concurrent infections and a shorter average length of hospital stay. This supports the earlier findings that diabetic patients have a higher tolerance for abnormal elevations in blood glucose [10] [18] [19]. Therefore, doctors typically establish different blood glucose control targets based on whether or not patients have a history of diabetes. Guidelines suggested maintaining blood glucose levels at 6.1 - 7.8 mmol/L in non-diabetic critically ill patients, and recommend less strict glycemic control (6.1 - 11.1 mmol/L) for critically ill patients with diabetes. In addition, guidelines recommend the target blood glucose level for patients with severe pancreatitis is 7.8 - 10.0 mmol/L [3].

In our subgroup analysis, we did find that more patients with diabetes were targeted to 6.1 to 11.1 mmol/L, but the improvements in mortality and length of hospital stay were not significant compared with other glycemic targets. Patients who stayed within the guideline-recommended glycemic target for pancreatitis (7.8 to 10.0 mmol/L) required more frequent glucose monitoring but did not improve outcomes and even had higher mortality than either target. We analysis the cause of the results are as follows：First, unlike previous studies, we included not only patients with severe or acute pancreatitis but also patients with chronic pancreatitis, for whom guideline-recommended glycemic targets may not be fully applicable, but the negative effect of chronic pancreatitis on glycemic control in patients has been well established [20] [21]. Second, in our study, patients with a mean blood glucose range of 7.8 to 10.0 mmol/L had a higher mortality rate and a higher severity score, so the multivariate regression analysis did not show a negative effect on the prognosis of patients, blood glucose has been regarded as one of the indicators that can evaluate the prognosis of patients [11], a patient with glycemic control in this range may not only be related to the glycemic target set by the physician, but also because his blood glucose is inherently difficult to control and is forced to be above the normal glycemic control target,

our study also found that indeed this part of the patient's blood sugar monitoring frequency is higher. In conclusion, there are a few limitations to our study. Firstly, despite being based on a large MIMIC-IV database, our study is still a single-center retrospective study. Therefore, more multicenter prospective studies are needed to validate our findings. Additionally, the blood glucose measurements in our study were not performed regularly in a laboratory setting, but rather through bedside monitoring in the ward. It is important to note that guidelines recommend using arterial blood glucose results from blood gas analysis for clinical observations. As a result, there may be some bias in the obtained results.

5. Conclusion

Further investigation is required to determine the optimal glycemic control in patients with pancreatitis. However, it is suggested that more frequent glucose monitoring and reduced variability could potentially contribute to a shorter hospital stay.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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