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Original Article

Relationship between blood glucose variability and death in patients with massive cerebral infarction: a retrospective study in China

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Abstract: Objective: To investigate the relationship between blood glucose variability and prognosis in patients with massive cerebral infarction. Materials and methods: From July 2013 to December 2015, a total of 111 patients with massive cerebral infarction were enrolled in this study, divided into survival group (n = 88) and death group (n = 23). We analyzed blood glucose levels in both groups, average blood glucose (GluAve), standard deviation of blood glucose (GluSD), blood glucose coefficient of variation (GluCV), large amplitude of glycemic excursion (LAGE), mean amplitude of glycemic excursion (MAGE), mean postprandial glucose excursion (MPPGE) was calculated and the relationship between blood glucose variability and patient mortality was compared between the two groups. Results: The difference in the GluAve, SD, GluCV, LAGE, MAGE, MPPGE between the death group and the survival group was all statistically significant ($P < 0.001$). The Pearson test results showed that, GluSD, GluCV, LAGE, MAGE and patients' outcomes were highly correlated (Pearson $r > 0.9$) and had significant differences ($P < 0.001$), respectively. But GluAve, MPPGE were middling correlated (Pearson $r < 0.5$), with patients' outcomes, respectively and had significant differences ($P < 0.001$). Conclusions: Blood glucose variability is closely related to the death of patients with massive cerebral infarction, which can better predict the prognosis of patients than the average blood glucose level.

Keywords: GluAve, GluCV, LAGE, MAGE, MPPGE

Introduction

Blood glucose variability refers to blood glucose fluctuations. In recent years, a number of studies confirmed that blood glucose variability and severe cerebrovascular disease prognosis is closely related [1, 2], it is an independent risk factor to increase the mortality of patients with severe cerebrovascular disease. There are several indicators to measure blood glucose variability, such as average blood glucose (GluAve), standard deviation of blood glucose (GluSD), blood glucose coefficient of variation (GluCV), large amplitude of glycemic excursion (LAGE), mean amplitude of glycemic excursion (MAGE), mean postprandial glucose excursion (MPPGE) etc. [3-6] Massive cerebral infarction is a common acute and critical diseases in neurology with high mortality and poor prognosis [7]. Whether the blood glucose variability is related to the death rate of patients with massive cerebral infarction is less. In this study, 111 cases of patients with massive cerebral infarction were retrospectively analyzed, and the relationship between blood glucose variability and mortality was compared.

Materials and methods

Patients

From July 2013 to December 2015, there were 111 patients with massive cerebral infarction who were hospitalized with NICU in our hospital, including 65 males and 46 females, the age distribution was 45-78 years old.

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients who meet the criteria for CT classification of massive cerebral infarction (more than 1 lobe, 5 cm^2 or more); (2) Patients underwent CT or MRI examination, cerebral hemorrhage excluded; (3) Within 24 hours of onset; (4) Hospital stay more than 3 days; (5) The patient was monitored after

Table 1. Characteristics of the death and survival groups

	Survival group (n = 88)	Death group (n = 23)	P
Sex female (%)	35 (39.8%)	11 (47.8%)	0.488
Severe pneumonia	65 (73.9%)	20 (87%)	0.27
Stress ulcer	30 (34.2%)	11 (47.8%)	0.236
Hypertension history	28 (31.8%)	11 (47.8%)	0.219
Diabetes	42 (47.7%)	16 (69.6%)	0.1
Age	61.78±8.69	62.04±10.21	0.902
Hospitalization time	11.40±3.32	12.35±2.57	0.205
APACHE II scores	9.32±3.17	12.74±2.03	0.023

Table 2. The blood glucose variability-related indicators of the survival group and death group

	Survival group (n = 88)	Death group (n = 23)	P
GluAve	8.39±1.91	8.94±4.69	< 0.001
GluSD	1.89±0.70	4.75±0.46	< 0.001
GluCV	26.06±4.82	53.66±4.82	< 0.001
LAGE	6.75±1.21	19.03±3.51	< 0.001
MAGE	2.69±0.47	8.73±0.69	< 0.001
MPPGE	2.98±0.87	10.96±0.30	< 0.001

Average blood glucose (GluAve), standard deviation of blood glucose (GluSD), blood glucose coefficient of variation (GluCV), large amplitude of glycemic excursion (LAGE), mean amplitude of glycemic excursion (MAGE), mean postprandial glucose excursion (MPPGE).

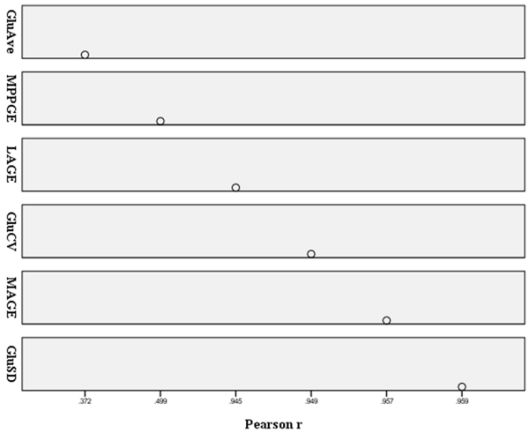

Figure 1. The Pearson r among blood glucose variability-related indicators, and death in patients with massive cerebral infarction. **statistically significant (P < 0.001). Standard deviation of blood glucose (GluSD) (Pearson r = 0.959), blood glucose coefficient of variation (GluCV) (Pearson r = 0.949), large amplitude of glycemic excursion (LAGE) (Pearson r = 0.945), mean amplitude of glycemic excursion (MAGE) (Pearson r = 0.957), average blood glucose (GluAve) (Pearson r = 0.372), mean postprandial glucose excursion (MPPGE) (Pearson r = 0.499).

admission for the first 24 hours of blood glucose.

Exclusion criteria: (1) Type 1 diabetes patients, patients with diabetic ketoacidosis; (2) Secondary cerebral infarction caused by the endocrine and blood system diseases; (3) Cerebral infarction caused by ertebral - basilar artery system hardening.

Treatment and measurement

All patients with glycemic control target of 7.8-10.0 mmoL/L, were not treated with intensive insulin therapy. blood glucose control: When the blood glucose is greater than 12 mmol/L, we began to use insulin intravenous pump, blood glucose below 10 mmol/L, stop the insulin pump. This study has been approved by the Ethics Committee of our hospital. All patients or their relatives sign an informed consent. All patients were tested for finger tip blood glucose 1 times per hour during the first 24 hours [3] after admission. GluAve, the mean value of the 24 measured blood glucoses of the monitored patients. GluSD, standard deviation of 24 measured values blood glucoses of the monitored patients. GluCV, standard deviation × 100/mean blood glucose. LAGE, the difference between the maximum value and the minimum value within 24 hours. MAGE, the absolute value of the difference between the two adjacent blood glucose in each patient is calculated, and we take the average of more than one SD. MPPGE, Calculate the difference between the highest blood glucose and the pre-meal blood glucose within 3 hours after each meal, and calculate the average of the difference in the three meals a day.

Statistical analysis

SPSS 19.0 statistical software (Chicago, Illinois) were used to process data. The quantitative data were expressed as mean ± standard deviation, and after the normality test, the independent sample T test were used to compare between the two groups. Multiple-group comparisons were performed using one-way

Table 3. The sample size of the variables in the multivariate logistic regression analysis

	1	2	3	4
APACHE II scores	< 10 (42)	10~15 (65)	15~20 (2)	> 20 (2)
GluSD	< 1.7 (28)	1.7~3.2 (61)	3.2~4.7 (12)	> 4.7 (11)
LAGE	< 4.2 (2)	4.2~6.8 (45)	6.8~9.4 (41)	> 9.4 (23)
GluCV	< 27 (77)	27~40 (11)	40~53 (11)	53~(12)

Table 4. The results of multivariate logistic regression analysis of all patients

	β	SE	Wald-X^2	P	OR (95% CL)
APACHE II scores	1.167	0.232	15.929	0.001	2.811 (1.953-3.231)
GluSD	1.341	0.349	9.565	0.001	3.302 (1.755~9.673)
LAGE	1.897	0.982	7.526	0.011	5.231 (1.685~32.452)
GluCV	1.043	0.427	8.877	0.019	4.408 (1.463~8.234)

Standard deviation of blood glucose (GluSD), blood glucose coefficient of variation (GluCV), large amplitude of glycemic excursion (LAGE).

ANOVA, qualitative data usage (composition ratio), and comparison between groups. Multivariate logistic regression analysis was performed on the statistically significant variables of univariate analysis. The Pearson test was used to detect the correlation between the two groups. $P < 0.05$ was considered statistically significant.

Result

The base characteristics and the blood glucose variability-related indicators of the death and survival groups

The age, length of hospital stay, and APACHE II scores of the survival group and death group were shown in **Table 1**. There were statistically significant differences in APACHE II scores between the death and survival groups ($P = 0.023$).

The blood glucose variability-related indicators of the survival group and death group were shown in **Table 2**. There was statistically significant differences in GluAve, GluSD, GluCV, LAGE,MAGE,MPPGE between the death and survival groups, respectively ($P < 0.001$). The Pearson test results showed that, GluSD, GluCV, LAGE,MAGE and patients' outcomes were highly correlated (Pearson $r > 0.9$) and had significant differences ($P < 0.001$), respectively. But GluAve, MPPGE were middling correlated (Pearson $r < 0.5$) with patients' outcomes, respectively, and had significant differences ($P < 0.001$) (**Figure 1**).

The multivariate logistic regression analysis result of all patients

Variables with $P < 0.1$ in univariate analysis were introduced into multivariate logistic regression analysis. The classification standard and the sample size of the different variables in the multivariate logistic regression analysis were shown in the **Table 3**. The results of multivariate logistic regression analysis (**Table 4**) of all patients also showed that, APACHE II scores ($P = 0.001$), GluSD ($P = 0.001$), LAGE ($P = 0.011$), GluCV ($P = 0.019$) were significantly highly correlated associated with death in patients with massive cerebral infarction.

Discussion

Blood glucose variability is the state of fluctuation between the highest and lowest values of blood glucose over a period of time, reflecting the unstable state of blood glucose. A number of studies have shown that high blood glucose variability is associated with increased progression and poor prognosis in patients with disease and is an independent predictor of adverse prognosis in critically ill patients [8]. Jiang et al. have shown that high blood glucose variability is associated with death in critically ill patients [9]. Zhang et al. have shown that the fluctuation range of blood glucose is related to the short-term prognosis of patients with acute coronary syndrome [10]. Guan et al. have shown that blood glucose variability is associated with diabetic complications - diabetic foot [11]. Lan et al. suggested that blood glucose variability is associated with diabetic microvascular complications [12]. Blood glucose variability can increase the risk of cerebral infarction after subarachnoid hemorrhage [4].

High blood glucose variability and poor prognosis of patients with severe differences, may

have the following factors: first, Small fluctuations in blood sugar may mean that more care for health care workers care, second, Low blood glucose variability prompted mild condition, third, high blood glucose variability itself is harmful to the body [13]. There is evidence that: high blood glucose variability will produce biological toxicity, which may have a bad effect to the body of the environment [14].

Massive cerebral infarction is a critically ill of neurology, brain tissue in patients with severely damaged, severe clinical symptoms, more complications, high morbidity, high mortality. Patients with stress state, the steady decline in the internal environment, and the existence of varying degrees of nutritional absorption disorders and glucose metabolism disorders, coupled with a variety of endocrine substances and inflammatory factors involved, patients with increased risk of hyperglycemia and hypoglycemia, blood glucose fluctuation significantly increased [15].

In this study, 116 patients with massive cerebral infarction were included, the results show that blood glucose variability-related indicators, GluSD, GluCV, LAGE, MAGE were highly correlated with death in patients with massive cerebral infarction, and these indicators could be used as independent predictors of prognosis in patients with large area of cerebral infarction. This is consistent with some previous reports [16-18]. In addition, the GluAve and mortality were not highly related.

Increased blood glucose variability, suggesting that the patient's condition deteriorates and is predictive of the prognosis of both diabetic and non-diabetic patients. There were required to closely monitor blood glucose, reduce blood glucose variability in clinical work, which may do help to improve the prognosis of patients, reduce mortality.

As the study selected patients with massive cerebral infarction only, the number of cases is limited, some patients may be subject to individual differences, nutritional support and other factors, may have some limitations. Later in the follow-up study, the number of samples will be increased, the other factors will be analyzed, to make a better analysis of blood glucose variability on the prognosis of patients. In addition, although we found that high blood glucose variability will increase the mortality rate, but there is no research shows that smooth control of blood glucose, lower blood glucose variability can improve the prognosis of patients. Expect more prospective studies to confirm this and provide a basis for clinical work.

Disclosure of conflict of interest

None.

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References

[1] Feng Z, Zhang JX. Study on the dynamic changes of blood glucose level after stroke. Chinese Critical Care Medicine 2014; 16: 247-248.

[2] Mazighi M, Labreuche J and Amarenco P. Glucose level and brain infarction: a prospective case-control study and prospective study. Int J Stroke 2009; 4: 346-351.

[3] Cesana F, Giannattasio C, Nava S, Soriano F, Brambilla G, Baroni M, Meani P, Varrenti M, Paleari F, Gamba P, Facchetti R, Alloni M, Grassi G and Mancia G. Impact of blood glucose variability on carotid artery intima media thickness and distensibility in type 1 diabetes mellitus. Blood Press 2013; 22: 355-361.

[4] Barletta JF, Figueroa BE, DeShane R, Blau SA and McAllen KJ. High glucose variability increases cerebral infarction in patients with spontaneous subarachnoid hemorrhage. J Crit Care 2013; 28: 798-803.

[5] Lipska KJ, Venkitachalam L, Gosch K, Kovatchev B, Van den Berghe G, Meyfroidt G, Jones PG, Inzucchi SE, Spertus JA, DeVries JH and Kosiborod M. Glucose variability and mortality in patients hospitalized with acute myocardial infarction. Circ Cardiovasc Qual Outcomes 2012; 5: 550-557.

[6] Jian Z, Zhou WJ. The significance and clinical evaluation of blood glucose stability. Natl Med J China 2006; 86: 2154-2157.

[7] Busing KA, Schulte-Sasse C, Fluchter S, Suselbeck T, Haase KK, Neff W, Hirsch JG, Borggrefe M and Duber C. Cerebral infarction: incidence and risk factors after diagnostic and interventional cardiac catheterization--prospective evaluation at diffusion-weighted MR imaging. Radiology 2005; 235: 177-183.

[8] Krinsley JS. Glycemic variability and mortality in critically ill patients: the impact of diabetes. J Diabetes Sci Technol 2009; 3: 1292-1301.

[9] Jiang HF, Jiang MC. Correlation of glycemic variability and the death of critically Ill patients with neurological. Chinese J Neurology 2012; 45: 734-738.
[10] Zhang XL, Zhang JL, Pan CY. Correlation between blood glucose control and short-term prognosis in patients with acute coronary syndrome. J Clinical Internal Med 2008; 25: 257-259.
[11] Guan LJ, Guan XW, Lu J. Changes and significance of blood glucose variability in patients with diabetic foot. Shandong Pharmaceutical 2016; 56: 60-61.
[12] Lizhen L, Lan JB, Tan F, Yang J. Acute blood glucose fluctuations exacerbated by oxidative stress caused by diabetic microvascular complications. Chinese Journal of Integrative Medicine on Cardio/Cerebrovascular Disease 2013; 11: 678-680.
[13] Egi M, Bellomo R, Stachowski E, French CJ and Hart G. Variability of blood glucose concentration and short-term mortality in critically ill patients. Anesthesiology 2006; 105: 244-252.
[14] Quagliaro L, Piconi L, Assaloni R, Martinelli L, Motz E and Ceriello A. Intermittent high glucose enhances apoptosis related to oxidative stress in human umbilical vein endothelial cells: the role of protein kinase C and NAD(P)H-oxidase activation. Diabetes 2003; 52: 2795-2804.
[15] Ali NA, O'Brien JM Jr, Dungan K, Phillips G, Marsh CB, Lemeshow S, Connors AF Jr and Preiser JC. Glucose variability and mortality in patients with sepsis. Crit Care Med 2008; 36: 2316-2321.
[16] Meyfroidt G, Keenan DM, Wang X, Wouters PJ, Veldhuis JD and Van den Berghe G. Dynamic characteristics of blood glucose time series during the course of critical illness: effects of intensive insulin therapy and relative association with mortality. Crit Care Med 2010; 38: 1021-1029.
[17] Farrokhi F, Chandra P, Smiley D, Pasquel FJ, Peng L, Newton CA and Umpierrez GE. Glucose variability is an independent predictor of mortality in hospitalized patients treated with total parenteral nutrition. Endocr Pract 2014; 20: 41-45.
[18] Wang LC, Wang XZ, Hu WL, Chen L,Ou HY, Kou QY. The association of glucose variability and mortality in critical ill patients. Chin J Clinicians (Electronic Edition) 2011; 5: 7291-7294.