Postoperative hyperglycemia in patients with traumatic brain injury: what should we care

Keywords
treatment, hyperglycemia, nursing, traumatic brain injury, glucose, operation, care

Abstract

Introduction

Blood glucose monitoring and management are very important for the prognosis of patients with traumatic brain injury (TBI). It is necessary to evaluate the status and influencing factor of hyperglycemia within 48 hours after operation in patients with TBI.

Material and methods

Patients with TBI who received craniocerebral surgery between March 1, 2022, and October 31, 2023, were enrolled. We assessed the clinical characteristics of TBI patients with and without the development of postoperative hyperglycemia. To identify potential risk factors associated with postoperative hyperglycemia, we performed both univariate and multivariate logistic regression analyses. Utilizing the regression coefficients derived from each significant risk factor, we subsequently constructed a predictive model aimed at forecasting postoperative hyperglycemia.

Results

A total of 216 TBI patients were included, the incidence of postoperative hyperglycemia was 31.48%. Correlation analysis indicated that the age(r=0.415), BMI(r=0.441), diabetes(r=0.513), GCS score(r=0.545) and length of hospital stay(r=0.456) were all corrected to the postoperative hyperglycemia in TBI patients (all P<0.05). Age ≥ 60y (OR=2.556, 95%CI: 1.831~3.641), BMI ≥ 24 kg/m2(OR=2.793, 95%CI: 2.305~3.679), diabetes (OR=3.081, 95%CI: 2.326~3.811) and GCS score≤8(OR=3.603, 95%CI: 1.956~4.086) were the independently influencing factors of postoperative hyperglycemia in TBI patients (all P<0.05). The area under the receiver operating characteristic curve and 95% CI were 0.795 (0.712, 0.849), the model had good discriminative ability to distinguish the occurrence of postoperative hyperglycemia in TBI patients (all P<0.05).

Conclusions

Postoperative hyperglycemia in patients with TBI is common. For TBI patient with a total score ≥ 6, early interventions and care are needed to reduce the postoperative hyperglycemia.

Title page

Title: Postoperative hyperglycemia in patients with traumatic brain injury: what should we care

Running title: Hyperglycemia & TBI

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Methods: Patients with TBI who received craniocerebral surgery between March 1, 2022, and October 31, 2023, were enrolled. We assessed the clinical characteristics of TBI patients with and without the development of postoperative hyperglycemia. To identify potential risk factors associated with postoperative hyperglycemia, we performed both univariate and multivariate logistic regression analyses. Utilizing the regression coefficients derived from each significant risk factor, we subsequently constructed a predictive model aimed at forecasting postoperative hyperglycemia.

Results: A total of 216 TBI patients were included, the incidence of postoperative hyperglycemia was 31.48%. Correlation analysis indicated that the age(r=0.415), BMI(r=0.441), diabetes(r=0.513), GCS score(r=0.545) and length of hospital stay(r=0.456) were all corrected to the postoperative hyperglycemia in TBI patients (all $P<0.05$). Age ≥ 60y (OR=2.556, 95%CI: 1.831~3.641), BMI ≥ 24 kg/m^2(OR=2.793, 95%CI: 2.305~3.679), diabetes (OR=3.081, 95%CI: 2.326~3.811) and GCS score≤8(OR=3.603, 95%CI: 1.956~4.086) were the independently influencing factors of postoperative hyperglycemia in TBI patients (all $P<0.05$). The area under the receiver operating characteristic curve and 95% CI were 0.795 (0.712, 0.849), the model had good discriminative ability to distinguish the occurrence of postoperative hyperglycemia in TBI

patients (all P<0.05).

Conclusion: Postoperative hyperglycemia in patients with TBI is common. For TBI patient with a total score ≥ 6, early interventions and care are needed to reduce the postoperative hyperglycemia.

Keywords: care; glucose; hyperglycemia; nursing; operation; traumatic brain injury; treatment.

Introduction

Traumatic brain injury (TBI) has a high rate of disability and fatality, and the incidence of TBI in China is about 0.2%[1]. Severe TBI accounted for about 20% TBI patients, of which the fatality rate of severe craniocerebral injury was 36.8% ~ 68.3%[2, 3]. An individual was deemed to have hyperglycemia if two distinct instances of random blood glucose tests showed a fasting glucose concentration above 6.1 mmol/L or a casual glucose concentration that surpassed 11.1 mmol/L[4]. After severe TBI, the hyperfunction of sympathetic-adrenal system is caused by the excitation of hypothalamus-pituitary-target gland axis, which leads to the increase of blood glucose[5, 6]. Some studies[7, 8] have found that the increase of blood glucose in patients with severe TBI is related to the degree and duration of disturbance of consciousness. In recent years, a large number of animal experiments and clinical studies have confirmed that the increase of blood glucose aggravates the secondary brain damage, and blood glucose is related to the prognosis of severe TBI[9, 10]. Therefore, the blood glucose management of patients with TBI is of great significance to the prognosis of patients.

It is currently recognized that the stress induced by TBI triggers a cascade of neuroendocrine

responses. Activation of the sympathetic nervous system and the adrenal medulla, along with increased secretion of hormones such as growth hormone, glucagon, adrenocorticotropin, and thyrotropin, can contribute to elevated blood glucose levels. These hormonal changes are part of the body's stress response, which, in the context of TBI, can have significant implications for glucose homeostasis and overall patient management[11, 12]. Although hyperglycemia in critically ill patients is transient, if not treated in time, it will cause serious damage to the body and affect the outcome of the disease[13-16]. At present, blood glucose is one of the important reasons that affect the prognosis of severe TBI. The longer the duration of hyperglycemia, the worse the prognosis[17, 18]. Blood glucose monitoring of patients with TBI has the characteristics of accurate, rapid, simple, easy and low cost for judging injury condition and prognosis[19]. It is an important means to monitor, guide treatment and judge prognosis of patients with TBI. The aim of this study was to conduct a comprehensive review and analysis of the prevailing conditions and contributing factors associated with hyperglycemia in patients with TBI within the initial 48 hours following surgical intervention. Furthermore, the study sought to create a predictive model for postoperative hyperglycemia specifically tailored to TBI patients. This model is intended to serve as a vital source of evidence-based support, informing and enhancing the treatment and nursing care strategies for individuals affected by TBI.

Methods

Ethics

This investigation was conducted as a retrospective cohort study focused on the status quo and influencing factors of postoperative hyperglycemia in patients with TBI. The research protocol

was reviewed and approved by the Suzhou Hospital, Affiliated Hospital of Medical School, Nanjing University, with the assigned approval number 20220046. All data collected were utilized solely for research purposes, ensuring the privacy and ethical treatment of the study participants.

Study population

In this study, we included patients who experienced TBI and subsequently underwent craniocerebral surgery at our facility between March 1, 2022, and October 31, 2023. The inclusion criteria were defined as follows: adult patients with age ≥ 18 years old; the patient had a clear history of brain trauma and was admitted to hospital within 8 hours after injury, and was diagnosed as "TBI" by brain CT scan[20]; the patients underwent surgery treatment in our hospital. The exclusion criteria were as follows: Patients with bilateral dilated pupils and dying TBI patients; TBI patients referred to our hospital from other hospitals; TBI patients with incomplete treatment data.

Data collection

The diagnosis of postoperative hyperglycemia was established based on the following criteria: a patient was considered to have hyperglycemia if two separate random blood glucose measurements revealed a fasting blood glucose level greater than 6.1 mmol/L or a random blood glucose level exceeding 11.1 mmol/L[21]. Blood glucose levels were closely monitored every three hours for the first 48 hours postoperatively. Once a TBI patient was diagnosed with hyperglycemia, they were promptly initiated on a standard insulin therapy regimen. Subsequently, the following data were meticulously gathered from the patients' medical and nursing record: age, gender, body mass index (BMI), hypertension, diabetes, hyperlipidemia, Glasgow coma scale

(GCS) score, duration of operation, length of hospital stay.

Statistical method

All collected data underwent analysis using the SPSS 23.0 software package. The measured data were presented as the mean ± standard deviation, with t-tests and analysis of variance (ANOVA) applied to analyze these data sets. Categorical data were assessed using the chi-square ($\chi 2$) test, while Pearson's correlation analysis was employed to examine the characteristics of the included TBI patients in relation to hyperglycemia. To pinpoint the independent contributing factors to postoperative hyperglycemia among TBI patients, logistic regression analysis was conducted. Scores were allocated to significant factors based on their respective partial regression coefficients in the logistic regression model. Subsequently, a risk prediction model for postoperative hyperglycemia in TBI patients was developed. The model's goodness-of-fit was evaluated using the Hosmer-Lemeshow (H-L) test. The sensitivity and specificity of the risk model were determined using the area under the receiver operating characteristic (ROC) curve. In this study, a difference was considered statistically significant if the P-value was less than 0.05.

Results

A total of 216 TBI patients were included in this study, of whom 68 patients had hyperglycemia within 48h after operation, the incidence of postoperative hyperglycemia in TBI patients was 31.48% in this study. As shown in Table 1, statistical differences in the age, BMI, diabetes, GCS score and length of hospital stay were found between hyperglycemia and no hyperglycemia patients with TBI (all $P<0.05$). No statistical differences in the gender, hypertension, hyperlipidemia and duration of operation were observed between hyperglycemia and no

hyperglycemia patients with TBI (all P>0.05).

Table 1 The characteristics of included TBI patients

As indicated in Table 2, results of correlation analysis indicated that the age(r=0.415), BMI(r=0.441), diabetes(r=0.513), GCS score(r=0.545) and length of hospital stay(r=0.456) were all corrected to the occurrence of postoperative hyperglycemia in TBI patients (all P<0.05).

Table 2 Correlation analysis on the characteristics of included TBI patients and hyperglycemia

The length of hospital stay was the result of hyperglycemia, so it was not taken as an independent variable in logistics regression analysis. This study included the other variables with statistical difference in the univariate analysis to further logistic regression analysis. The variable assignment for multivariate logistic regression analysis in this study is presented in Table 3. As presented in Table 4, the findings from the logistic regression analysis revealed that age ≥ 60y (OR=2.556, 95%CI: 1.831~3.641), BMI ≥ 24 kg/m^2(OR=2.793, 95%CI: 2.305~3.679), diabetes (OR=3.081, 95%CI: 2.326~3.811) and GCS score≤8(OR=3.603, 95%CI: 1.956~4.086) were the significant independent risk factors for postoperative hyperglycemia in TBI patients (all P<0.05).

Table 3 The variable assignment for multivariate logistic regression analysis

Table 4 Logistic regression analysis on the influencing factors of hyperglycemia in TBI patients

As shown in Table 5, this study developed the scoring criteria of the predictive model of

postoperative hyperglycemia in TBI patients. Based on the ROC curve (Figure 1) and scoring standard of the risk prediction model, the sensitivity and specificity of the prediction model under different cut-off scores were calculated and compared, and the according Youden index (sensitivity + specificity -1) was calculated. As presented in Table 6, the Youden index was higher when the total score was between 5.5 to 6.5. Thus the total score= 6 was used as the cuff value of this risk predicting model. The sensitivity and specificity of the prediction model were all high when the total score= 6. The area under the ROC curve (AUC) and 95% CI were 0.795 (0.712, 0.849), indicating that the risk predicting model had good discriminative ability to distinguish the occurrence of postoperative hyperglycemia in TBI patients (all $P<0.05$).

Table 5 The scoring method of the logistic model for the risk of hyperglycemia in TBI patients

Figure 1 The ROC curve of the risk prediction model for hyperglycemia in TBI patients

Table 6 The sensitivity and specificity of the prediction model under different cuff values

Discussions

Hyperglycemia represents a metabolic response of the body following traumatic or stressful events. While it may be transient in nature, failure to address it promptly can lead to significant harm to the body and adversely impact the disease's prognosis[22-24]. A number of previous studies[25-27] have confirmed that hyperglycemia has an adverse effect on the prognosis of critically ill patients. It has been reported that the control of hyperglycemia will be beneficial to

the prognosis of TBI[28]. The results of this study show that the incidence of postoperative hyperglycemia in TBI patients is 31.48%, and age ≥ 60y, BMI ≥ 24 kg/m^2, diabetes and GCS score≤8 are the independently influencing factors of postoperative hyperglycemia in TBI patients. Besides, this study has developed a useful predicting model for postoperative hyperglycemia in TBI patients, which is easy and helpful for the clinical treatment and nursing care of TBI patients.

Hyperglycemia is very common in postoperative patients. There is a strong stress response after craniocerebral injury, which leads to the over-excitation of the sympathetic-adrenal medulla system and the increase of catecholamine in the blood[29, 30]. The sympathetic efferent pathway of the hypothalamus and brainstem is damaged by primary or secondary reasons, which excitates the sympathetic nerve and leads to a sharp increase in the secretion of catecholamine in the body, stimulating the release of glucagon, decomposing liver glycogen and inhibiting insulin secretion[31-33]. On the one hand, the increase of blood glucose after TBI strengthens glycolysis and the production of lactic acid, which leads to a large number of Na+ entering into the cell and induces cellular brain edema[34]. On the other hand, the strengthening of anaerobic metabolism can lead to the disturbance of energy generation, resulting in intracellular high sodium, extracellular high potassium and calcium overload, increasing the catabolism of adenosine 5'-triphosphate, cellular protein and lipid, and damaging the cellular skeleton system and membrane system[35, 36]. All of the above factors can further aggravate the degree of intracellular brain edema and then aggravate the increase of intracranial pressure after TBI[37, 38]. If it cannot be effectively controlled, it will fall into a vicious circle of intracranial hypertension, brain edema, cerebral hypoxia and aggravate intracranial hypertension, resulting in the death of patients[39-41].

Therefore, dynamic monitoring of blood glucose and active control of blood glucose level has become one of the keys to the treatment of TBI patients.

Hyperglycemia has been paid more and more attention in clinical work. Hyperglycemia will prolong the wound recovery time and hospitalization time of patients, and delay the time of early recovery of patients[42]. At present, under the advocacy of the concept of accelerated rehabilitation surgery, higher requirements and standards have been put forward for the treatment and nursing of TBI patients. Currently most hospitals still use venous blood or peripheral blood to monitor patients' blood glucose level, and use combined intravenous infusion of insulin to treat hyperglycemia response in critically ill patients[43]. However, frequent blood collection and simple peripheral or venous blood collection bring discomfort to patients, at the same time, they only reflect the instantaneous blood glucose level at a fixed time point, and cannot find the abnormal blood glucose in real time[44, 45]. Many studies[46-48] have shown that blood glucose fluctuation is one of the important factors affecting the prognosis of patients with severe diseases. Some study[49] has used a dynamic blood glucose monitoring system, through blood glucose monitoring at as many as 288 time points a day, the results show that there is a correlation between blood glucose fluctuation and the condition of patients with craniocerebral trauma. Therefore, the continuous monitoring and management of blood glucose in patients with TBI has an important impact on the prognosis of patients. The predictive model for postoperative hyperglycemia in TBI patients developed in this study exhibits good fit, as evidenced by the H-L test and the ROC curve analysis. These results affirm that the model possesses high predictive accuracy and discriminative power. Patients with a total score of 6 or greater are at an increased

risk for the development of postoperative hyperglycemia. Consequently, prompt recognition and vigilant nursing care are essential to mitigate the incidence of postoperative hyperglycemia in this patient population. It is necessary to continuously observe the relationship between the use of hypoglycemic drugs and the fluctuation of blood glucose, keep blood glucose in a safe range, detect abnormalities as soon as possible and deal with them, and reduce secondary brain damage to a minimum, so as to improve the quality of life of patients with brain trauma[50, 51].

Several limitations in this study must be considered. Firstly, this study was a single-centered study, the sample size is small, it may be underpowered to detect the potentially associated factors of postoperative hyperglycemia. Secondly, due to the retrospective nature of this study design, there may exist additional factors that could influence the development of postoperative hyperglycemia which were not accounted for in the analysis. Thirdly, this study lacks an assessment of glycated hemoglobin, or glycated albumin, to correct patients' recent blood sugar levels. In clinical practice, the combination of glycated hemoglobin and glycated albumin, can more accurately reflect the changes of blood glucose control in patients. The standardization of detection methods and indicators, as well as the development of portable devices, can help diabetic patients better understand their blood glucose control level and achieve a better effect of blood sugar control. Finally, the predicting model for postoperative hyperglycemia in TBI patients in this study needs to be verified by more prospective studies with lager sample size in the future. Our research team will expand the sample size and increase the number of positive samples in the future to further verify the predicting performance of this risk model, to provide useful and reliable evidence for clinical TBI treatment and care.

Conclusion

In conclusion, this study has found that the incidence of postoperative hyperglycemia in TBI patients is 31.48%, and for TBI patients with age ≥ 60y, BMI ≥ 24 kg/m^2, diabetes and GCS score≤8, they have higher risk of postoperative hyperglycemia. Furthermore, this study has developed a useful predicting model for postoperative hyperglycemia in TBI patients. The model is easy and convenience for clinical use, which is helpful for the risk evaluation of TBI patients.

List of abbreviations

TBI, traumatic brain injury

BMI, body mass index

GCS, Glasgow coma scale

ROC, receiver operating characteristic

Declarations

Ethics approval and consent to participate

In this study, all methods were performed in accordance with the relevant guidelines and regulations. The study has been reviewed and approved by the ethics committee of Suzhou Hospital, Affiliated Hospital of Medical School, Nanjing University (approval number: 20220046). And written informed consents had been obtained from all the included patients.

Consent for publication

Not applicable.

Availability of data and materials

The data associated with the paper are not publicly available but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

XY, Y X, X M designed research; X Y, Y X, L S, X Z, L L, X M conducted research; Y X, L S analyzed data; X Y, Y X, L S wrote the first draft of manuscript; L L, X M had primary responsibility for final content. All authors read and approved the final manuscript.

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Figure legend

Figure 1 The ROC curve of the risk prediction model for hyperglycemia in TBI patients

Table 1 The characteristics of included TBI patients

Variables	Hyperglycemia group (n=68)	No hyperglycemia group(n=148)	t/χ^2	P
Age(y)	64.01±8.12	52.38±9.74	12.005	0.011
Male/female	40/28	93/55	1.944	0.106
BMI (kg/m^2)	25.10±3.92	22.82±2.97	4.746	0.013
Hypertension	25(36.76%)	58(39.19%)	1.097	0.187
Diabetes	46(67.65%)	49(33.11%)	1.206	0.005
Hyperlipidemia	21(30.88%)	40(27.03%)	1.691	0.147
GCS score	7.06±2.15	11.63±3.02	1.977	0.012
Duration of operation (min)	80.21±24.77	69.86±25.27	16.033	0.065
Length of hospital stay(days)	7.24±2.08	4.07±3.13	1.665	0.045

TBI, traumatic brain injury; BMI, body mass index; GCS, Glasgow coma scale

Table 2 Correlation analysis on the characteristics of included TBI patients and hyperglycemia

Variables	r	P
Age(y)	0.415	0.016
Gender	0.209	0.118
BMI (kg/m^2)	0.441	0.014
Hypertension	0.086	0.105
Diabetes	0.513	0.023
Hyperlipidemia	0.091	0.147
GCS score	0.545	0.007
Duration of operation (min)	0.113	0.104
Length of hospital stay(days)	0.456	0.041

TBI, traumatic brain injury; BMI, body mass index; GCS, Glasgow coma scale

Table 3 The variable assignment for multivariate logistic regression analysis

Factors	Variables	Assignment
Hyperglycemia	Y	Yes=1, no=2
Age(y)	X_1	≥60=1, <60=2
BMI (kg/m^2)	X_2	≥24=1, <24=2
Diabetes	X_3	Yes=1, no=2
GCS score	X_4	≤8=1, >8=2

BMI, body mass index; GCS, Glasgow coma scale

Table 4 Logistic regression analysis on the influencing factors of hyperglycemia in TBI patients

Variables	β	Wald	OR	95%CI	P
Age ≥ 60y	0.188	0.104	2.556	1.831~3.641	0.015
BMI ≥ 24 kg/m^2	0.117	0.124	2.793	2.305~3.679	0.036
Diabetes	0.126	0.212	3.081	2.326~3.811	0.012
GCS score≤8	0.175	0.185	3.603	1.956~4.086	0.008

TBI, traumatic brain injury; BMI, body mass index; GCS, Glasgow coma scale.

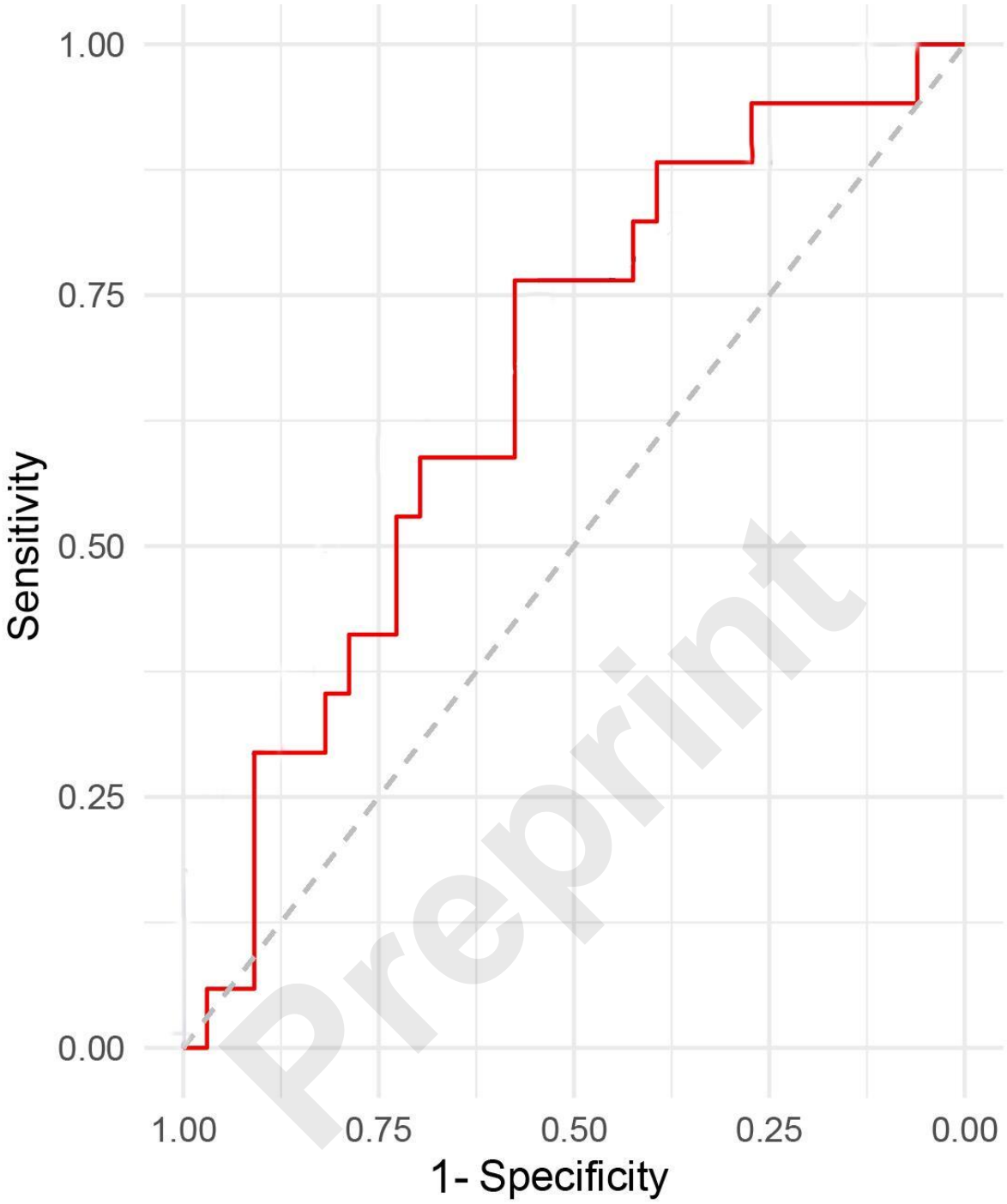
Table 5 The scoring method of the logistic model for the risk of hyperglycemia in TBI patients

Variable	Score
Age ≥ 60y	2
BMI ≥ 24 kg/m^2	2
Diabetes	3
GCS score≤8	3

Table 6 The sensitivity and specificity of the prediction model under different cuff values

Total score	Sensitivity	Specificity	Yorden Index
-1.0	1.000	0.000	0.000
1.0	1.000	0.125	0.125
1.5	0.977	0.231	0.208
2.5	0.921	0.384	0.305
3.5	0.862	0.559	0.421
4.5	0.823	0.702	0.525
5.5	0.680	0.864	0.544
6.5	0.678	0.891	0.569
7.5	0.226	0.904	0.130
8.5	0.127	0.922	0.049
9.5	0.109	0.937	0.046

10.5	0.023	1.000	0.023
11	0.000	1.000	0.000


1.00
0.75
0.50
0.25
0.00
Sensitivity
1.00
0.75
0.50
0.25
0.00
1- Specificity

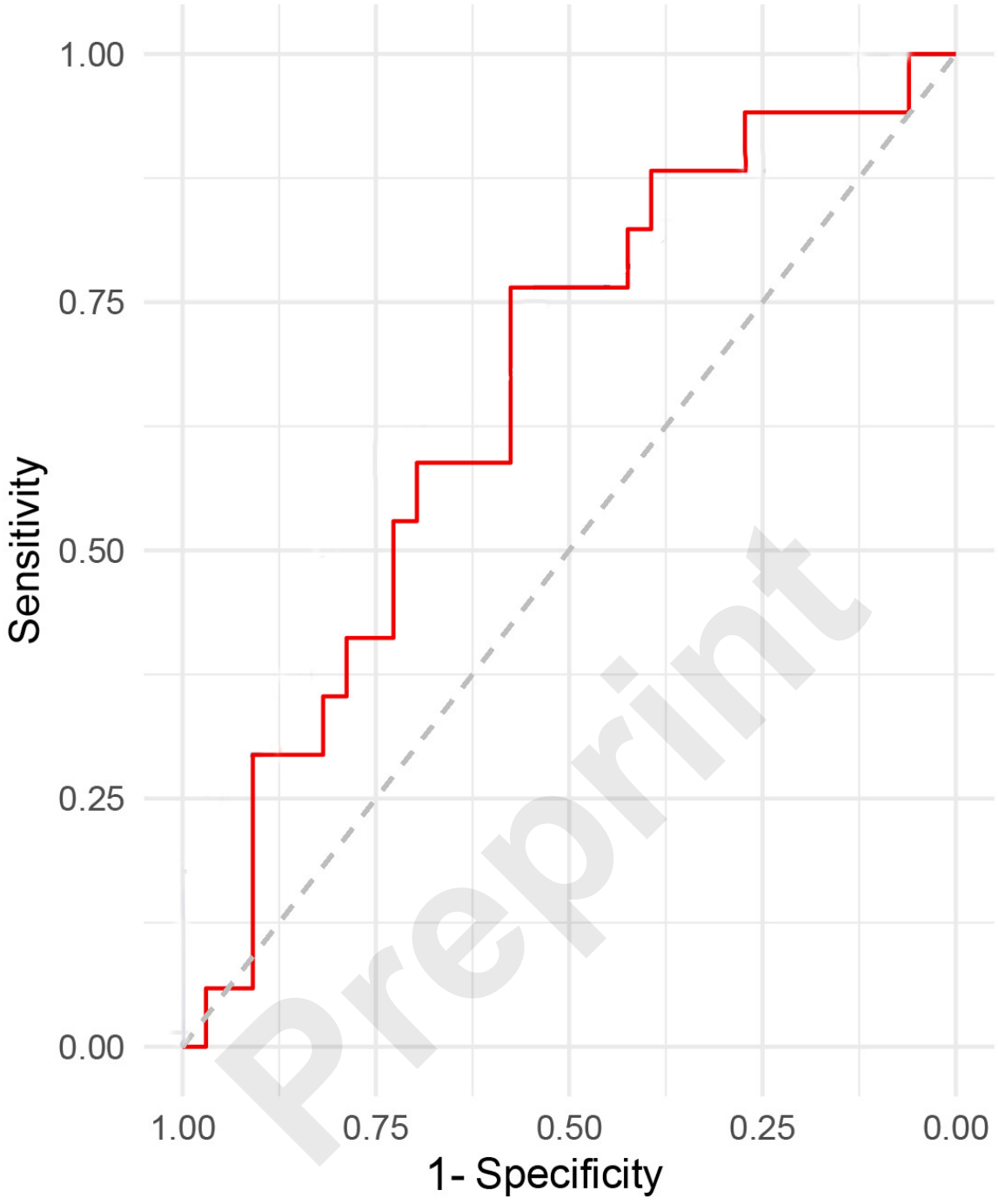


Figure 1 The ROC curve of the risk prediction model for hyperglycemia in TBI patients