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Original Article

Plasma glucose, serum albumin, and serum triglyceride, could influence and predict the prognosis of patients with supratentorial hypertensive intracerebral hemorrhage

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Abstract: Objective: To analyze the relationship among the clinical factors and the prognoses of patients with supratentorial hypertensive intracerebral hemorrhage and to identify the prognosis-related factors. Method: Patients suffering from supratentorial hypertensive intracerebral hemorrhage were divided into a low score group (GOS1~3) and a high score group (GOS 4&5). Univariate and multiple variate logistic regression analyses were used to explore the risk factors affecting GOS. The independent factors of the low score GOS were analyzed in the multiple factor logistic regression model using the single factor logistic regression analysis results in the multiple factor logistic regression model. The ROC curve and the area under the ROC curve were used to predict the effect of the first fasting plasma glucose, serum albumin, and serum triglyceride in patients with low GOS scores and to determine the best sensitivity and specificity according to the approximate value of the ROC curve. All statistical analyses were performed using bilateral tests; and $P < 0.05$ was considered statistically significant. Result: 125 patients were recruited for this study and divided into high score (GOS1~3) and low score groups (GOS4 &5). Univariate and multiple variate logistic regression revealed that first fasting plasma glucose, serum albumin, and serum triglyceride could influence the prognoses of patients with supratentorial hypertensive intracerebral hemorrhage. An ROC curve analysis indicated that the combination of first fasting plasma glucose, serum albumin and serum triglyceride could predict patient prognosis. Conclusion: The first fasting plasma glucose, serum albumin, and serum triglyceride can influence and predict the prognosis of patients with supratentorial hypertensive intracerebral hemorrhage.

Keywords: Supratentorial hypertensive intracerebral hemorrhage, GOS, first fasting plasma glucose, serum albumin, serum triglyceride

Introduction

Supratentorial hypertensive intracerebral cerebral hemorrhage (sHICH), also known as supratentorial cerebral bleed caused by long time hypertension, is a type of intracranial bleed that occurs within the brain tissue or ventricles [1]. Many patients suffering from supratentorial hypertensive intracerebral cerebral hemorrhage usually leave adverse sequelae, such as paralysis, aphasia and dysphasia, which bring about physical and psychological pain and heavy economic pressure on the patients and their families [1-3]. The causes of sHICH should preclude brain trauma, aneurysms, arteriovenous malformations. and brain tumors [1, 4, 5]. The largest risk factors for spontaneous supratentorial intracerebral cerebral hemorrhage are high blood pressure and amyloidosis. Other specific risk factors include alcoholism, low cholesterol, blood thinners, and cocaine use [6-9].

In order to analyze the risk factors which affect or predict the prognosis of sHICH, a retrospective clinical analysis at a single center was carried out. The prognosis was assessed by the Glasgow Outcome Score (GOS) six months after treatment. Many of the clinical factors were statistically analyzed by univariate and multiple

variate logistic regression analyses, including an ROC curve analysis, which looked at sex, age, hospitalization days, systolic blood pressure, diastolic blood pressure, the side of hematoma, the areas of involvement, hemorrhage broken into ventricles, hematoma volume, cerebral hernia, GCS of disease onset, plasma glucose of disease onset, fasting plasma glucose, serum uric acid, serum total cholesterol, serum triglyceride, serum albumin, and the treatment method.

Materials and methods

Patients

Clinical data from patients suffering from supratentorial hypertensive cerebral hemorrhage (ICH) and receiving residential treatment in Sun Yat-sen Memorial Hospital, Zengcheng Branch was collected and retrospectively analyzed. The factors we focused on included sex (male or female), age, length of hospital stay, systolic blood pressure, diastolic blood pressure, the side of hematoma (left or right), the areas of involvement, hemorrhage broken into ventricles (yes or no), hematoma volume, cerebral hernia (yes or no), GCS of disease onset, plasma glucose of disease onset, fasting plasma glucose, serum uric acid, serum total cholesterol, serum triglyceride, serum albumin, treatment method, and the patient's prognosis (GOS). The Glasgow Outcome Score (GOS) is a scale for patients with brain damage who can be divided into groups that allow standardized descriptions of the objective degree of recovery in five categories [10]. Patients with GOS 1 were assessed with severe injury or death without the recovery of consciousness; patients with GOS 2 were assessed with severe damage with a prolonged state of unresponsiveness and a lack of higher mental functions; patients with GOS 3 were assessed with severe injury with the permanent need for help with daily living; patients with GOS 4 were assessed with no need for assistance in everyday life; employment is possible but may require special equipment; patients with GOS 4 were assessed with light damage with minor neurological and psychological deficits. Patients with GOS 1-3 were regarded as severe sequela and poor prognosis; and Patients with GOS 4-5 were regarded as having light sequela and better prognoses. All patients were followed up for more than 6 months. Inclusion criteria: 1. Spontaneous intracerebral hemorrhage; 2. Imaging studies confirmed the diagnosis; 3. Supratentorial cerebral hemorrhage. Exclusion criteria: 1. Hemorrhage due to cerebral AVMs and aneurysms; 2. Traumatic ICH; 3. Tumor bleeding; 4. Cerebellar or brainstem hemorrhage; 5. Patients or their immediate family members refused further treatment.

Statistical analysis

Demographics and baseline characteristics of the subjects were presented as the mean ± standard deviation for continuous data with a normal distribution and median (25th to 75th percentiles) for continuous data with skewed variables and compared by Student's *t* test and an Mann-Whitney U test, respectively. Categorical data were presented as the percentage and compared using the Chi-square or Fisher's exact test, as appropriate. Odds ratios (ORs) and 95% confidence intervals (95% CI) were calculated in unadjusted and multivariate-adjusted logistic regression model analyses. To build the multiple logistic regression model, we selected variables with clinical significance and all the association factors with $P \leq 0.05$ at the univariable level. A receiver operating characteristic (ROC) curve was used to evaluate the predictive value of the three predicators including first blood glucose, triglyceride and albumin. Area under the curve (AUC) was used to evaluate the "overall diagnostic accuracy" of the test in relation to GOS. All statistical assessments were performed using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA). A two-tailed $P < 0.05$ was considered indicative of statistical significance.

Result

General statistical description

Data from 125 patients with supratentorial hypertensive cerebral hemorrhage (sHICH) receiving residential treatment were collected and retrospectively analyzed based on inclusion and exclusion criteria. All the patients were divided into the low GOS group or the high GOS group based on the prognosis. In all 43 females and 82 males were included in the study, and their ages ranged from 35-75 years old. 86 patients received conservative treatment and

Table 1. General characteristics of the research subjects

	GOS		χ2	*P*
	Low GOS (classes 1-3)	High GOS (classes 4-5)		
Sex				
Male	38 (46.3)	44 (53.7)	0.530	0.466
Female	17 (39.5)	26 (60.5)		
Years				
≤ 50	12 (32.4)	25 (67.6)	3.052	0.217
51-60	24 (51.1)	23 (48.9)		
≥ 61	19 (46.3)	22 (53.7)		
Days				
≤ 10	18 (56.3)	14 (43.8)	3.899	0.142
11-20	18 (34.6)	34 (65.4)		
≥ 21	19 (46.3)	22 (53.7)		
Left or Right				
Left	23 (41.8)	32 (58.2)	0.190	0.663
Right	32 (45.7)	38 (54.3)		
Involvement				
1 area	31 (32.0)	66 (68.0)		
2 areas	16 (80.0)	4 (20.0)	26.409	< 0.001
3 areas	8 (100.0)	0		
Hemorrhage broken into ventricles				
No	33 (38.4)	53 (61.6)	3.543	0.060
Yes	22 (56.4)	17 (43.6)		
Cerebral hernia				
No	52 (42.6)	70 (57.4)	3.912	0.048
Yes	3 (100.0)	0		

39 patients received an operation or either trepanation and drainage or eliminating the hematoma and decompressive craniotomy. 55 patients were assessed at GOS 1-3, and 70 patients were assessed at GOS 4-5. The detailed information showed in **Table 1**.

Univariate and multiple variate logistic regression

In this study, as the results shown in **Tables 2** and **3**. Univariate and multiple variate logistic regression revealed that at the first time fasting plasma glucose, serum albumin and serum triglyceride could influence the prognosis of patients with supratentorial hypertensive intracerebral hemorrhage. The analysis showed that the median and four-digit spacing of the first fasting blood glucose at high GOS group (GOS 4&5) after hospitalization was 5.67 (4.86~6.60), and the median and four-digit spacing of the first fasting blood glucose in low GOS group (GOS 1-3) was 6.93 (5.90~8.89), and the GOS score was negatively correlated with the first fasting blood glucose (GOS 4) after hospitalization (GOS 4&5 vs. GOS 1-3 = 5.67 vs. 6.93). Notably, the first time fasting blood glucose value in the GOS 5 group was the lowest compared with GOS 1-4 respectively after hospitalization. The results suggested that good blood sugar control after hospitalization helps to improve postoperative GOS score. Additionally, the correlation analysis of the first time serum albumin level and the GOS score was completed after the patients were released from the hospital. Comparing the average level of the first time serum albumin in the GOS 4&5 group 41.88 ± 3.44 with the GOS 1-3 group 40.16 ± 5.87, the difference was statistically significant (P = 0.031). Furthermore, the correlation analysis of the first time serum triglyceride level and GOS score was completed after the patients were released from the hospital. Comparing the average level of the first time serum triglyceride in the GOS 4&5 group with the GOS 1-3

Table 2. Univariate logistic regression analysis of low GOS

	Patients (%)	Low GOS (%)	OR (95% CI)	*P*
Sex				
Male	82	38 (46.3)	1.00	0.467
Female	43	17 (39.5)	0.76 (0.36-1.60)	
Ages				
≤ 50	37	12 (32.4)	1.00	0.223
51-60	47	24 (51.1)	2.17 (0.89-5.32)	0.089
≥ 61	41	19 (46.3)	1.80 (0.72-4.53)	0.212
Days				
≤ 10	32	18 (56.3)	1.00	0.147
11-20	52	18 (34.6)	0.41 (0.17-1.02)	0.054
≥ 21	41	19 (46.3)	0.67 (0.27-1.70)	0.402
Systolic pressure (mmHg)				
≤ 150	38	14 (36.8)	1.00	0.605
151-167	25	10 (40.0)	1.14 (0.41-3.22)	0.801
168-180	24	12 (50.0)	1.71 (0.61-4.83)	0.308
≥ 181	38	19 (50.0)	1.71 (0.69-4.28)	0.249
Diastolic pressure (mmHg)				
< 90	29	15 (51.7)	1.00	0.197
90-94	34	12 (35.3)	0.51 (0.19-1.40)	0.191
95-105	34	12 (35.3)	0.51 (0.19-1.40)	0.191
≥ 106	28	16 (57.1)	1.24 (0.44-3.54)	0.682
Left or Right				
Left	55	23 (41.8)	1.00	0.663
Right	70	32 (45.7)	1.17 (0.57-2.39)	
Involvement				
1 area	97	31 (32.0)	1.00	0.002
2 areas	20	16 (80.0)	8.52 (2.63-27.60)	< 0.001
3 areas	8	8 (100.0)	-	-
Hemorrhage broken into ventricles				
No	86	33 (38.4)	1.00	0.062
Yes	39	22 (56.4)	2.08 (0.96-4.48)	
Hematoma volume (mL)				
≤ 10	54	10 (18.5)	1.00	< 0.001
11-20	35	14 (40.0)	2.93 (1.12-7.69)	0.029
≥ 21	36	31 (86.1)	27.28 (8.49-87.70)	< 0.001
Cerebral hernia				
No	122	52 (42.6)	1.00	0.048
Yes	3	3 (100.0)	-	
GCS of disease onset				
≤ 10	32	28 (87.5)	1.00	< 0.001
≥ 11	93	27 (29.0)	0.06 (0.02-0.18)	
Plasma glucose of disease onset (mmol/L)				
≤ 6.11	31	10 (32.3)	1.00	0.044
6.12-7.13	32	10 (31.3)	0.96 (0.33-2.76)	0.932
7.14-8.43	31	19 (61.3)	3.33 (1.17-9.44)	0.024
≥ 8.44	31	16 (51.6)	2.24 (0.80-6.28)	0.125
Fasting Plasma Glucose (mmol/L)				

≤ 5.16	31	9 (29.0)	1.00	0.002
5.17-6.15	32	8 (25.0)	0.82 (0.27-2.48)	0.719
6.16-7.62	31	18 (58.1)	3.39 (1.18-9.71)	0.023
≥ 7.63	31	20 (64.5)	4.44 (1.53-12.94)	0.006
Serum Uric Acid (μmol/L)				
≤ 240.5	31	13 (41.9)	1.00	0.446
240.6-312.0	32	18 (56.3)	1.78 (0.66-4.83)	0.258
312.1-422.0	31	12 (38.7)	0.87 (0.32-2.41)	0.796
≥ 422.1	31	12 (38.7)	0.87 (0.32-2.41)	0.796
Serum Total Cholesterol (mmol/L)				
≤ 4.11	32	14 (43.8)	1.00	0.298
4.12-4.83	31	11 (35.5)	0.71 (0.26-1.95)	0.503
4.84-5.57	31	12 (38.7)	0.81 (0.30-2.22)	0.685
≥ 5.58	31	18 (58.1)	1.78 (0.66-4.83)	0.258
Serum Triglyceride (mmol/L)				
≤ 0.64	33	12 (36.4)	1.00	0.122
0.65-0.97	30	19 (63.3)	3.02 (1.08-8.44)	0.035
0.98-1.37	31	12 (38.7)	1.11 (0.40-3.04)	0.846
≥ 1.38	31	12 (38.7)	1.11 (0.40-3.04)	0.846
Serum Albumin (g/L)				
≤ 38.26	31	21 (67.7)	1.00	0.008
38.27-41.38	32	11 (34.4)	0.25 (0.09-0.71)	0.009
41.39-44.45	31	8 (25.8)	0.17 (0.06-0.50)	0.001
≥ 44.46	31	15 (48.4)	0.45 (0.16-1.25)	0.125
Treatment Method				
Conservative Treatment	86	22 (25.6)	1.00	< 0.001
Trepanation and Drainage	30	24 (80.0)	11.64 (4.21-32.18)	< 0.001
Decompressive craniotomy	9	9 (100.0)	-	-

group, the difference was statistically significant. As shown in **Figures 1** and **2**.

Receiver operating characteristic (ROC) analysis

An ROC curve is a graphical plot that illustrates the diagnostic ability of a binary classifier system as its discrimination threshold is varied. In this study, the factors affecting the GOS low score event (GOS 1-3) in the multivariate logistic regression analysis were included, including first time fasting plasma glucose, serum albumin and serum triglyceride after hospitalization. According to the four quantile spacings of the three above, such three indexes were independent factors that influenced the occurrence of a GOS low score event (GOS 1-3). In order to analyze the ability of such three indexes predicting the ability of a GOS low score event (GOS 1-3), a receiver operating characteristic (ROC) analysis was carried out via the area under the ROC curve. As shown in the ROC chart, the area under the ROC curve (AUC) is 0.778 (AUC = 0.778, 95% CI: 0.698-0.857, P < 0.001), indicating that the combination of the first time fasting plasma glucose, serum albumin, and serum triglyceride after the patient's hospitalization can better predict and influence the patient's GOS. Based on the ROC curve area, the best sensitivity and specificity were determined according to the Jordan index. In this study, the best Jordan index was 0.417, the sensitivity was 94.5% and the specificity was 47.1%. In summary, as for predicting the patients' GOS, the first time fasting plasma glucose, serum albumin and serum triglyceride after hospitalization are good predictive indexes of the patients' prognosis (As shown in **Figure 3**).

Discussion

Risk factors for supratentorial hypertensive intracerebral cerebral hemorrhage (sHICH) have

Table 3. Multivariate logistic regression analysis of low GOS

	β	S.E.	Wald	OR (95% CI)	*P*
Sex (male *vs.* female)	-0.77	0.71	1.18	0.47 (0.12-1.85)	0.277
Ages (≤ 50 *vs.* 51-60)	2.66	0.98	7.14	13.76 (2.01-94.13)	0.008
Ages (≤ 50 *vs.* ≥ 61)	2.16	1.00	4.63	8.64 (1.21-61.61)	0.031
Days (≤ 10 *vs.* 11-20)	1.09	1.04	1.10	2.98 (0.39-23.06)	0.295
Days (≤ 10 *vs.* ≥ 21)	1.51	0.99	2.31	4.51 (0.65-31.55)	0.129
Involvement (1 area *vs.* 2 areas)	0.56	1.27	0.19	1.75 (0.15-21.00)	0.661
Hemorrhage broken into ventricles (No *vs.* Yes)	-0.89	0.77	1.32	0.41 (0.09-1.87)	0.250
Hematoma volume(mL) (≤ 10 *vs.* 11-20)	1.13	0.71	2.50	3.09 (0.76-12.49)	0.114
Hematoma volume(mL) (≤ 10 *vs.* ≥ 21)	1.40	1.31	1.14	4.07 (0.31-53.21)	0.285
GCS of disease Onset (≤ 10 *vs.* ≥ 11)	-0.87	1.08	0.66	0.42 (0.05-3.44)	0.420
Plasma glucose of disease Onset (mmol/L) (≤ 6.11 *vs.* 6.12-7.13)	0.66	0.93	0.50	1.93 (0.31-11.94)	0.481
Plasma glucose of disease Onset (mmol/L) (≤ 6.11 *vs.* 7.14-8.43)	0.26	1.05	0.06	1.29 (0.17-10.10)	0.806
Plasma glucose of disease Onset (mmol/L) (≤ 6.11 *vs.* ≥ 8.44)	-0.30	1.13	0.07	0.74 (0.08-6.82)	0.794
Fasting Plasma Glucose (mmol/L) (≤ 5.16 *vs.* 5.17-6.15)	0.13	0.98	0.02	1.14 (0.17-7.79)	0.892
Fasting Plasma Glucose (mmol/L) (≤ 5.16 *vs.* 6.16-7.62)	2.07	1.05	3.86	7.94 (1.01-62.63)	0.049
Fasting Plasma Glucose (mmol/L) (≤ 5.16 *vs.* ≥ 7.63)	2.08	1.12	3.43	8.01 (0.89-72.40)	0.064
Serum Triglyceride(mmol/L) (≤ 0.64 *vs.* 0.65-0.97)	1.46	0.87	2.85	4.32 (0.79-23.57)	0.091
Serum Triglyceride(mmol/L) (≤ 0.64 *vs.* 0.98-1.37)	0.52	0.93	0.31	1.68 (0.27-10.47)	0.577
Serum Triglyceride(mmol/L) (≤ 0.64 *vs.* ≥ 1.38)	0.80	0.88	0.83	2.23 (0.40-12.54)	0.363
Serum Albumin(g/L) (≤ 38.26 *vs.* 38.27-41.38)	-1.28	0.89	2.08	0.28 (0.05-1.58)	0.150
Serum Albumin(g/L) (≤ 38.26 *vs.* 41.39-44.45)	-2.72	1.08	6.38	0.07 (0.01-0.54)	0.012
Serum Albumin(g/L) (≤ 38.26 *vs.* ≥ 44.46)	-0.76	0.86	0.78	0.47 (0.09-2.53)	0.466
Treatment Method (Conservative Treatment *vs.* trepanation and drainage)	2.74	1.39	3.90	15.44 (1.02-233.85)	0.048

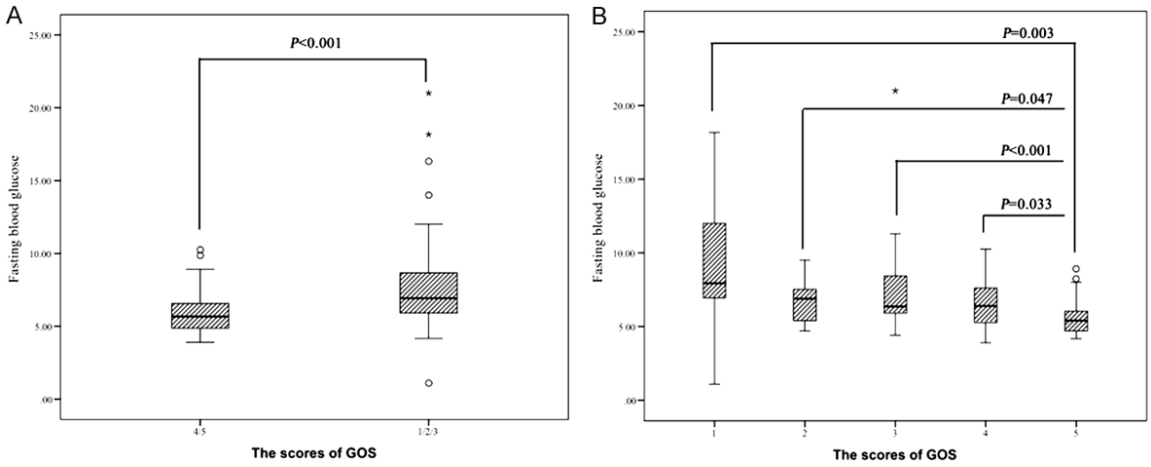

Figure 1. Correlation analysis of the first day fasting blood glucose and GOS score after hospitalization. A. Comparison of the 2 main groups. GOS score was negatively correlated with the first fasting blood glucose (GOS 4) after hospitalization (GOS 4&5 vs. GOS 1-3 = 5.67 vs. 6.93). B. Comparison among 5 groups. The changes of the first time fasting blood glucose for GOS 1-5 were analyzed respectively. GOS 5 vs. GOS 4: 5.41 (4.71~6.08) vs. 6.40 (5.23~7.64), P = 0.033; GOS 5 vs. GOS 3; 5.41 (4.71~6.08) vs. 6.36 (5.91~8.67), P < 0.001; GOS 5 vs. GOS 2; 5.41 (4.71~6.08) vs. 6.89 (5.27~7.66), P = 0.047; GOS 5 vs. GOS 1; 5.41 (4.71~6.08) vs. 7.94 (6.35~12.50), (P = 0.003).

been assessed in some other studies [7, 9, 11-15] which suggested that the prognosis of sHICH might be associated with different surgical treatments, the Glasgow Outcome Scale scores at the onset, hemorrhage volume, age, blood pressure, blood glucose level and serum

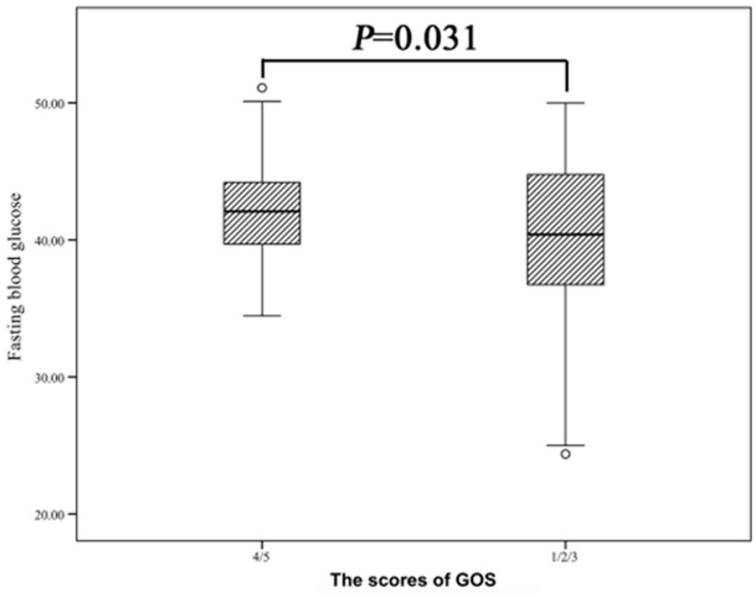

Figure 2. Correlation analysis of the first time serum albumin level and GOS score after hospitalization. The average level of the first albumin in the GOS 4 & 5 group was 41.88 ± 3.44 after hospitalization. The average level of the first albumin in the GOS 1-3 group was 40.16 ± 5.87, and the difference was statistically significant (P = 0.031).

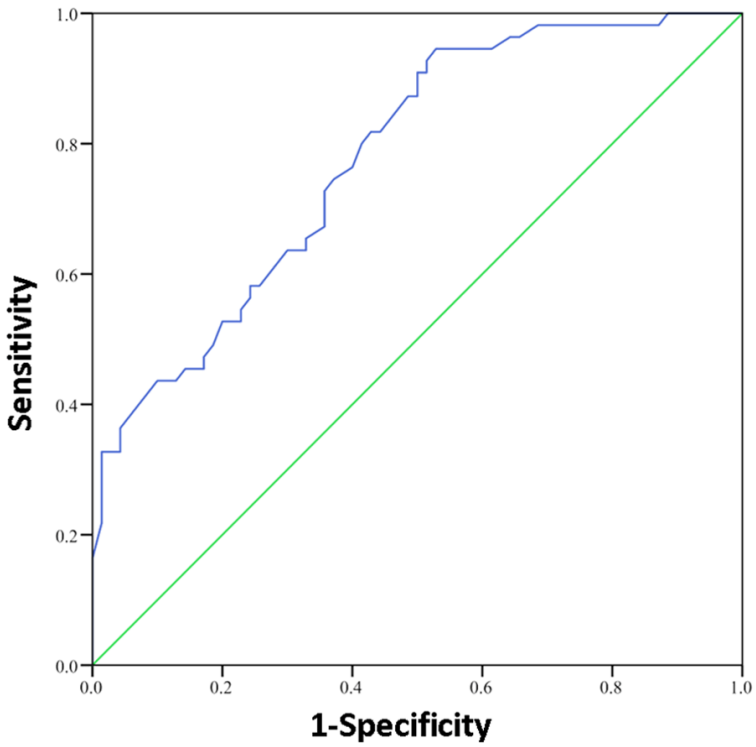

Figure 3. ROC curve for first time fasting plasma glucose, serum albumin, and serum triglyceride combinationally predicting a low GOS event (GOS 1-3). AUC = 0.778, 95% CI: 0.698-0.857, (P < 0.001).

cholesterol and lipids. However, some studies were slightly contradictory in terms of identifying the risk factors to some extent. For example, Zhao et al. indicated that decompressive craniotomy is more suitable for treating HICH patients than minimally invasive aspiration [11], but Wang et al. considered minimally as a better surgical method [16]. Therefore, we assessed the possible risk factors for sHICH and attempted to figure out a fitted curve of risk factors for prognosis.

In the present study, some factors were found to be related to different prognoses of sHICH, such as hematoma volume, the occurrence of cerebral hernia, GCS score on admission, treatment method, serum triglyceride and plasma glucose levels. On the other hand, factors like age, the degree of hypertension and serum total cholesterol et al. were not associated with the prognosis of sHICH based on our research. Among all these risk factors, a further multivariate logistic regression analysis was carried out to determine the independent variables for the prognosis of sHICH, which were subsequently analyzed using an ROC curve. As a result, high plasma glucose levels, low serum albumin levels and high serum triglyceride could jointly predict the low GOS which represented the poor prognosis of sHICH.

As Wang Y et al. [17] have reported, those patients with normal serum glucose enjoyed a better prognosis than those with diabetes or hyperglycemia. Stollerger et al. [18] also came to a similar conclusion. These results were similar to those from the present study. Regarding triglyceride, Li, W et al. [19] reported that the low levels of serum triglycerides and total cholesterol were related to increased 3-month poor

outcome in ischemic stroke and ICH. However, the present study showed that total cholesterol did not appear as a significant risk factor with P > 0.05 while serum triglyceride was, on the contrary, positively related to the poor outcome of sHICH. The difference might result from the different study design with which the former study paid attention to both ischemic stroke and ICH, but the present study only focused on the sHICH.

Few studies have reported the relation between serum albumin level and the prognosis of sHICH, but Zavertailo et al. showed that an enteral feeding protocol involving low glucose or albumin would significantly lead to a poor recovery from cerebral damage. The present study directly focused on serum albumin which would predict the outcome of sHICH. To conclude, the present study not only analyzed the risk factors for the prognosis of sHICH, but it also figured out a ROC curve involving three serum factors to predict the outcome of patients with sHICH, which is a more thorough guideline for clinical residents than some other studies have reported.

Conclusion

First time fasting plasma glucose after hospitalization is a risk factor for GOS, the higher the plasma glucose level, the lower the GOS; the lower the plasma glucose level, the higher the GOS. First-time serum albumin after hospitalization is good for GOS, and the higher the serum albumin level, the higher the GOS; the lower the serum albumin level, the lower the GOS. First-time serum triglyceride after hospitalization is a risk for GOS, and the higher the serum triglyceride level, the lower the GOS; the lower the serum triglyceride level, the higher the GOS. The predictive factors including first time fasting plasma glucose, and serum albumin, and serum triglyceride after hospitalization can predict the GOS.

Disclosure of conflict of interest

None.

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