MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2018; 24: 6237-6244
DOI: 10.12659/MSM.910024

Received: 2018.03.18
Accepted: 2018.05.02
Published: 2018.09.07

Hyperglycemia Predicts Blend Sign in Patients with Intracerebral Hemorrhage

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEFG 1,2 Fan Zhang
BCF 1 Hao Li
EF 3 Juan Qian
BCE 1 Chuanyuan Tao
BCD 1 Jun Zheng
ACFG 1 Chao You
ACE 1,4,5 Mu Yang

1 Department of Neurosurgery, West China Hospital, Sichuan University, Chengdu, Sichuan, P.R. China
2 Department of Pathology, Case Western Reserve University, Cleveland, OH, U.S.A.
3 Department of Population and Quantitative Health, School of Medicine, Case Western Reserve University, Cleveland, OH, U.S.A.
4 Department of Neurology and Neurosurgery, McGill University, Montreal, QC, Canada
5 Alan Edwards Centre for Research on Pain, McGill University, Montreal, QC, Canada

Corresponding Authors: Mu Yang, e-mail: mu.yang@mcgill and Chao You, e-mail: youchao0118@sina.com
Source of support: Departmental sources

Background: Predictive values of admission blood glucose for early hematoma expansion in patients with intracranial hemorrhage (ICH) remain controversial. Blend sign is a novel image predictor for early hematoma growth that suggests presence of active bleeding. We investigated the association between hyperglycemia and blend sign in predicting early hematoma growth in ICH patients.

Material/Methods: All patients with intracranial hemorrhage were retrospectively reviewed. Clinical characteristics and radiological parameters were collected. Blood glucose was measured within 24 h after onset. CT scan results for hematoma expansion and blend sign were evaluated by 2 readers. Multivariate logistic regression analyses were applied to reveal the associations between hematoma growth and blend sign, as well as other variables.

Results: Out of 164 patients with ICH, 52 exhibited early hematoma growth and 18 of these were diagnosed with blend sign. Average blood glucose was 7.53 mmol/L among all patients. By using multivariate analyses, the time of CT scan baseline, GCS score, hematoma size, blend sign, and blood glucose were associated with hematoma expansion, whereas only hyperglycemia was associated with blend sign.

Conclusions: Admission hyperglycemia is associated with hematoma expansion in the presence of blend sign. These findings suggest that elevated blood glucose is a possible factor predicting continuous bleeding. Strategies to control blood glucose and ameliorate hematoma growth are urgently needed and will be investigated in our future studies.

MeSH Keywords: Cerebral Hemorrhage • Diagnostic Imaging • Hematoma • Hyperglycemia • Neuroimaging

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/910024

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Background

Intracranial hemorrhage (ICH) is a serious disease accounting for 10%–30% of all strokes [1]. Serum glucose [2] and early hematoma expansion [3] have been reported to be associated with prognosis in patients with ICH. Although the correlation of hyperglycemia with early hematoma expansion is controversial, findings from experimental studies demonstrate that increased blood glucose promotes continuous bleeding by accelerating the brain blood barrier damage and impairing microvascular integrity around the initial bleeding location [4–6].

Blend sign was first identified by medical imaging scientists to indicate active bleeding, and this phenomenon has also been recently used as a novel imaging biomarker to predict early hematoma expansion in patients with ICH [7]. Accordingly, we hypothesized that there might be a correlation between hyperglycemia and blend sign in the process of hematoma expansion. Therefore, we evaluate whether admission blood glucose is associated with blend sign during hematoma expansion in patients with ICH.

Material and Methods

Patients

All ICH cases between September 2015 and November 2016 in West China Hospital were retrospectively enrolled. This study was approved by the Biomedical Ethics Committee of West China Hospital and all patients or their relatives signed informed consents. This study followed the requirements of relevant regulations and guidelines of Sichuan University.

Inclusion criteria were: (1) Diagnosis of intracranial hemorrhage was confirmed by CT; (2) Admission blood glucose was examined within 24 h after onset; (3) CT scan was performed within 8 h after initial ictus and the follow-up CT scan was performed within 24 h; (4) ages of all patients were over 18 years.

Exclusion criteria were: (1) ICH resulting from tumor, aneurysm, trauma, arteriovenous malformation, or Moyamoya disease; (2) ICH patients without follow-up CT scan; (3) Patients with ICH were under treatment using warfarin and/or anticoagulants; (5) Hematoma evacuation was performed before follow-up CT scan; (6) A stroke history within 6 months.

Data on all clinical characteristics were collected: age; sex; admission blood pressure; smoking and alcohol use; hypertension or diabetes history; family history of ICH, cerebral infarction, or aneurysm; and admission blood glucose.

Image features

At least 2 radiologists independently evaluated all CT scan results without being aware of clinical conditions or patient information. Any conflict between the 2 radiologists would be evaluated by the third one. Radiological results were collected from head CT scan within 8 h after initial ictus, including hematoma location, hematoma size, presence of intraventricular hemorrhage (IVH), subarachnoid hemorrhage (SAH), cerebral infarction, and blend sign. Hematoma volume was estimated by using ABC/2 method. Hematoma expansion was defined as increased hematoma volume above 33% by follow-up CT scan results, or the absolute growth volume is above 12.5 ml^3. According to previous studies, blend sign was identified as a hematoma with a hypoattenuating area and hyperattenuating area that possessed a well-defined margin that can be easily recognized by the unaided eye. An 18-Hounsfield unit difference between 2 areas is necessary and the relatively hypodense region should not be encapsulated by the hyperdense area [7].

Statistical analysis

All statistical analyses were performed using SPSS 23.0. Baseline clinical characteristics, laboratorial parameters, and imaging features were compared between patients with or without hematoma expansion. Data are expressed as the mean ±SD or median with interquartile range (IQR) or frequency with percentage. Comparisons were conducted with the independent-samples *t* test, Mann-Whitney U test, chi-square test, or Fisher's exact test. Multivariable logistic regression analysis was performed to adjust the association between blend sign and hyperglycemia on hematoma expansion when the P-value of the variable was below 0.15 in univariate analysis. K-value was used to analyze the interobserver reliability of blend sign. Receiver-operator analysis was conducted to evaluate the predictive abilities of admission blood glucose for hematoma expansion and blend sign. The variables with $P<0.05$ were considered statistically significant.

Results

In this study, there are 164 eligible patients (125 males and 39 females, detail exclusions in Figure 1) in total. The average age was 59.26±11.92 years with a range from 31 to 89 years. The mean hematoma size was 28.16±16.38 ml and the mean admission blood glucose was 7.53±2.58 mmol/L. The average period from symptom onset to initial CT scan was 3.81 h. There were 148 patients with supratentorial hematoma and 16 patients with subtentorial hematoma. Early hematoma expansions were observed in 52 patients and of these, blend signs were observed in 18. The K-value of interobserver reliability

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

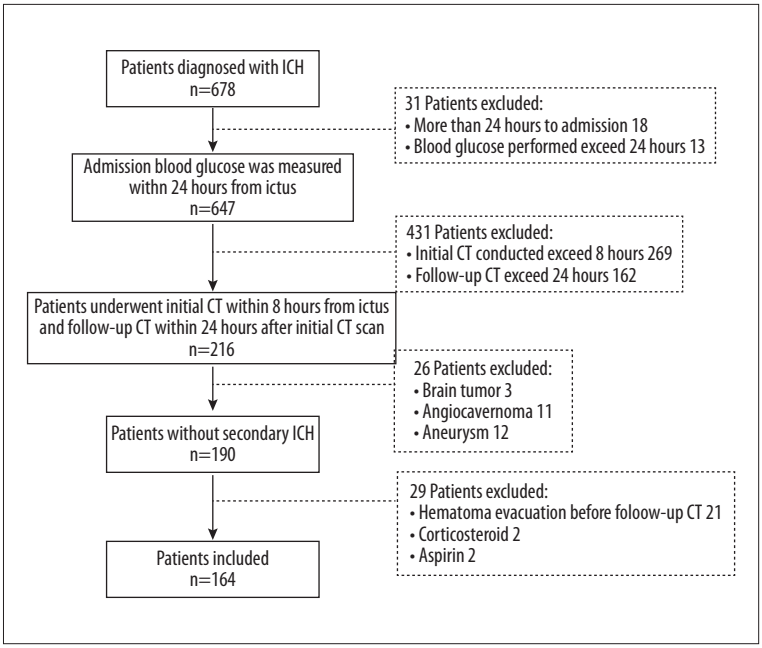


Figure 1. Flowchart of patient enrollment.

Table 1. Clinical characteristics related to hematoma expansion in patients with ICH.

Characteristic	Patients with HE (n=52)	Patients without HE (n=112)	P
Male	39	86	0.803
Age (years)	60.31±11.96	58.78±11.92	0.446
Systolic blood pressure (mmHg)	169.09±26.45	168.94±35.55	0.977
Diastolic blood pressure (mmHg)	97.65±18.05	97.95±19.95	0.926
Mean arterial pressure (mmHg)	120.41±19.75	121.56±23.77	0.763
Medical history			
Hypertension	25	62	0.385
Diabetes mellitus	4	9	0.941
Ischemic stroke	3	12	0.307
Smoker	26	51	0.594
Alcohol (>3 drinks per 24 hours)	27	47	0.233
Time to CT (hour)	3.20±1.84	4.10±2.04	0.007*
GCS score on admission	7.90±3.37	10.59±3.52	<0.001*
Hematoma size (ml)	39.98±14.83	22.64±14.00	<0.001*
Presence of SAH	27	24	<0.001*
Presence of IVH	16	19	0.045*
Supratentorial hematoma	50	98	0.082
Blend sign	15	3	<0.001*
Blood Glucose	8.63±3.13	7.02±2.11	0.001*

Data are expressed as n(%), mean±standard deviation, median(interquartile range), as appropriate. SAH – subarachnoid hemorrhage; IVH – intraventricular hemorrhage; GCS – Glasgow coma scale; WBC – white blood cells; ANC – admission neutrophil count; ALC – admission lymphocyte count; AMC – admission lymphocyte count; NLR – neutrophil to lymphocyte ratio; PLR – platelet to lymphocyte ratio; PLT – platelet count.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 2. Clinical characteristics related to blend sign in patients with ICH.

Characteristic	patients with blend sign (n=18)	patients without blend sign (n=146)	P
Male	13	112	0.673
Age (years)	59.44±13.01	59.24±11.83	0.945
Systolic blood pressure (mmHg)	172.89±21.22	168.51±34.03	0.595
Diastolic blood pressure (mmHg)	92.61±17.29	98.51±19.51	0.223
Mean arterial pressure (mmHg)	115.99±18.41	121.84±22.95	0.301
Medical history			
Hypertension	7	80	0.202
Diabetes mellitus	2	11	0.596
Ischemic stroke	4	11	0.041*
Smoker	9	68	0.784
Alcohol (>3 drinks per 24 hours)	10	64	0.346
Time to CT (hour)	3.04±1.89	3.91±2.01	0.085
GCS score on admission	9.94±3.09	9.71±3.76	0.802
Hematoma size (ml)	36.60±11.51	27.13±16.62	0.021*
Presence of SAH	5	46	0.747
Presence of IVH	5	30	0.48
Supratentorial hematoma	18	130	0.139
Blood glucose	11.20±4.11	7.08±1.90	0.001*

Data are expressed as n(%), mean ± standard deviation, median(interquartile range), as appropriate. SAH – subarachnoid hemorrhage; IVH – intraventricular hemorrhage; GCS – Glasgow coma scale; WBC – white blood cells; ANC – admission neutrophil count; ALC – admission lymphocyte count; AMC – admission lymphocyte count; NLR – neutrophil to lymphocyte ratio; PLR – platelet to lymphocyte ratio; ABG – admission blood glucose; PLT – platelet count.

for identifying blend sign was 91.7%, thus exhibit an excellent interobserver agreement between the 2 radiologists. The clinical characteristics of patients with or without hematoma expansions are listed in Table 1 and the comparison of detailed information on clinical variables between ICH patients with or without blend signs is presented in Table 2. No significant difference was found in age, sex blood pressure, hypertension, diabetes mellitus, smoking, or drinking.

Univariate analysis demonstrated that there was a significantly shorter period between initial ictus and CT scan in ICH patients with hematoma expansions, as well as lower GCS score on admission, larger hematoma size, higher prevalence of SAH, higher prevalence of IVH, and higher admission blood glucose. Multivariable logistic regression analyses were performed when the P-value of a variable was below 0.15 in univariate analyses. Multivariate analysis revealed that the time to baseline CT scan (OR 0.788, 95%CI 0.618–0.989, p=0.048 or OR 0.771, 95%CI 0.610–0.976, p=0.03), GCS scores (OR 0.817, 95%CI 0.717–0.931, p<0.01 or OR 0.851, 95%CI 0.753–0.960, p=0.01), hematoma sizes (OR 1.080, 95%CI 1.046–1.116, p<0.01 or OR 1.082, 95%CI 1.048–1.116, p<0.01), blend sign (OR 16.242, 95%CI 3.528–74.762, p<0.01), and admission blood glucose (as continuous data, OR 1.263, 95%CI 1.056–1.510, p=0.01 or as categorical data, OR 3.536, 95%CI 1.419–8.510, p<0.01) can independently predict early hematoma expansion (Table 3). The univariate logistic analysis also indicated the time to baseline CT scan, history of ischemic stroke, hematoma volume, and blood glucose were associated with blend sign; after the adjustment of potential confounders, although admission blood glucose (OR 1.713, 95%CI 1.357–2.163, p<0.01), time to baseline CT, ischemic stroke, and hematoma size were not significantly associated with blend sign (Table 4). Receiver operating characteristic analyses was used to estimate the ability of admission blood glucose to predict early hematoma expansion and blend sign. Hyperglycemia exhibited a better predictive value for hematoma growth compared with blend sign (area under the curve [AUC] 0.674, p<0.001 *vs.* AUC 0.631, p<0.001,

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 3. Multivariable logistic regression of blend sign and blood glucose on hematoma expansion after ICH.

Characteristic	Crude		Model 1 (blend sign)		Model 2 (blood glucose >7.15)		Model 3 (blood glucose)	
	OR (CI)	P	OR (CI)	P	OR (CI)	P	OR (CI)	P
Time to CT	0.779 (0.645–0.940)	0.09	0.788 (0.618–0.989)	0.05	0.734 (0.576–0.936)	0.01	0.771 (0.610–0.976)	0.03
GCS score on admission	0.808 (0.731–0.894)	<0.01	0.817 (0.717–0.931)	<0.01	0.865 (0.767–0.975)	0.02	0.851 (0.753–0.960)	0.01
Hematoma volume	1.087 (1.055–1.120)	<0.01	1.080 (1.046–1.116)	<0.01	1.086 (1.051–1.122)	<0.01	1.082 (1.048–1.116)	<0.01
Presence of SAH	3.960 (1.953–8.029)	<0.01	2.198 (0.737–6.558)	0.16	1.847 (0.614–5.555)	0.28	1.793 (0.617–5.210)	0.28
Presence of IVH	2.175 (1.009–4.690)	0.04	0.529 (0.162–1.726)	0.29	0.550 (0.183–1.652)	0.29	0.562 (0.185–1.708)	0.31
Blend sign#	14.730 (4.037–53.750)	<0.01	16.242 (3.528–74.762)	<0.01	–	–	–	–
Blood glucose (>7.15)*#	3.619 (1.765–7.420)	<0.01	–	–	3.536 (1.419–8.510)	<0.01		
Blood glucose#	1.049 (1.014–1.085)	<0.01	–	–	–	–	1.263 (1.056–1.510)	0.01

CI – confidence interval; OR – odds ratio; GCS – Glasgow coma scale. # Adjustment by time interval from onset to initial CT, presence of SAH, presence of IVH, GCS score and hematoma volume. Blood glucose * was analyzed as categorical variable by dichotomizing blood glucose from the cut-off points identified in receiver operating characteristic analysis while blood glucose was analyzed as a continuous variable.

Table 4. Associations of admission blood glucose with blend sign in patients with ICH.

Characteristic	Crude			Adjusted		
	OR (CI)		P	OR (CI)		P
Time to CT (hour)	0.768	(0.564–1.046)	0.09	0.913	(0.653–1.278)	0.59
Ischemic stroke	3.506	(0.985–12.484)	0.05	1.333	(0.209–8.505)	0.76
Hematoma size (ml)	1.032	(1.004–1.062)	0.03	1.030	(0.993–1.068)	0.11
Blood glucose	1.695	(1.236–2.008)	<0.01	1.713	(1.357–2.163)	<0.01

CI – confidence interval; OR – odds ratio. Adjustment by time interval from onset to initial CT, ischemic stroke, hematoma volume and admission blood glucose.

Figure 2). Hyperglycemia also showed an excellent ability to predict blend sign (cut-off value 7.96, sensitivity 83.33%, specificity 70.55%, positive predictive value 25.9, negative predictive value 97.2, AUC 0.819, p<0.001, Figure 3).

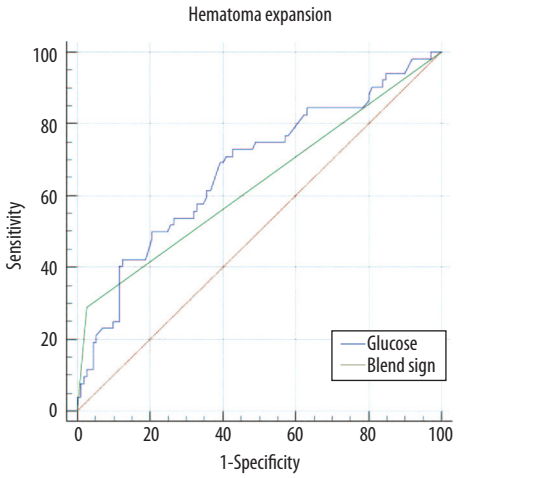
Discussion

We found that elevated admission blood glucose and blend sign were independently associated with early hematoma growth, while hyperglycemia exhibited a better predictive value. This is the first study to show hyperglycemia is an independent predictor of blend sign.

As a common secondary disease, early hematoma expansion occurs in many patients with ICH. Previous studies reported one-third of ICH patients had a significantly hematoma growth, and the incidence of absolute hematoma expansion was as high as 70% of all ICH patients [8–10].

Since both hematoma growth and blood glucose level are preventable in patients with ICH, research on identifying good

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]



	Sensitivity	Specificity	PPV	NPV	Cut-off value	AUC	P
Admission blood glucose	73.10%	57.10%	44.20%	82.10%	7.15	0.674	<0.001
Blend sign	28.80%	97.30%	83.30%	74.70%	0	0.631	<0.001

Figure 2. Receiver operating characteristic curves of blood glucose and blend sign with their corresponding areas under the curve (AUC) for predicting hematoma expansion. The best cut-off points were identified with their sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

predictors for both symptoms is important. Numerous studies over the last 2 decades have indicated that hyperglycemia [11–14] and hematoma expansion [15–17] are associated with adverse outcome in patients with ICH. Bejot [2] demonstrated that elevated admission blood glucose independently predicted 1-month fatality rate and poor functional outcome at discharge in a France population-based study. Fogelholm [18] reported that admission hyperglycemia was associated with early death regardless of diabetic status in Finland. On the other hand, Davis et al. [3] reported that hematoma expansion was an independent predictor for morbidity and mortality. Dowlatshahi et al. [19] discussed the different definitions of hematoma growth and suggested that all definitions could independently predict poor outcome after ICH.

There is also plentiful evidence from basic research documenting that inflammation [20,21], oxygen-free radical generation [22], and blood-brain barrier breakdown [23,24] participate in the pathological processes, and experimental studies [6,25–31] showed that hyperglycemia affects hematoma expansion. Liu et al. [4] proved that elevated blood glucose could induce hematoma growth by plasma kallikrein, which is characterized by production of bradykinin. Bradykinin increases BBB permeability and induces brain edema, which affects the

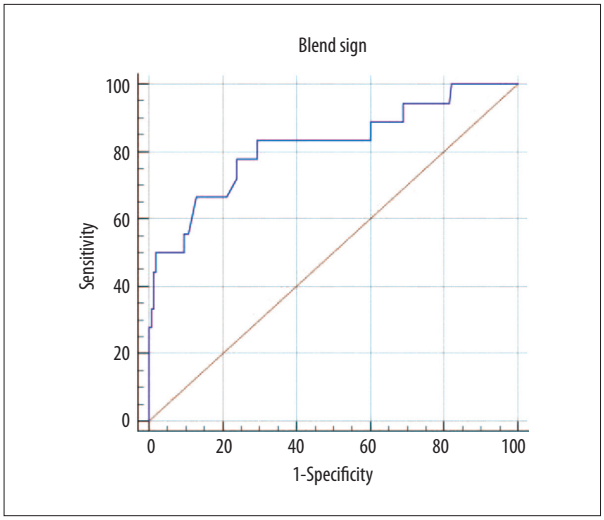


Figure 3. Receiver operating characteristic curves of admission blood glucose for predicting blend sign.

prognosis [32], and may also be involved in the pathological processes of hematoma growth and poor prognosis. Additionally, experimental studies found that elevated blood glucose leads to hematoma expansion in an animal model of brain hemorrhage [5]. However, the relationship between hyperglycemia and hematoma growth remains controversial in clinical studies. Qureshi AI [33] and other authors [18,34,35] pointed out that hyperglycemia was associated with hematoma expansion as well as brain edema. However, the INTERACT 2 study [36] demonstrated that neither hematoma growth nor perihematomal edema was detected in ICH patients with elevated blood glucose. As the main surgical hospital for the INTERACT 2 study, we have to admit that there are several potential limitations to our works, which could explain the discrepancy. Firstly, patients involved in the INTERACT2 study have relatively lower rates of hematoma growth [37] because all the patients undergoing emergency surgical treatment were excluded. Then, patients who underwent hematoma expansion were also excluded due to massive hematoma or poor prognosis. In addition, the follow-up CT scans were supposed to be conducted over 30 h and patients had a higher systolic blood pressure.

Our results further confirmed that hyperglycemia has strong predictive ability for early hematoma growth in patients with ICH. Moreover, the present study is the first to report that elevated blood glucose independently predicts the presence of blend sign, which is emerging as a novel and easy-to-use imaging predictor for hematoma expansion that shows the liquid blood from active bleeding [7,38]. Experimental studies have suggested the deleterious effect of increased blood glucose-accelerated blood-brain barrier damage, impaired microvascular integrity, and promoting continuous bleeding [39]. In addition to results from animal model studies, our results directly show that hyperglycemia is associated with the pathological

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

process of active bleeding in patients with ICH. In consideration of the risk of hematoma growth in patients with blood glucose level of >7.15 mmol/L, which is more than 3 times that of those with glucose level of <7.15 mmol/L, we want to highlight the management of glucose-lowering, which improve the prognosis and should be performed to decrease the prevalence of hematoma growth.

Several limitations should be taken into account when interpreting our results. Firstly, all the patients enrolled in this study came from a single institution (West China Hospital), which is one of the largest hospitals in China; therefore, the patients usually have worse clinical grades than in other hospitals due to the lack of a medical referral system. Furthermore, a small number of patients can be examined by CT scan within 8 h after initial ictus and a large proportion of patients do not meet the criterion, which may have resulted in selection bias. Third, this was a retrospective clinical study and the sample size was relatively small. In addition, the black hole sign [40] and the island sign [41], which also indicate active bleeding, were are not studied and further studies are urgently needed to investigate the associations between hyperglycemia and these signs.

Conclusions

Although hyperglycemia has been reported to be associated with high mortality in patients with ICH, the relationship between admission blood glucose level and hematoma expansion remains controversial. Our study demonstrates that hyperglycemia is not only associated with early hematoma expansion, but also is a predictor for blend sign, which to the best of our knowledge has never been documented before. Because blend sign can indicate active bleeding, we further raise the possibility that hyperglycemia also participates in the pathological process of bleeding in ICH patients.

Conflict of interests

None.

References:

1. Qureshi AI, Mendelow AD, Hanley DF: Intracerebral haemorrhage. Lancet, 2009; 373: 1632–44
2. Bejot Y, Aboa-Eboule C, Hervieu M et al: The deleterious effect of admission hyperglycemia on survival and functional outcome in patients with intracerebral hemorrhage. Stroke, 2012; 43: 243–45
3. Davis SM, Broderick J, Hennerici M et al: Hematoma growth is a determinant of mortality and poor outcome after intracerebral hemorrhage. Neurology, 2006; 66: 1175–81
4. Liu J, Gao BB, Clermont AC et al: Hyperglycemia-induced cerebral hematoma expansion is mediated by plasma kallikrein. Nat Med, 2011; 17: 206–10
5. Zheng Y, Hu Q, Manaenko A et al: 17beta-Estradiol attenuates hematoma expansion through estrogen receptor alpha/silent information regulator 1/nuclear factor-kappa b pathway in hyperglycemic intracerebral hemorrhage mice. Stroke, 2015; 46: 485–91
6. Allen CL, Bayraktutan U: Antioxidants attenuate hyperglycaemia-mediated brain endothelial cell dysfunction and blood-brain barrier hyperpermeability. Diabetes Obes Metab, 2009; 11: 480–90
7. Li Q, Zhang G, Huang YJ et al: Blend sign on computed tomography: Novel and reliable predictor for early hematoma growth in patients with intracerebral hemorrhage. Stroke, 2015; 46: 2119–23
8. Brott T, Broderick J, Kothari R et al: Early hemorrhage growth in patients with intracerebral hemorrhage. Stroke, 1997; 28: 1–5
9. Delcourt C, Huang Y, Arima H et al: Hematoma growth and outcomes in intracerebral hemorrhage: The INTERACT1 study. Neurology, 2012; 79: 314–19
10. Dowlatshahi D, Wasserman JK, Momoli F et al: Evolution of computed tomography angiography spot sign is consistent with a site of active hemorrhage in acute intracerebral hemorrhage. Stroke, 2014; 45: 277–80
11. Kimura K, Iguchi Y, Inoue T et al: Hyperglycemia independently increases the risk of early death in acute spontaneous intracerebral hemorrhage. J Neurol Sci, 2007; 255: 90–94
12. Koga M, Yamagami H, Okuda S et al: Blood glucose levels during the initial 72 h and 3-month functional outcomes in acute intracerebral hemorrhage: The SAMURAI-ICH study. J Neurol Sci, 2015; 350: 75–78
13. Zhang G, Wu F, Xu Y et al: Prestroke glycemic status is associated with the functional outcome in spontaneous intracerebral hemorrhage. Neurol Sci, 2015; 36: 927–34
14. Tao C, Hu X, Wang J, You C: Effect of admission hyperglycemia on 6-month functional outcome in patients with spontaneous cerebellar hemorrhage. Med Sci Monit, 2017; 23: 1200–7
15. Yaghi S, Dibu J, Achi E et al: Hematoma expansion in spontaneous intracerebral hemorrhage: Predictors and outcome. Int J Neurosci, 2014; 124: 890–93
16. Cheung RTF, Zou LY: Use of the original, modified, or new intracerebral hemorrhage score to predict mortality and morbidity after intracerebral hemorrhage. Stroke, 2003; 34: 1717–22
17. Leira R, Davalos A, Silva Y et al: Early neurologic deterioration in intracerebral hemorrhage: Predictors and associated factors. Neurology, 2004; 63: 461–67
18. Fogelholm R, Murros K, Rissanen A, Avikainen S: Admission blood glucose and short-term survival in primary intracerebral haemorrhage: A population-based study. J Neurol Neurosurg Psychiatry, 2005; 76: 349–53
19. Dowlatshahi D, Demchuk AM, Flaherty ML et al: Defining hematoma expansion in intracerebral hemorrhage: Relationship with patient outcomes. Neurology, 2011; 76: 1238–44
20. Pampfer S, Cordi S, Dutrieux C et al: Interleukin 1beta mediates the effect of high D-glucose on the secretion of TNF-alpha by mouse uterine epithelial cells. Cytokine, 1999; 11: 500–9
21. Asakawa H, Miyagawa J, Hanafusa T et al: High glucose and hyperosmolarity increase secretion of interleukin-1 beta in cultured human aortic endothelial cells. J Diabetes Complications, 1997; 11: 176–79
22. Rehncrona S, Hauge HN, Siesjo BK: Enhancement of iron-catalyzed free radical formation by acidosis in brain homogenates: Differences in effect by lactic acid and CO2. J Cereb Blood Flow Metab, 1989; 9: 65–70
23. Won SJ, Tang XN, Suh SW et al: Hyperglycemia promotes tissue plasminogen activator-induced hemorrhage by increasing superoxide production. Ann Neurol, 2011; 70: 583–90
24. Chiu CD, Chen CC, Shen CC et al: Hyperglycemia exacerbates intracerebral hemorrhage via the downregulation of aquaporin-4: Temporal assessment with magnetic resonance imaging. Stroke, 2013; 44: 1682–89
25. Slowik A, Turaj W, Pankiewicz J et al: Hypercortisolemia in acute stroke is related to the inflammatory response. J Neurol Sci, 2002; 196: 27–32
26. Esposito K, Nappo F, Marfella R et al: Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans: Role of oxidative stress. Circulation, 2002; 106: 2067–72
27. Chan S, Conell C, Veerina KT et al: Prediction of intracerebral haemorrhage expansion with clinical, laboratory, pharmacologic, and noncontrast radiographic variables. Int J Stroke, 2015; 10: 1057–61

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

28. Feng W, Tauhid S, Goel S et al: Hyperglycemia and outcome in intracerebral hemorrhage: From bedside to bench-more study is needed. Transl Stroke Res, 2012; 3: 113–18
29. Song EC, Chu K, Jeong SW et al: Hyperglycemia exacerbates brain edema and perihematomal cell death after intracerebral hemorrhage. Stroke, 2003; 34: 2215–20
30. Chiu CD, Chen TY, Chin LT et al: Investigation of the effect of hyperglycemia on intracerebral hemorrhage by proteomic approaches. Proteomics, 2012; 12: 113–23
31. Liu RY, Wang JJ, Qiu X, Wu JM: Acute hyperglycemia together with hematoma of high-glucose blood exacerbates neurological injury in a rat model of intracerebral hemorrhage. Neurosci Bull, 2014; 30: 90–98
32. Schulz J, Plesnila N, Eriskat J et al: LF16-0687 a novel non-peptide bradykinin B2 receptor antagonist reduces vasogenic brain edema from a focal lesion in rats. Acta Neurchir Suppl, 2000; 76: 137–39
33. Qureshi AI, Palesch YY, Martin R et al: Association of serum glucose concentrations during acute hospitalization with hematoma expansion, perihematomal edema, and three-month outcome among patients with intracerebral hemorrhage. Neurocrit Care, 2011; 15: 428–35
34. Kazui S, Minematsu K, Yamamoto H et al: Predisposing factors to enlargement of spontaneous intracerebral hematoma. Stroke, 1997; 28: 2370–75
35. Passero S, Ciacci G, Ulivelli M: The influence of diabetes and hyperglycemia on clinical course after intracerebral hemorrhage. Neurology, 2003; 61: 1351–56
36. Saxena A, Anderson CS, Wang X et al: Prognostic significance of hyperglycemia in acute intracerebral hemorrhage: The INTERACT2 study. Stroke, 2016; 47: 682–88
37. Anderson CS, Heeley E, Huang Y et al: Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. N Engl J Med, 2013; 368: 2355–65
38. Zheng J, Yu Z, Xu Z et al: The accuracy of the spot sign and the blend sign for predicting hematoma expansion in patients with spontaneous intracerebral hemorrhage. Med Sci Monit, 2017; 23: 2250–57
39. Chen S, Zhao B, Wang W et al: Predictors of hematoma expansion predictors after intracerebral hemorrhage. Oncotarget, 2017; 8: 89348–63
40. Li Q, Zhang G, Xiong X et al: Black hole sign: Novel imaging marker that predicts hematoma growth in patients with intracerebral hemorrhage. Stroke, 2016; 47: 1777–81
41. Li Q, Liu QJ, Yang WS et al: Island sign: An imaging predictor for early hematoma expansion and poor outcome in patients with intracerebral hemorrhage. Stroke, 2017; 48: 3019–25

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]