Observational Study

Medicine®

OPEN

Hyperglycemia is associated with poor in-hospital outcome in elderly patients with acute ischemic stroke

Lei Zhao, MS*, Li Wang, MD, Meihua Lu, BS, Wei Hu, MS, Shuangling Xiu, MD

Abstract

Fasting hyperglycemia is associated with poor neurologic outcome in acute ischemic stroke (AIS), but its relationship with in-hospital outcome in elderly patients remains largely unknown. To assess the association of in-hospital outcome with fasting plasma glucose (FPG) levels at admission in individuals with AIS.

This retrospective propensity score-matched case–control study included patients aged over 60 years suffering from AIS and who were admitted to the emergency department from November 2013 to October 2016. Subjects were grouped into the poor-outcome and good-outcome groups based on mortality and intensive care unit (ICU) admission.

The poor- and good-outcome groups comprised 74 and 1927 cases, respectively, before propensity score matching (PSM), and 74 and 296 cases, respectively, after PSM. Univariable logistic regression analysis showed that initial FPG after admission was associated with poor in-hospital outcome. Multivariable logistic regression analysis showed that initial FPG after admission was an independent predictor of poor in-hospital outcome (odds ratio = 1.11, 95% confidence interval: 1.037–1.188, $P = .003$).

This study used PSM and strongly suggests that FPG is an independent predictive factor of poor in-hospital outcome in elderly patients with AIS. High initial FPG levels after admission may predict poor in-hospital outcome. Prospective studies are needed to confirm these findings.

Abbreviations: AIS = acute ischemic stroke, ALT = alanine aminotransferase, CI = confidence interval, CKD = chronic kidney disease, FPG = fasting plasma glucose, GFR = glomerular filtration rate, GOG = good-outcome group, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein, ICU = intensive care unit, LDL-C = low-density lipoprotein cholesterol, NIHSS = National Institutes of Health Stroke Scale, OR = odds ratio, POG = poor-outcome group, PSM = propensity score matching, TC = total cholesterol, TG = triglyceride, UKPDS = United Kingdom Prospective Diabetes Study.

Keywords: acute ischemic stroke, fasting plasma glucose, in-hospital outcome prognosis, propensity score matching

1. Introduction

Stroke is one of the leading causes of death[1] and probably the greatest reason for adult permanent disability worldwide.[1] It occurs more frequently in the elderly, with one-third of the ischemic stroke cases occurring in individuals 80 years and above.[2–4] Recently, the incidence and burden of stroke in China have increased rapidly, as in other developing countries. Indeed, about 2 million people of all ages suffer a new stroke every year, with 15 million stroke-related deaths occurring each year.[1]

It is widely accepted that hyperglycemia is associated with increased incidence of stroke in rural China.[5] Therefore, minimizing glucose fluctuations and reducing hemoglobin A1c (HbA1c) levels could help prevent ischemic stroke.[6] Meanwhile, it was found that stroke patients have higher fasting plasma glucose (FPG) levels compared with their nonstroke counterparts.[7] A study revealed the detrimental effects of hyperglycemia on morbidity and mortality in patients diagnosed with acute ischemic stroke (AIS),[8] both with or without diabetes.[9] In addition, multivariable logistic regression analysis indicated that FPG is associated with mortality in stroke.[10] Nevertheless, the association between FPG and in-hospital mortality remains largely undetermined. This study focused on in-hospital outcome to assess its association with FPG levels at admission in AIS patients.

2. Materials and methods

2.1. Patients

This retrospective propensity score-matched case–control study enrolled all patients with ischemic stroke admitted to the emergency department of Xuanwu Hospital from November 2013 to October 2016. The inclusion criteria were: age ≥60 years; AIS diagnosis by computed tomography or magnetic resonance imaging; and complete clinical information. The

Editor: Hidetaka Hamasaki.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The authors have no funding and conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

Department of Endocrinology, Xuanwu Hospital of Capital Medical University, Beijing, China.

* Correspondence: Lei Zhao, Department of Endocrinology, Xuanwu Hospital of Capital Medical University, Beijing, China (e-mail: zhaolei8346@163.com).

Medicine (2019) 98:31(e16723)

Received: 27 March 2019 / Received in final form: 1 July 2019 / Accepted: 12 July 2019

http://dx.doi.org/10.1097/MD.0000000000016723

patients who received thrombolytic therapy were excluded. The eligible patients were divided into 2 groups: poor-outcome (POG; individuals admitted in the intensive care unit [ICU] and/or died in the hospital) and good-outcome (GOG; patients never admitted in the ICU who were discharged from the hospital). The ethics committee of Xuanwu Hospital approved the study and waived the requirement for obtaining informed consent. All procedures were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

2.2. Treatment

All patients received aspirin, clopidogrel, statins, and symptomatic treatment. Those with diabetes maintained their original hypoglycemic regimens. When 2-hour postprandial blood glucose levels were higher than 20 mmol/L, an insulin pump was used at 0.1 IU/kg/h until blood glucose fell to 15 mmol/L.

2.3. Measurements

The FPG and HbA1c were measured the first morning upon admission after at least 8 hours of fasting. Hypertension was defined as systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg, or current use of antihypertensive drugs.[11,12] Diabetes was defined as HbA1c ≥6.5% or current use of antidiabetic drugs. FPG was not considered in the present study for the diagnosis of diabetes because of the metabolic disturbances associated with AIS. Since HbA1c represents the long-term glycemic burden, it was considered as more reliable for the diagnosis of diabetes,[13] as per the Chinese guidelines.[14,15] Initial stroke severity was evaluated on the 1st day of admission according to the National Institute of Health Stroke Scale (NIHSS).[16] Chronic kidney disease (CKD) was classified according to the KDOQI 2002 guidelines[17] as follows: CKD 1, renal injury with glomerular filtration rate (GFR) ≥90 mL/(min · 1.73 m^2); CKD 2, 60 ≤ GFR < 90 mL/(min · 1.73 m^2); CKD 3, 30 ≤ GFR < 60 mL/(min · 1.73 m^2); CKD 4, 15 ≤ GFR < 30 mL/(min · 1.73 m^2); and CKD 5, GFR < 15 mL/(min · 1.73 m^2)]. Hypoproteinemia was defined as albumin < 3.5 g/dL.[18] Alanine aminotransferase (ALT), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were detected the morning following admission. HbA1c was measured using Variant II Turbo (Bio-Rad Laboratories, Philadelphia, PA). The measurements of all other metabolites were performed on a Hitachi 7600 automatic biochemical analyzer (Hitachi High-Technologies, Tokyo, Japan).

2.4. Grouping

Since poor outcome cases were rare in the present study (3.4%), we included 1 patient in the POG matched to 4 patients in the GOG by propensity score matching (PSM) using the R software. The propensity score was estimated in a multivariable logistic regression model. Age, sex, ALT, CKD stage, and NIHSS score are associated with outcome in AIS, and hence included in the PSM model.[16,17,19–21]

2.5. Statistical analysis

Continuous data with nonnormal distribution were presented as median (range), and assessed by the Mann–Whitney *U* test. The distribution of categorical variables was evaluated by the Chi-squared test. Parameters with $P < .1$ in univariable logistic regression analyses were included in a multivariable logistic regression analysis. SPSS 22.0 (IBM, Armonk, NY) was used for all statistical analyses. $P < .05$ was considered statistically significant.

3. Results

3.1. Patient baseline characteristics

A total of 2001 subjects fulfilled the eligibility criteria, including 74 and 1927 in the POG and GOG before PSM, respectively. After PSM, there were 74 POG and 296 GOG patients. No significant differences were found in baseline features, including age, sex, ALT, CKD, and NIHSS score between the 2 groups after PSM. Nevertheless, FPG was higher in the POG (mean, 7.32 mmol/L; range, 3.67–22.44 mmol/L) compared with the GOG (mean, 6.4 mmol/L; range, 3.57–22.33 mmol/L; $P = .005$). The baseline characteristics are summarized in Table 1.

3.2. Factors affecting in-hospital outcome and NIHSS score before matching

Univariable logistic regression analysis before PSM suggested that age, CKD, malignant tumor, gout history, ALT, TG, TC, HDL-C, LDL-C, and FPG were the potential influencing factors for in-hospital outcome ($P < .1$). The results of multivariable analysis showed that CKD (odds ratio [OR] = 8.105, 95% confidence interval [CI]: 4.241–15.489, $P < .001$), malignant tumor (OR = 5.334, 95% CI: 2.124–13.398; $P < .001$), gout history (OR = 4.141, 95% CI: 1.041–16.477; $P = .044$), TG (OR = 0.527, 95% CI: 0.32–0.869; $P = .012$), and FPG (OR = 1.199, 95% CI: 1.118–1.285; $P < .001$) were found to independently affect in-hospital outcome in patients with AIS (Table 2). Further subgroup analyses were performed based on age. Among patients aged 60 to 75 years, CKD (OR = 14.788, 95% CI: 6.824–32.046; $P < .001$), HDL-C (OR = 2.889, 95% CI: 1.044–7.999; $P = .041$), and FPG (OR = 1.206, 95% CI: 1.097–1.325; $P < .001$) are the independent factors associated with the in-hospital outcomes (Supplementary Table S1, http://links.lww.com/MD/D157). Among patients aged >75 years, malignant tumor (OR = 7.999, 95% CI: 2.285–28.002; $P = .001$) is the independent factor associated with the in-hospital outcomes (Supplementary Table S2, http://links.lww.com/MD/D157).

3.3. FPG upon admission independently predicts poor in-hospital outcome in AIS

Univariable logistic regression analysis was performed after PSM to identify potential influencing factors for in-hospital outcome. As shown in Table 3, malignant tumor, gout history, hypoproteinemia, and FPG were found to affect in-hospital outcome in patients with AIS ($P < .1$). Next, multivariable logistic regression analysis was performed to locate the independent factors, which showed that FPG upon admission was an independent predictor of poor in-hospital outcome (OR = 1.11, 95% CI: 1.037–1.188; $P = .003$).

4. Discussion

This study included AIS patients grouped according to poor or good in-hospital outcomes after age, sex, ALT, CKD stage, and

Table 1

Clinical features before and after matching.

Variables	Before matching			After matching		
	POG (n = 74)	GOG (n = 1927)	*P*	POG (n = 74)	GOG (n = 296)	*P*
Age, yrs	70.5 (61–93)	68 (60–97)	.003	70.5 (61–93)	72 (60–92)	.426
Male	47 (63.5%)	1362 (70.7%)	.185	47 (63.5%)	171 (57.8%)	.369
Hypertension	56 (75.7%)	1426 (74.0%)	.747	56 (75.7%)	220 (74.3%)	.811
Diabetes	35 (47.3%)	784 (40.7%)	.256	35 (47.3%)	124 (41.9%)	.401
CKD	19 (25.7%)	71 (3.7%)	<.001	19 (25.7%)	62 (20.9%)	.379
Malignant tumor	7 (9.5%)	43 (2.2%)	<.01	7 (9.5%)	12 (4.1%)	.075
Gout history	3 (4.1%)	25 (1.3%)	.082	3 (4.1%)	3 (1.0%)	.097
NIHSS score	12 (0–35)	4 (0–42)	<.001	12 (0–35)	12 (0–42)	.721
Hypoproteinemia	1 (1.4%)	38 (2%)	>.999	1 (1.4%)	21 (7.1%)	.094
ALT, IU/L	17 (3–447)	15 (2–362)	.235	17 (3–447)	15 (5–268)	.355
TG, mmol/L	1.15 (0.34–3.13)	1.29 (0.36–10.29)	.074	1.15 (0.34–3.13)	1.24 (0.39–8.39)	.448
TC, mmol/L	4.155 (2.56–6.3)	3.92 (1.3–8.28)	.052	4.155 (2.56–6.3)	4.04 (1.65–6.71)	.281
HDL-C, mmol/L	1.205 (0.59–2.84)	1.18 (0.32–2.77)	.170	1.205 (0.59–2.84)	1.2 (0.33–2.76)	.352
LDL-C, mmol/L	2.63 (0.99–4.79)	2.36 (0.33–6.35)	.040	2.63 (0.99–4.79)	2.385 (0.55–4.75)	.119
FPG, mmol/L	7.32 (3.67–22.44)	5.77 (1.47–22.33)	<.001	7.32 (3.67–22.44)	6.4 (3.57–22.33)	.005
HbA1c, %	6.1 (4.4–13.2)	6 (3.8–13.4)	.675	6.1 (4.4–13.2)	6.1 (4.2–12.2)	.959
Length of stay, d	12 (1–49)	9 (0–501)	.006	12 (1–49)	10 (0–59)	.401

ALT = alanine aminotransferase, CKD = chronic kidney disease, FPG = fasting plasma glucose, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein, LDL-C = low-density lipoprotein cholesterol, NIHSS = National Institutes of Health Stroke Score, TC = total cholesterol, TG = triglyceride.

NIHSS score were brought into a PSM model, and suggests that FPG is an independent predictive factor of poor in-hospital outcome.

Diabetes is considered one of the most important risk factors for poor outcome after stroke,[22,23] not only because of high blood glucose levels but also their fluctuation.[6] Even in healthy people without a history of diabetes, elevated levels of postprandial plasma glucose have been found to be a predictor of stroke mortality.[24] Therefore, strict glycemic control during hospitalization might improve prognosis after stroke. However, this may be controversial as the benefit of tight glycemic control in different population of critically ill patients in the ICU, not just stroke cases, remains debatable.[25] While most studies agree that hyperglycemia is a risk for ICU patients, the major risk of strict glycemic control is increased hypoglycemia, which offsets the benefit of any intervention.[26] Similarly, hyperglycemic patients undergoing surgery have worse outcome compared with other individuals, but tight glycemic control does not appear to change this outcome.[27] Therefore, current opinion suggests that effective continuous monitoring systems are needed to ensure that safe levels of glucose are maintained.[28] Hyperglycemia in patients after stroke is sometimes caused by stress[25] and associated with changes in body composition because of aging, obesity, and sedentary behavior.[26]

Until now, FPG has not been reported as a predictor of in-hospital outcome in patients with stroke. In this study, we found that FPG was valuable in predicting in-hospital outcome in such patients. It should be noted that the adjusted OR was close to 1

Table 2

Logistic regression analysis for in-hospital outcome before matching.

Variables	Univariable logistic regression		Multivariable logistic regression	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	1.048 (1.016, 1.08)	.003	1.031 (0.996, 1.068)	.086
Sex	1.385 (0.854, 2.245)	.187		
Hypertension	1.093 (0.637, 1.877)	.747		
Diabetes	1.308 (0.822, 2.084)	.258		
CKD	9.03 (5.092, 16.014)	<.001	8.105 (4.241, 15.489)	<.001
Malignant tumor	4.578 (1.986, 10.552)	<.001	5.334 (2.124, 13.398)	<.001
Gout history	3.215 (0.948, 10.897)	.061	4.141 (1.041, 16.477)	.044
Hypoproteinemia	0.681 (0.092, 5.028)	.706		
ALT	1.008 (1.002, 1.014)	.010	1.007 (0.996, 1.017)	.202
TG	0.692 (0.467, 1.025)	.066	0.527 (0.32, 0.869)	.012
TC	1.239 (0.993, 1.546)	.058	1.184 (0.519, 2.701)	.688
HDL-C	2.05 (1.079, 3.896)	.028	1.484 (0.586, 3.76)	.405
LDL-C	1.311 (1.009, 1.703)	.043	1.203 (0.522, 2.769)	.665
FPG	1.198 (1.13, 1.27)	<.001	1.199 (1.118, 1.285)	<.001
HbA1c	1.023 (0.87, 1.204)	.782		

ALT = alanine aminotransferase, CKD = chronic kidney disease, FPG = fasting plasma glucose, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein, LDL-C = low-density lipoprotein cholesterol, NIHSS = National Institutes of Health Stroke Score, TC = total cholesterol, TG = triglyceride.

Table 3

Logistic regression analysis for in-hospital outcome after matching.

Variables	Univariable logistic regression		Multivariable logistic regression	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	0.988 (0.954–1.022)	.472		
Sex	0.786 (0.464–1.33)	.370		
Hypertension	1.075 (0.595–1.942)	.811		
Diabetes	1.245 (0.746–2.076)	.401		
CKD	1.304 (0.721–2.357)	.380		
Malignant tumor	2.473 (0.938–6.519)	.067	2.612 (0.956–7.137)	.061
Gout history	4.127 (0.816–20.877)	.087	4.641 (0.886–24.32)	.069
Hypoproteinemia	0.179 (0.024–1.356)	.096	0.14 (0.018–1.085)	.060
ALT	1.003 (0.997–1.01)	.318		
TG	0.823 (0.555–1.222)	.335		
TC	1.16 (0.901–1.494)	.251		
HDL-C	1.703 (0.871–3.329)	.120		
LDL-C	1.24 (0.928–1.658)	.146		
FPG	1.084 (1.015–1.157)	.015	1.11 (1.037–1.188)	.003
HbA1c	0.994 (0.833–1.187)	.949		

ALT = alanine aminotransferase, CKD = chronic kidney disease, FPG = fasting plasma glucose, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein, LDL-C = low-density lipoprotein cholesterol, NIHSS = National Institutes of Health Stroke Score, TC = total cholesterol, TG = triglyceride.

(1.11), although the significance of FPG was strongly supported by the 95% CI and *P*-value (.003) obtained. Further larger studies are needed to support this finding. Nevertheless, based on the above data, clinicians should consider treatment methods as well as other factors that might affect FPG while dealing with stroke patients.[27] According to current reports, hyperglycemia is an indicator of severe stroke; while it cannot increase cerebral glucose content, it promotes further ischemia in the brain.[28] Hyperglycemia is associated with severe stroke and poor clinical outcomes; therefore, blood glucose monitoring and management are essential tools for healthcare professionals.[29] The United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that 1% reduction in HbA1c is associated with 12% stroke occurrence.[30] In addition, many studies have confirmed that intensive glucose control results in fewer major cardiovascular events, including stroke, compared with standard therapy.[31–33] Although FPG independently predicted in-hospital outcome, HbA1c was not associated with this parameter in the present study. On the contrary, a recent report demonstrated that elevated HbA1c is an independent predictor of 1-year all-cause mortality after acute 1st-ever ischemic stroke.[34]

On a clinical perspective, the results may suggest that paying more attention to the patients with diabetes to avoid overt hyperglycemia while avoiding hypoglycemic events could lead to improved AIS outcome. In the nondiabetic patients, blood glucose levels should be monitored to detect any hyperglycemia that could be related to stress or stroke-associated metabolic disturbance. The compensatory and self-recovery abilities of younger AIS patients are better than that of elderly AIS patients.[35] Hyperglycemia and hypoglycemia affect elderly AIS patients more deeply than younger AIS patients.[35]

The present study has some limitations. First, it was a retrospective and single-center study, with PSM, and may not comprehensively represent the clinical situation. In addition, the sample size was relatively small. Furthermore, only in-hospital outcome (mortality and ICU admission) was assessed, with no long-term outcome analysis due to lack of follow-up data. Future larger prospective studies should address these shortcomings, especially assessing the degree of disability using modified Rankin scale in these patients, by extending follow-up duration.

Overall, this study showed that FPG after admission is an independent predictor of in-hospital outcome in stroke patients. An initial high level of FPG after admission may predict poor in-hospital outcome. Prospective studies are needed to confirm these findings.

Author contributions

Conceptualization: Lei Zhao.
Data curation: Lei Zhao, Wei Hu.
Formal analysis: Li Wang, Wei Hu.
Investigation: Meihua Lu.
Methodology: Wei Hu.
Project administration: Lei Zhao, Li Wang, Shuangling Xiu.
Resources: Meihua Lu, Shuangling Xiu.
Supervision: Li Wang.
Visualization: Meihua Lu.
Writing – original draft: Lei Zhao.
Writing – review & editing: Lei Zhao, Shuangling Xiu.

References

[1] Katan M, Luft A. Global burden of stroke. Semin Neurol 2018;38:208–11.
[2] Hollander M, Koudstaal PJ, Bots ML, et al. Incidence, risk, and case fatality of first ever stroke in the elderly population. The Rotterdam Study. J Neurol Neurosurg Psychiatry 2003;74:317–21.
[3] Allen CL, Bayraktutan U. Risk factors for ischaemic stroke. Int J Stroke 2008;3:105–16.
[4] Teh WL, Abdin E, Vaingankar JA, et al. Prevalence of stroke, risk factors, disability and care needs in older adults in Singapore: results from the WiSE study. BMJ Open 2018;8:e020285.
[5] Wang J, An Z, Li B, et al. Increasing stroke incidence and prevalence of risk factors in a low-income Chinese population. Neurology 2015;84:374–81.
[6] Lin CC, Yang CP, Li CI, et al. Visit-to-visit variability of fasting plasma glucose as predictor of ischemic stroke: competing risk analysis in a national cohort of Taiwan Diabetes Study. BMC Med 2014;12:165.
[7] Lipska K, Sylaja PN, Sarma PS, et al. Risk factors for acute ischaemic stroke in young adults in South India. J Neurol Neurosurg Psychiatry 2007;78:959–63.

[8] Clark ME, Payton JE, Pittiglio LI. Acute ischemic stroke and hyperglycemia. Crit Care Nurs Q 2014;37:182–7.
[9] Di Bonito P, Di Fraia L, Di Gennaro L, et al. Impact of known and unknown diabetes on in-hospital mortality from ischemic stroke. Nutr Metab Cardiovasc Dis 2003;13:148–53.
[10] Zuliani G, Cherubini A, Ranzini M, et al. Risk factors for short-term mortality in older subjects with acute ischemic stroke. Gerontology 2006;52:231–6.
[11] Chen Y, Hu S, Wu L, et al. Clinical practice guidelines for hypertension in China: a systematic review of the methodological quality. BMJ Open 2015;5:e008099.
[12] Hua Q, Fan L, Li J. Joint Committee for Guideline Revision2019 Chinese guideline for the management of hypertension in the elderly. J Geriatr Cardiol 2019;16:67–99.
[13] Chai TY, Tonks KT, Campbell LV. Long-term glycaemic control (HbA1c), not admission glucose, predicts hospital re-admission in diabetic patients. Australas Med J 2015;8:189–99.
[14] Weng J, Ji L, Jia W, et al. Standards of care for type 2 diabetes in China. Diabetes Metab Res Rev 2016;32:442–58.
[15] Jia W, Weng J, Zhu D, et al. Standards of medical care for type 2 diabetes in China 2019. Diabetes Metab Res Rev 2019;e3158.
[16] Ghotra SK, Johnson JA, Qiu W, et al. Age at stroke onset influences the clinical outcome and health-related quality of life in pediatric ischemic stroke survivors. Dev Med Child Neurol 2015;57:1027–34.
[17] Haast RA, Gustafson DR, Kiliaan AJ. Sex differences in stroke. J Cereb Blood Flow Metab 2012;32:2100–7.
[18] Vincent JL. Relevance of albumin in modern critical care medicine. Best Pract Res Clin Anaesthesiol 2009;23:183–91.
[19] Weikert C, Drogan D, di Giuseppe R, et al. Liver enzymes and stroke risk in middle-aged German adults. Atherosclerosis 2013;228:508–14.
[20] Hojs Fabjan T, Hojs R. Stroke and renal dysfunction. Eur J Intern Med 2014;25:18–24.
[21] Shrestha S, Poudel RS, Khatiwada D, et al. Stroke subtype, age, and baseline NIHSS score predict ischemic stroke outcomes at 3 months: a preliminary study from Central Nepal. J Multidiscip Healthc 2015;8:443–8.
[22] Zhu Z, Yang J, Zhong C, et al. Abnormal glucose regulation, hypoglycemic treatment during hospitalization and prognosis of acute ischemic stroke. J Neurol Sci 2017;379:177–82.
[23] Zhu XR, Zhang YP, Bai L, et al. Prediction of risk of diabetic retinopathy for all-cause mortality, stroke and heart failure: evidence from epidemiological observational studies. Medicine (Baltimore) 2017;96: e5894.
[24] Hyvarinen M, Qiao Q, Tuomilehto J, et al. Hyperglycemia and stroke mortality: comparison between fasting and 2-h glucose criteria. Diabetes Care 2009;32:348–54.
[25] Tziomalos K, Dimitriou P, Bouziana SD, et al. Stress hyperglycemia and acute ischemic stroke in-hospital outcome. Metabolism 2017;67: 99–105.
[26] Ferriolli E, Pessanha FP, Marchesi JC. Diabetes and exercise in the elderly. Med Sport Sci 2014;60:122–9.
[27] Liu J, Liu J, Fang D, et al. Fasting plasma glucose after intensive insulin therapy predicted long-term glycemic control in newly diagnosed type 2 diabetic patients. Endocr J 2013;60:725–32.
[28] Zhang S, Zuo W, Guo XF, et al. Cerebral glucose transporter: the possible therapeutic target for ischemic stroke. Neurochem Int 2014;70:22–9.
[29] Laird E. Blood glucose monitoring and management in acute stroke care. Nurs Stand 2014;28:52–6.
[30] Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000;321:405–12.
[31] Hayward RA, Reaven PD, Wiitala WL, et al. Follow-up of glycemic control and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2015;372:2197–206.
[32] Chalmers J, Arima H, Woodward M, et al. Effects of combination of perindopril, indapamide, and calcium channel blockers in patients with type 2 diabetes mellitus: results from the Action In Diabetes and Vascular Disease: Preterax and Diamicron Controlled Evaluation (ADVANCE) trial. Hypertension 2014;63:259–64.
[33] The Action to Control Cardiovascular Risk in Diabetes Follow-On (ACCORDION) Eye Study Group and the Action to Control Cardiovascular Risk in Diabetes Follow-On (ACCORDION) Study GroupPersistent effects of intensive glycemic control on retinopathy in type 2 diabetes in the action to control cardiovascular risk in diabetes (ACCORD) follow-on study. Diabetes Care 2016;39:1089–100.
[34] Wu S, Wang C, Jia Q, et al. HbA1c is associated with increased all-cause mortality in the first year after acute ischemic stroke. Neurol Res 2014;36:444–52.
[35] Lui SK, Nguyen MH. Elderly stroke rehabilitation: overcoming the complications and its associated challenges. Curr Gerontol Geriatr Res 2018;2018:9853837.