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Original Article

Expressions of serum adiponectin and visfatin in patients with hypertension in cerebrovascular accidents and analysis of risk factors

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Abstract: Objective: To determine the expressions of serum adiponectin and visfatin in patients with hypertension and cerebrovascular accidents and to analyze the risk factors. Methods: Data of 161 patients with hypertension treated in The Affiliated Hospital of Shandong University of Traditional Chinese Medicine from March 2019 to July 2021 were retrospectively analyzed. There were 72 patients with cerebrovascular accidents assigned to an occurrence group. The remaining 89 patients without cerebrovascular accidents were assigned to a non-occurrence group. The two groups were compared in terms of the coagulation function (activated partial thromboplastin time, prothrombin time, and fibrinogen), liver function (aspartate aminotransferase (AST), glutamic pyruvic transaminase (GPT), albumin and total bilirubin (TB)), blood lipid indexes (cholesterol, triglyceride, high-density lipoprotein (HDL), low-density lipoprotein (LDL)), serum adiponectin, and visfatin levels. Pearson's correlation coefficient was performed to analyze the correlation of serum adiponectin and visfatin with blood lipid indexes. Logistics regression was performed to analyze the risk factors of stroke in patients with hypertension. Results: The two groups were similar in terms of sex, age, education level, smoking, drinking, and diabetes histories (P>0.05). There were more patients ≥65 years old with body mass index ≥20 kg/m^2 and with hyperlipidemia in the occurrence group than those in the non-occurrence group (P<0.05). The two groups were not notably different in activated partial thromboplastin time, prothrombin time, fibrinogen, AST, GPT, albumin, TB, total cholesterol, and HDL (P>0.05). The occurrence group showed significantly higher triglyceride, LDL and adiponectin levels, and a notably lower visfatin level than the non-occurrence group (P<0.05). Adiponectin showed a positive correlation with triglyceride and a negative association with LDL (P<0.05). Visfatin showed only a negative correlation with triglyceride (P<0.05), but no correlation with LDL (P>0.05). A multivariate logistics regression analysis reported that hyperlipidemia, triglyceride, LDL, adiponectin, and visfatin were independent risk factors for stroke in patients with hypertension (P<0.05). Conclusion: Serum adiponectin and visfatin were differentially expressed in patients with both hypertension and stroke. Our regression analysis revealed that serum adiponectin and visfatin were independent risk factors for stroke in patients with hypertension.

Keywords: Hypertension, adiponectin, visfatin, cerebrovascular accident

Introduction

Hypertension is a frequentlyseen risk factor of cardiovascular and cerebrovascular diseases in adults. It is the primary risk factor of total human mortality [1]. A USA epidemiological survey stated that 7 million people die from hypertension every year [2]. As blood pressure increases, the blood pressure-associated target organs, including heart, blood vessels, kidney, and brain, will have corresponding subclinical damage, forming a vicious circle and triggering death [3, 4]. Stroke, known as cerebrovascular accident, is an acute cerebrovascular disease. It is a group of diseases that cause brain tissue damage by sudden rupture of blood vessels in the brain or blockage of blood vessels [5]. Stroke can be classified into ischemic stroke and hemorrhagic stroke. An ischemic stroke is the most common type in clinical

practice, accounting for 60-80% of all stroke cases. Ischemic stroke refers to the cerebrovascular disease caused by blood supply disturbance in local brain tissue. It leads to ischemic and hypoxic necrosis of brain tissue, resulting in neurological deficit and seriously compromises the quality of life of patients [6, 7]. There is a lack of target molecules that take a crucial part in stroke in patient with hypertension.

Adiponectin is a special protein secreted by adipocytes, discovered in recent years. Adiponectin is closely linked to insulin resistance, arteriosclerosis, and inflammation [8]. It improves the body's insulin resistance in many ways to protect vascular endothelium. It plays an anti-inflammatory and protective role in myocardial ischemia-reperfusion injury [9]. Visfatin is a cytokine found in active peripheral blood lymphocytes, with the function of promoting the maturation of B lymphocytes [10]. Recent research shared that visfatin is mainly secreted by adipocytes, with insulin activity, and its expression is bound up with obesity and type 2 diabetes [11]. There are few reports about adiponectin and visfatin in patients with both hypertension and stroke. Whether they can be adopted as indicators to predict stroke in patients with hypertension is under investigation.

This study was designed to analyze the value of serum adiponectin and visfatin in patients with both hypertension and stroke, to provide reference for clinical prediction.

Methods and data

Clinical data

Data of 161 patients with hypertension treated in The Affiliated Hospital of Shandong University of Traditional Chinese Medicine from March 2019 to July 2021 were retrospectively analyzed. There were 72 patients with cerebrovascular accidents who were assigned to an occurrence group. The remaining 89 patients without cerebrovascular accidents were assigned to a non-occurrence group. This study was performed with approval from the Medical Ethics Committee of Affiliated Hospital of Shandong University of Traditional Chinese Medicine, with ethnical approval number of 2019044 (review).

Inclusion and exclusion criteria

Inclusion criteria: Patients met the criteria of diagnosis and treatment of acute ischemic stroke in China [12], patients with hyperhomocysteinemia ≥10 μmol/L, patients with ischemic stroke, patients who met the diagnostic criteria in Chinese guidelines for prevention and treatment of hypertension [13], patients with detailed clinical data, and patients who were 55 years old or older.

Exclusion criteria: Patients with severe systemic diseases including the liver, kidney, or electrolyte dysfunction; patients with severe coagulation dysfunction; patients with malignant tumor; pregnant women; women in pre- or postpartum confinement; patients with secondary hypertension; or patients with thyroid dysfunction.

Collection of general medical history data

The data including sex, age, height, weight, education level, smoking and drinking history, lifestyle, and previous medical history of basic diseases including diabetes and hyperlipidemia were collected.

Collection of laboratory indicators

Fasting venous blood was acquired from each patient within 24 h after admission. The coagulation function (activated partial thromboplastin time, prothrombin time, and fibrinogen), liver function (aspartate aminotransferase (AST) and glutamic pyruvic transaminase (GPT), albumin and total bilirubin (TB)), blood lipid indexes (cholesterol, triglyceride, high-density lipoprotein (HDL), low-density lipoprotein (LDL)), serum adiponectin, and visfatin were determined. Except for serum adiponectin and visfatin, all other laboratory indexes were detected with the use of a Beckman Coulter Uni Cel DXC600 automatic biochemical analyzer with reagents from instrument kits. Serum adiponectin and visfatin were quantified by enzyme-linked immunosorbent assay (ELISA) with the kit from Shanghai MLBIO Co., Ltd.

Outcome measures

Primary outcome measures: The two groups were compared in terms of coagulation function, liver function, blood lipid indexes, serum

Table 1. General data

Factor	Occurrence group (n=72)	Non-occurrence group (n=89)	*P* value
Sex			
Male	37	49	0.642
Female	35	40	
Age (years)			
≥65	43	35	0.010
<65	29	54	
BMI (kg/m^2)			
≥20	66	56	<0.001
<20	6	33	
Education level			
≥ High school	23	30	0.812
< high school	49	59	
History of smoking			
Yes	43	51	0.756
No	29	38	
History of alcoholism			
Yes	15	22	0.802
No	57	59	
Diabetes			
Yes	38	52	0.472
No	34	37	
Hyperlipoidemia			
Yes	17	8	0.010
No	55	81	

Note: Body Mass Index (BMI).

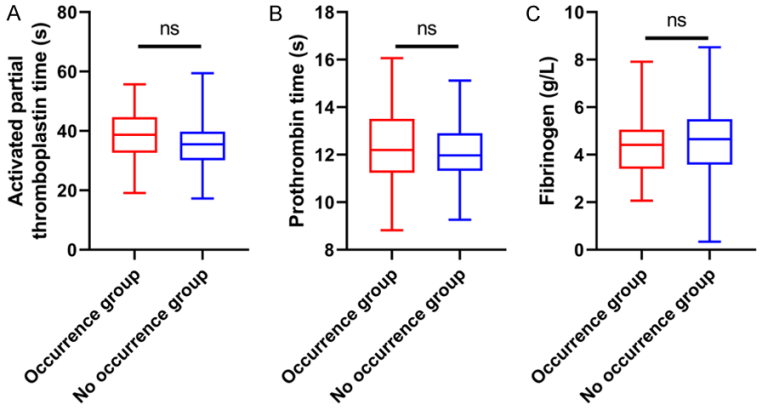

Figure 1. Comparison of coagulation function between the two groups. A. Comparison of activated partial prothrombin time. B. Comparison of prothrombin time. C. Comparison of fibrinogen. Note: ns means P>0.05.

adiponectin, and visfatin levels. Pearson's correlation coefficient was conducted to analyze the correlation of serum adiponectin and visfatin with blood lipid indexes.

Secondary outcome measures: Clinical data of the two groups were compared. Logistics regression was performed to analyze the risk factors of stroke in patients with hypertension.

Statistical analysis

This study adopted SPSS 20.0 software for statistical analyses of the collected data. GraphPad Prism 8 software was used for data visualization. Counting data (rate, %) were analyzed using the Chi-square test. The measured data (mean ± standard deviation) were analyzed by the t test. Their inter-group comparison and intra-group comparison were carried out using the independent-sample t test and paired t test, respectively. Logistic regression was performed for analysis of risk factors of stroke in patients with hypertension. P<0.05 indicated a significant difference.

Results

Comparison of general data

A comparison of baseline data between the occurrence group and the non-occurrence group explained that the two groups were not greatly different in sex, age, education level, smoking, drinking, and diabetes history (P>0.05, **Table 1**). There were more patients ≥65 years old with a body mass index (BMI) ≥20 kg/m^2 and with hyperlipidemia in the occurrence group than those in the non-occurrence group (P<0.05).

Comparison of coagulation function

A comparison of coagulation function showed that there was no great difference in activated

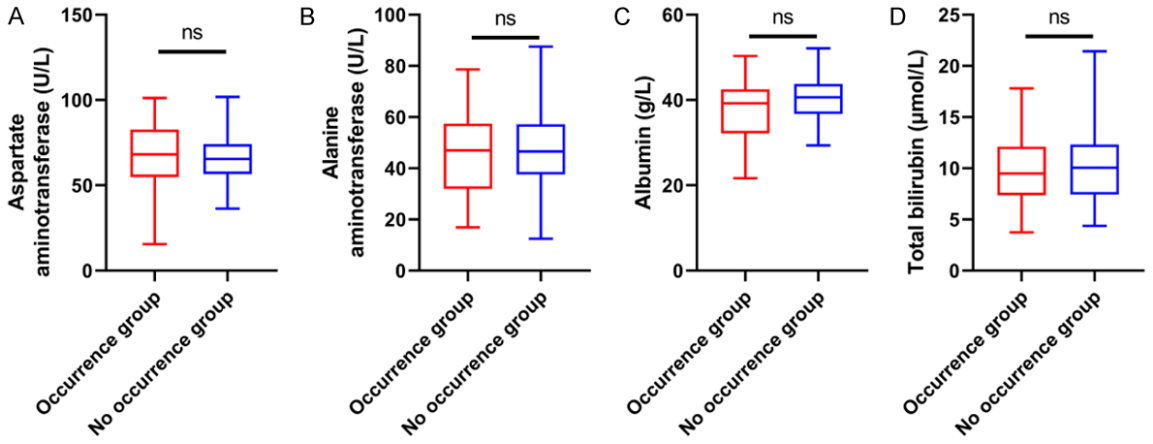

Figure 2. Comparison of liver function between the two groups. A. Comparison of aspartate aminotransferase. B. Comparison of glutamic-pyruvic transaminase. C. Comparison of albumin. D. Comparison of total bilirubin. Note: ns means P>0.05.

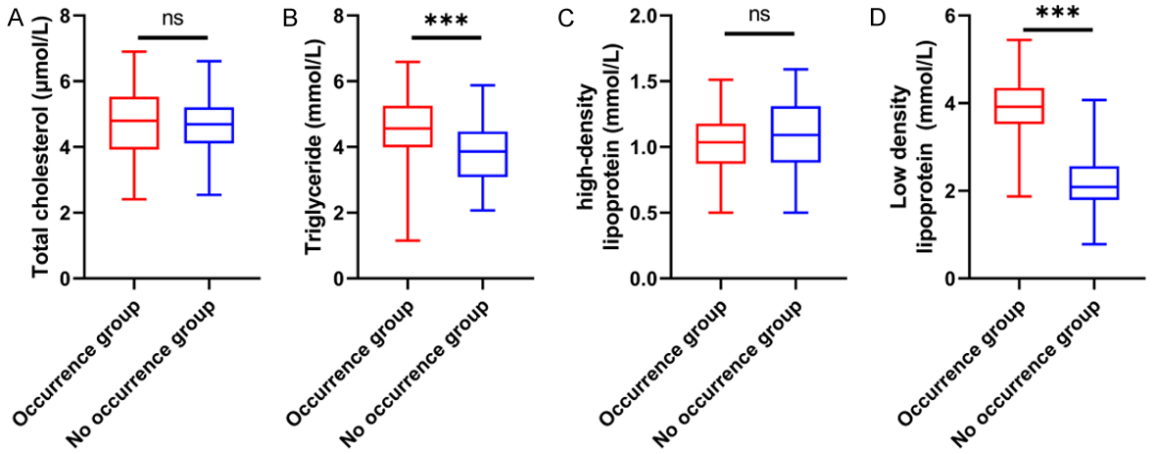

Figure 3. Comparison of blood lipid indexes between the two groups. A. Comparison of total cholesterol. B. Comparison of triglycerides. C. Comparison of high-density lipoprotein. D. Comparison of low-density lipoprotein. Note: ns means P>0.05, and *** means P<0.001.

partial thromboplastin time, prothrombin time, and fibrinogen between the occurrence group and the non-occurrence group (P>0.05, **Figure 1**).

Comparison of liver function

A comparison of liver function showed that there was no notable difference in AST, GPT, albumin, and TB between the two groups (P>0.05, **Figure 2**).

Comparison of blood lipid indexes

A comparison of the blood lipid indexes between the two groups showed that the total cholesterol and HDL of the two groups were not greatly different (P>0.05). The occurrence group showed notably higher triglyceride and LDL levels than the non-occurrence group (P<0.05, **Figure 3**).

Comparison of adiponectin and visfatin

As for adiponectin and visfatin, the occurrence group showed a higher adiponectin level and a notably lower visfatin level than the non-occurrence group (P<0.05, **Figure 4**).

Correlation of adiponectin and visfatin with blood lipid indexes

Adiponectin showed a positive correlation with triglycerides and a negative association with

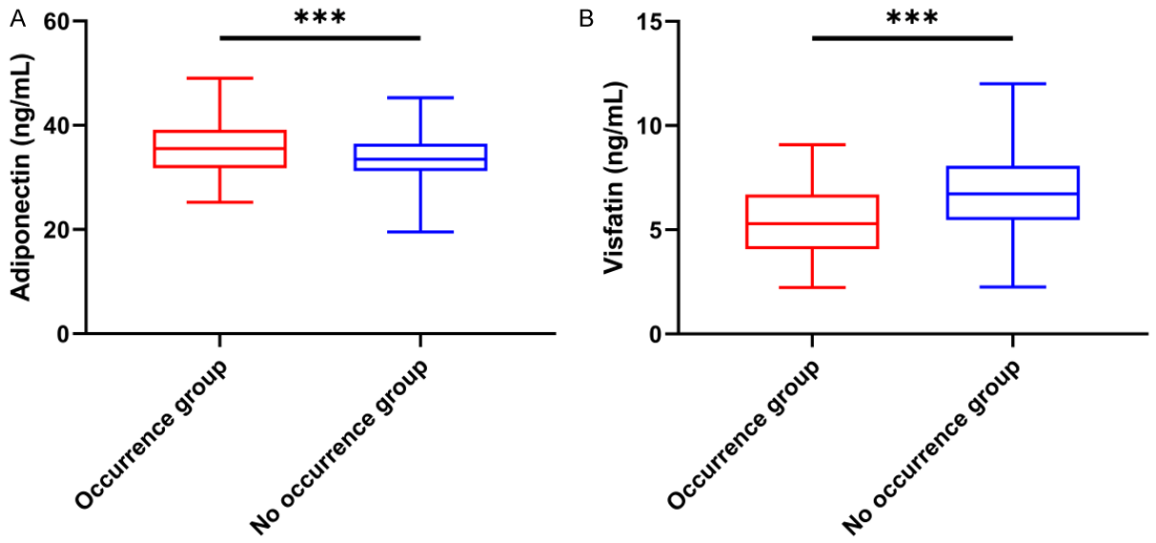

Figure 4. Comparison of adiponectin and visfatin between the two groups. A. Comparison of adiponectin. B. Comparison of visfatin. Note: *** means P<0.001.

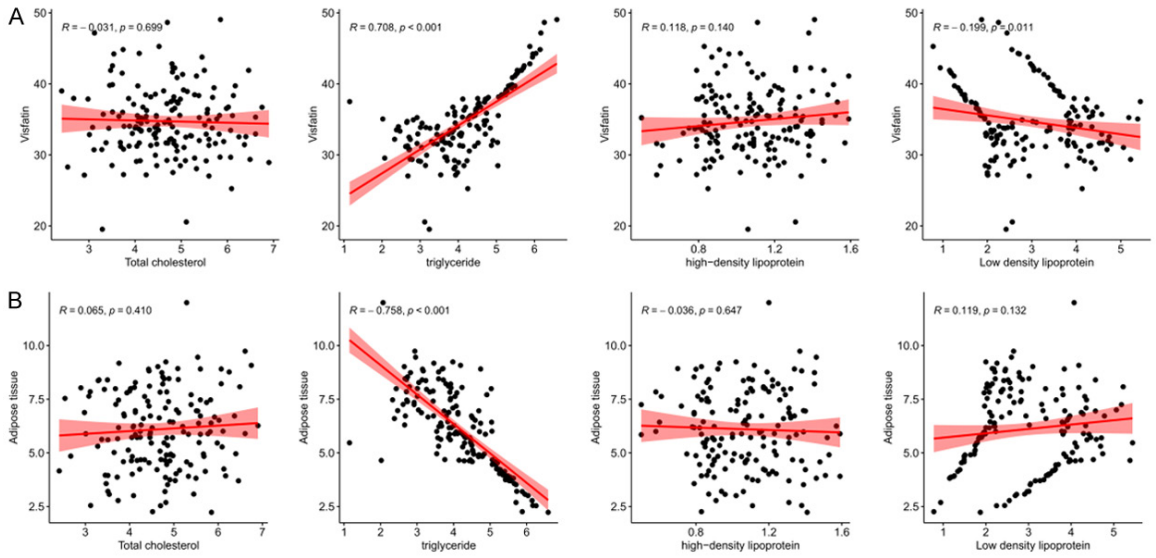

Figure 5. Correlation of adiponectin and visfatin with blood lipid indexes. A. Correlation of adiponectin with blood lipid indexes. B. Correlation of visfatin with blood lipid indexes.

LDL (P<0.05). Visfatin showed a negative association with triglycerides (P<0.05), but no correlation with LDL (P>0.05). Neither adiponectin nor visfatin were linked to total cholesterol or HDL (P>0.05, **Figure 5**).

Risk factors of stroke in patients with hypertension

The univariate analysis reported that age, BMI, hyperlipidemia, triglycerides, LDL, adiponectin, and visfatin were risk factors for stroke in patients with hypertension. To determine the independent factors influencing stroke in patients with hypertension, the data were assigned (**Table 2**). It was found that hyperlipidemia, triglyceride, LDL, adiponectin, and visfatin were independent risk factors for stroke in patients with hypertension (P<0.05, **Table 3**).

Discussion

The latest statistics stated that there was approximately 390 million adult patients with hypertension in China. This accounted for 28.0% of the total population in China [14].

Table 2. Assignment

Factor	Assignment
Age	≥65 years old =1, <65 years old =0
BMI	≥20 kg/m^2 =1, <20 kg/m^2 =0
Hyperlipoidemia	Yes =1, No =0
Triglycerides	Data belonging to continuous variables were their raw data
Low-density lipoprotein	Data belonging to continuous variables were their raw data
Adiponectin	Data belonging to continuous variables were their raw data
Visfatin	Data belonging to continuous variables were their raw data
Group	Occurrence group =1, Non-occurrence group =0

Note: Body Mass Index (BMI).

Table 3. Multivariate analysis

Factor	β	SE	X^2	*P* value	OR value	95% CI	
						Lower limit	Upper limit
Age	0.068	0.060	1.282	0.257	1.070	0.952	1.203
BMI	-0.026	0.181	0.020	0.886	0.974	0.683	1.390
Hyperlipoidemia	2.473	1.242	3.966	0.046	11.858	1.040	135.217
Triglycerides	1.650	0.482	11.695	0.001	5.207	2.022	13.404
Low-density lipoprotein	3.696	0.740	24.911	<0.001	40.280	9.436	171.949
Adiponectin	-0.629	0.240	6.888	0.009	0.533	0.333	0.853
Visfatin	0.260	0.093	7.832	0.005	1.297	1.081	1.557

Note: Body Mass Index (BMI).

Hypertension harms health through cardiovascular and cerebrovascular complications. Stroke is the most common complication [15]. Statistics showed the incidence ratio of stroke among hypertensive people in China was approximately (5-8): The high disability rate of stroke greatly compromises the quality of life for the survivors [16]. Finding and controlling the risk factors of stroke in patients with hypertension can be a shortcut to prevent and control stroke.

In this study, age, BMI, hyperlipidemia, triglycerides, LDL, adiponectin, and visfatin were found to be risk factors for stroke in patients with hypertension. Prior research has revealed that with the increase of age and BMI, strokes in patients with hypertension obviously increase [17, 18]. A multivariate analysis in this study reasoned that age and BMI were not risk factors of stroke in patients with hypertension. This was different from prior research. The reason was that the age and BMI data of the samples collected in this study were concentrated. The regression analysis was not based on a large sample size.

Blood lipid is a general type of lipid contained in human plasma. Hyperlipidemia is the high content of lipids in the blood [19]. Hyperlipidemia can directly increase the incidence of some harmful diseases. The main consequence of hyperlipidemia is the deposition of lipids in vascular endothelium. Research reported that acute stroke is greatly increased in patients with hyperlipidemia. Hyperlipidemia is a risk factor for acute stroke [20, 21]. In this study, stroke in patients with hyperlipidemia was 11 times that in patients without hyperlipidemia. It is of profound importance to prevent hyperlipidemia and related diseases.

Triglyceride is an organic compound, formed by esterification of three hydroxyl groups of glycerol with three fatty acid molecules. As a non-polar substance stored in the body in the form of non-hydration, it is the energy substance with the largest reserve and the most productive capacity in the body [22]. LDL refers to a lipoprotein particle with a diameter of 18-25 nanometers. LDL is responsible for carrying fatty acid molecules in the blood to the whole body for cell use [23]. It is the final stage of LDL produced by the liver. With the publica-

tion of new large-scale research results and the update of prevention and treatment guidelines, the role of dyslipidemia in the primary prevention and treatment of ischemic stroke is highlighted [24]. Like the present study, prior research revealed that the increase of serum total cholesterol and serum LDL cholesterol levels were the main risk factors for atherosclerotic cardiovascular disease [25]. The results suggested that patients with hypertension need control of LDL and triglycerides levels and insistence on exercise to improve their diet to prevent the occurrence of stroke.

Adipocyte factor is closely bound up with blood lipid. Visfatin is a kind of adipocyte factor secreted by visceral adipose tissue [26, 27]. Prior research indicated that visfatin can promote cell proliferation, participate in inflammatory response, resist cell apoptosis, and regulate insulin secretion [28, 29]. Adiponectin is a cytokine secreted by adipocytes with anti-atherosclerosis, endothelial protection, and anti-inflammatory effects [30]. A study revealed a notably lower serum adiponectin level in patients with cerebral infarction than that of the control patients. This suggested that the decrease of adiponectin level was a crucial factor in the development and progression of vascular diseases including acute cerebral infarction [31]. In the present study, a correlation analysis revealed a positive association of adiponectin with triglycerides, a negative association of adiponectin with LDL, and a negative association of visfatin with triglyceride. The results indicated that both adiponectin and visfatin were strongly linked to the blood lipids in patients with stroke. The blood lipids in patients with stroke increased significantly. This suggested the involvement of adiponectin and visfatin in the development of stroke in patients with hypertension. In the logistics regression analysis, adiponectin and visfatin were found to be independent risk factors of stroke in patients with hypertension. This was the first time that adiponectin and visfatin were found to be risk factors of stroke in patients with hypertension. The specific mechanism needs further exploration.

This study determined that serum adiponectin and visfatin are independent risk factors of stroke in patients with hypertension. This study has some limitations. This was a retrospective study. The patients were not followed long term. There were some differences between the results of this study and those of prior literature because of the small sample size. We did not analyze the changes of serum adiponectin and visfatin before or after the treatment in this study. It is unknown if there were differences between them after the treatment, or if they could be adopted as prognostic indicators for patients with both hypertension and stroke. This needs to be further analyzed. We hope to carry out more experiments in the future to improve the research findings.

Serum adiponectin and visfatin were differentially expressed in patients with both hypertension and stroke. The regression analysis revealed that serum adiponectin and visfatin were independent risk factors of stroke in patients with hypertension.

Disclosure of conflict of interest

None.

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