The use of susceptibility-weighted imaging to detect cerebral microbleeds after lacunar infarction

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Abstract. – OBJECTIVE: To study the value of susceptibility-weighted imaging (SWI) technology to detect cerebral microbleeds (CMBs) in senile cerebral lacunar infarction patients; and to evaluate the complicated cerebral hemorrhage risk after patients with CMBs took aspirin, an antiplatelet medication or received anticoagulant therapy.

PATIENTS AND METHODS: MRI scanning, using GRE-T2*WI, SWI and FSE sequences (T1WI, T2WI, and T2FLAIR), was performed on the three groups: (1) a cerebral lacunar infarction group; (2) cerebral lacunar infarction with cerebral microbleeds (CMBs) group; and (3) a healthy elderly group. A total of 60 cases were in each group (180 total patients). In addition, the lacunar infarction group and lacunar infarction with CMBs groups were both treated with formal antiplatelet or anticoagulant therapy, according to medical guidelines. Patients were followed for 12 months, during which time their cerebral hemorrhages and post-event effects were observed. The relativity of CMBs, antiplatelet therapy, anticoagulant therapy and cerebral hemorrhage transformation was analyzed and defined. The two groups of research patients with lacunar infarctions were scanned with relevant sequences.

RESULTS: The SWI scanning sequence showed the highest positive rate of CMBs, followed by GRE-T2*WI and other conventional scanning sequences. T1WI, T2WI and T2FLAIR showed a relatively lower positive rate of CMBs. In the cerebral lacunar infarction group and healthy elderly group, 34 cases in the SWI sequence showed 84 positive sites; 18 cases in the GRE-T2*WI sequence showed 40 positive sites; 2 cases in the T1WI sequence showed 4 positive sites; and 6 cases in the T2WI sequence showed 11 positive sites. After a chi-squared test, the differences between the sequences were statistically significant ($p < 0.05$). In the lacunar infarction group, 26 cases (43.33%) exhibited microbleeding lesions, while the normal control group represented 8 cases (13.33%). The lacunar infarction group exhibited mild, moderate and severe cases, the three types of CMBs. The normal control group only showed mild hemorrhaging. The degree of lacunar infarction was significantly related to the severity of CMBs ($p < 0.05$). After patients with CMBs had received formal antiplatelet therapy and anticoagulation therapy, one case in the lacunar infarction with microbleeds group showed cerebral hemorrhaging, but this had no statistical significance ($p > 0.05$).

CONCLUSIONS: The SWI scanning sequence is more sensitive than the GRE-T2*WI sequence. The GRE-T2*WI sequence is more sensitive than the conventional FSE sequence. SWI is highly sensitive and specific to the diagnosis of CMBs. It is an accurate and effective method for the analysis and diagnosis of CMBs. If patients with CMBs caused by lacunar infarction are treated with antiplatelet and anticoagulant therapy, the risk of cerebral hemorrhagic transformation is relatively smaller within 12 months. However, this needs to be observed further to define possible long-term risks.

Key Words:
CMBs, Magnetic susceptibility-weighted imaging, Cerebral lacunar infarction, Anti-platelet therapy, Anticoagulation therapy.

Introduction

Cerebral microbleeds (CMBs) refer to the tiny blood vessels in the brain that seep blood. This microbleeding causes a series of morphological changes that can be detected by MRI scanning. The general bleeding diameter is less than 5 mm, which pertains to the category of small bleeding lesions[1]. The present study suggests that CMBs are a risk factor of patients after the onset of cerebral infarction for hemorrhagic transformation complicated with cerebral hemorrhage[2]. The application of existing CT or MRI scanning for

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routine inspection has limited diagnostic value for patients suffering from lacunar infarction complicated with CMBs. Thus, this experiment used magnetic susceptibility-weighted imaging (SWI) technology to examine the patients suffering from lacunar infarction. This was compared with conventional MRI scanning to study the application value of SWI technology in the diagnosis of these patients complicated with CMBs. Concurrently, the preliminary analysis was conducted for the influencing factors related to the incidence of CMBs in old-age lacunar infarction, as well as the administration of aspirin antiplatelet therapy or anticoagulant therapy, to explore the risk of brain hemorrhaging for patients suffering from lacunar infarction, to enhance the judgment on clinical prognosis, and to provide a reliable theory basis for clinical diagnosis, treatment and prognosis.

Patients and Methods

Patients

A total of 60 patients with lacunar infarction and 60 patients with lacunar infarction complicated with microbleeds (CMBs) were admitted in our hospital from July to December 2015. These patients were identified as the focus of our research. All patients with lacunar infarction were confirmed with the medical diagnosis criteria for the condition. Patients with brain tumors, brain trauma, cerebral hemorrhage, cerebral venous malformation, blood system diseases, and severe heart and lung disease were excluded after further inspection of the patient subjects. In the group of lacunar infarction patients, there were 33 male patients and 27 female patients aged 59-76 years old, with an average age of 68.54±6.58 years old. In the group of lacunar infarction patients complicated with CMBs, there were 31 male patients and 29 female patients aged 57-77 years old, with an average age of 66.74±7.65 years old.

A total of 60 healthy elderly volunteers identified during the same period was taken as the control group, including 29 cases of male patients and 31 cases of female patients aged 58-76 years old, with an average age of 67.12±6.33 years old. None of the selected patients were found to exhibit any lesions during regular MRI scanning. This study was approved by the Ethics Committee of Xuzhou First Hospital. Signed written informed consents were obtained from the patients and/or guardians.

Clinical Data

Age, gender and risk factors (smoking history, atrial fibrillation, stroke, diabetes mellitus, high blood pressure, hyperlipidemia, etc.) of all patients in the lacunar infarction group and the lacunar cerebral infarction complicated with CMBs group were noted and recorded for the study. The diagnosis of diabetes, high blood pressure, hyperlipidemia and atrial fibrillation was based on World Health Organization (WHO) criteria. A history of stroke was confirmed by old lesions found in iconography or previous definite diagnosis and treatment in a hospital.

Methods

Scanner: GEExciteHDt 3.0TMR. Scanning sequence: axial view T2WI, TR5000 ms, TE120 ms, TI2300 ms; axial T1WI fluid attenuated inversion recovery (FLAIR), TR1772 ms, TE24 ms, TI800 ms; axial T2WI FLAIR, TR8000 ms, TE167 ms, TI2000 ms; matrix 384×384, number of excitation (NEX) was 1; DWI, TR5000 ms, TE75 ms, b value = 1000, thickness of layer = 6 mm, layer spacing = 1 mm, field of view (FOV) = 20 cm × 20 cm, matrix 416 x 320; SWI sequence: TR51.3 ms, TE26 ms, NEX2, fully flow compensated, the image wholly or partially covering the whole brain, 3D gradient echo sequence. A GEAW4.2 workstation was used for SWI data processing, and through the SWI, the processing software automatically produced the correction of the phase diagram and negative phase mask, then the minimum density projection was conducted.

Image Observation and Analysis

Cerebral lacunar infarction is defined by abnormal signal lesions with a clear boundary of less than 15 mm in diameter, where the core density within the brain parenchyma is the same as cerebrospinal fluid.

Lesions were observed through the application of the SWI sequence, FSE sequence (T1WI, T2WI, T2FLAIR) and GRE-T2*WI sequence. T1WI scanning showed low signal and quasi-circular shadows. T2WI and T2WIFLAIR both showed slightly low signal and ring or quasi-circular shadows. Diffusion-weighted magnetic resonance imaging (DWI) showed multiple points of low signal shadows. Lesions of the SWI sequence scan showed low signal shadows of strip, pointed and ring or quasi-circular forms, and the edge of the lesions were clear without edema. Then, according to position, each lesion was divided by the region in which it was located: cortex-sub-

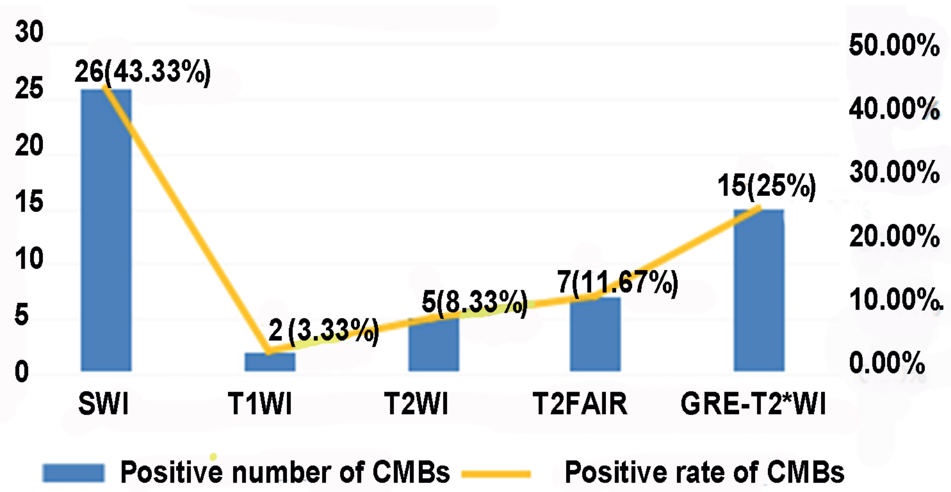

Figure 1. The detection rate of different-sequence CMBs in the lacunar infarction group.

cortex (CSC), basal ganglia/thalami (DGM) and infratentorial (IT). According to the number of lesions, the study divided the cases into three categories: mild (1-3), moderate (4-10) and severe (> 10)[3].

The observation and analysis of the images were independently evaluated by two senior neuroimaging physicians and two senior neurologists using a double-blind method.

Statistical Analysis

SPSS 19.0 software (SPSS Inc., Chicago, IL, USA) was used for all statistical analysis and data summary. The McNemar test was used to compare positive rates for CMBs among SWI, T1W1, T2W1, T2FLAIR and GRE-T2* WI. To counteract any issues with multiple comparisons, the significant level was corrected by the Bonferroni correction method. Comparisons of CMB lesion detection rates underwent X^2 testing. The Kaplan-Meier product-limit method was used to evaluate cumulative probability of intracerebral hemorrhage of 6 months and 12 months ($p < 0.05$ suggested statistical differences).

Results

There were 60 cases for the lacunar infarction group and 60 cases for the healthy control group, shown by different sequences for scanning. The detection rate of different-sequence CMBs in the lacunar infarction group is shown in Figure 1. The detection rate of different-sequence CMBs in the healthy control group is shown in Figure 2. A review of these rates

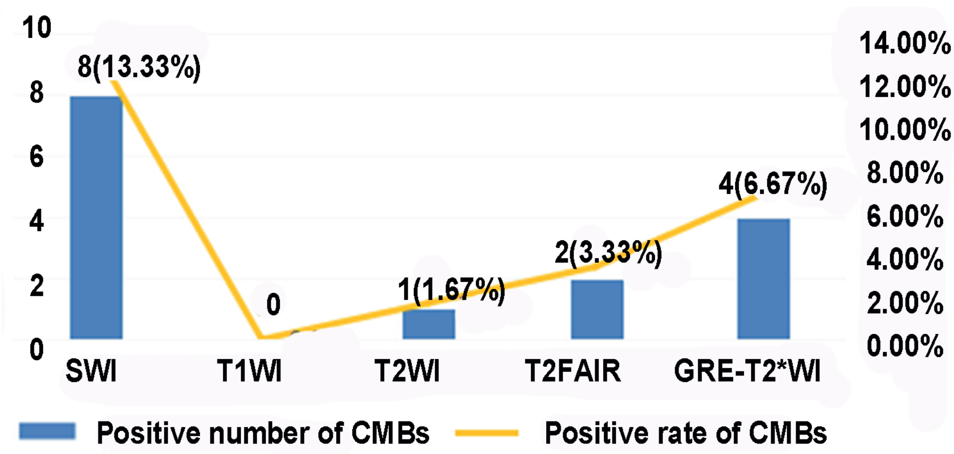

Figure 2. The detection rate of different-sequence CMBs in the healthy control group.

Table I. Comparison of parts where microbleeds often occur between the two groups.

Group microbleeds	Incidence (%)	Cortex-subcortex (CSC)	Basal ganglia/thalami (DGM)	Infratentorial (ITE)
Normal and healthy control group (n = 8,10 sites)	13.33%	2 (20%)	7 (70%)	1 (10%)
Lacunar infarction group (n = 26, 74 sites)	43.33%	16 (21.62%)	46 (62.16%)	12 (16.22%)

shows that the application of the SWI sequence scan improved the discovery of lesions more than other sequences.

During the McNemar test, the positive rate for CMBs of the SWI sequence in the lacunar infarction group was higher than that of the T1W1, T2W1, T2FLAIR and GRE-T2*WI sequences ($p < 0.001$).

During the McNemar test, the positive rate for CMBs of the SWI sequence in the healthy control group was higher than that of the T1W1, T2W1, T2FLAIR and GRE-T2*WI sequences ($p < 0.001$). In the normal healthy control group, there were 10 cases of lesions in which 2 sites of lesions were detected in the cortical-subcortical area (CSC), accounting for 20%; 7 sites of lesions were detected in basal ganglia/thalamus area (DGM), accounting for 70%; and 1 lesion site was detected in the subtentorial area (IT), accounting for 10%. All of these cases were categorized as mild situations.

There were 74 sites of microbleeding lesions in the lacunar infarction group, in which 16 sites of the lesions were detected in the cortical-subcortical (CSC) area, accounting for 21.62%; 46 sites of lesions were detected in the basal ganglia/hypothalamic area (DGM), accounting for 62.16%; and 12 sites were detected in the subtentorial area (IT), accounting for 16.22%. All of these cases were categorized as mild, moderate or severe situations.

It can be concluded from the above two groups of data that CMBs mostly occurred in the basal ganglia/hypothalamic area, followed by the cortical-subcortical area and subtentorial area. To compare the basal ganglia/hypothalamic area with the cortical-subcortical area and subtentorial area, the difference was statistically significant ($p < 0.05$) (Table I).

As for the prevalence rate, the percentage of the lacunar infarction group with CMBs was significantly higher than the normal healthy control group, where the difference was statistically significant ($p < 0.05$) (Table I).

After the SWI scans were conducted for 6o cases of patients in the lacunar infarction group, the lacunar infarction degree and CMBs were classified to analyze their relevance and severity. The results showed that the lacunar infarction degree was significantly related to the severity of the CMBs ($p < 0.05$) (Table II).

Cerebral Hemorrhage Cases After Treatment

The baseline conditions such as gender, age, smoking, hypertension, diabetes mellitus, hyperlipidemia and atrial fibrillation created no obvious difference between the two infarction groups ($p > 0.05$). However, the lacunar infarction group accompanied by microbleeds had significantly more cases of stroke history than the lacunar infarction group, where the difference was statistically significant ($p < 0.05$) (Table III).

After Treatment Follow-Up

Two groups of patients were in accordance with the guideline recommendations to start antiplatelet or anticoagulant therapy. After six months, these two groups were not found to have any cerebral hemorrhaging. Further, after 7 months of treatment, CMBs in patients in the lacunar cerebral infarction group appeared in 1

Table II. Classification of cerebral microbleeds.

		Non	Mild	Moderate	Severe	Total
Severity degree of lacunar cerebral infarction	Mild	20	3	0	0	23
	Moderate	13	13	4	0	30
	Severe	1	2	2	2	7
Total		**34**	**18**	**6**	**2**	**60**

case, occurring in the right basal ganglia. The difference was not statistically significant ($p > 0.05$) (Table IV).

Discussion

As shown in the recent epidemiological studies for four cities in China, patients suffering from lacunar infarction accounted for 42.3% of all ischemic stroke victims[5]. The occurrence of tiny blood vessel lesions inside the brain increase with the increase of the age of the patients suffering from lacunar infarction[6,7]. The occurrence of tiny blood vessel diseases, such as those exhibited by CMBs inside the brain, represent a higher bleeding tendency. Severe tiny vascular lesions are created in the process of the treatment and rehabilitation of patients, affecting the mortality of stroke patients[8]. Therefore, the early detection and identification of lesions have a very important clinical significance.

The research showed that the main cause of CMBs was the degeneration of fibers in the arteriole, causing the trace exosmosis of blood and leading to the chromatosis of heme containing iron[9]. Lipid transparent degeneration plays an important role in the occurrence of CMBs[10]. Currently, the use of conventional head CT or MRI to detect lesions in patients suffering from lacunar infarction has limited diagnostic value. However, in recent years, compared with the conventional scanning sequence, magnetic susceptibility-weighted imaging (SWI) offers the characteristics of high signal-to-noise ratio, high spatial resolution and the three directions imposing liquidity compensation, with very high sensitivity to paramagnetic substances. Because of its simplicity and convenience, SWI is becoming increasingly important for clinical and image doctors[11].

This study used different sequences for scanning and found in the two groups of objects that the SWI sequence had the highest percentage of CMBs detected. This was followed by GRE-T2*W and T2FLAIR sequences, while T2WI and T1WI sequences had the lowest percentage of CMBs detected. The CMBs positive rate of SWI sequence was higher than that of the T1W1, T2W1, T2FLAIR and GRE-T2*WI sequences. This showed that the application of the SWI sequence scan had a better effect on the discovery of lesions than other sequences, which was consistent with current research[12]. In addition,

Table III. Baseline conditions of the research objects in the two groups.

Group Items	Gender (male/female)	Age (yrs)	Smoking rate (%)	History of high blood pressure (%)	History of diabetes (%)	Hyperlipidemia (%)	Atrial fibrillation (%)	History of stroke (%)
Lacunar infarction group	33/27	68.54 ± 6.58	30 (50.0)	38 (63.33)	21 (35.0)	23 (38.33)	5 (8.33)	8 (13.33)
Lacunar infarction complicated with microbleeds group	31/29	66.74 ± 7.65	27 (45.0)	39 (65.0)	19 (31.67)	26 (43.33)	4 (6.67)	24 (40.0)
p value	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	< 0.01

Table IV. Follow-up situation of cerebral hemorrhage after treatment.

	6 months after treatment	12 months after treatment	*p* value
Lacunar infarction group (n = 60)	0	0	–
Lacunar infarction complicated with microbleeds group (n = 60)	0	1	$p > 0.05$

the incidence of CMBs was slightly higher in the normal healthy group of this experiment, which parallels other research[13]. This could be due to this research adopting the more advanced SWI sequence scanning, while previous research used GRE-T2*WI sequence scanning.

After determining the location and number of CMBs in the healthy control group and the lacunar infarction group, it was discovered that lesions mostly occurred in the basal ganglia/hypothalamus area. The regions with the next highest totals were the cortical, subcortical and the subtentorial areas, respectively. However, past research has shown that, in healthy people, CMBs mostly occur in the cortex and subcortical areas, followed by the basal ganglia, thalamus and subtentorial areas[14]. This research considered differences to be related to the collection of the case number, race and regions of patients. However, the predilection site of CMBs in the lacunar infarction group was consistent with other research[15]. In addition, this study found that, when the severity of the lacunar infarction was higher, the severity of the CMBs was also higher, so both were positively correlated. Other research has suggested that, from the perspective of the pathology, lacunar infarction and CMBs have the same pathological manifestations, hence they have certain relevance[16].

Both CMBs and lacunar infarction are classified as microvascular lesions[17,18]. For patients with lacunar infarction, the multiple lesions mean an increase in the risk of brain hemorrhaging[19]. Therefore, CMBs can be used to predict the occurrence of brain hemorrhaging in patients with lacunar infarction after the use of antiplatelet aggregation or anticoagulant drugs for treatment. This study collected 120 cases of lacunar infarction patients with basically the same baseline situation, divided into a lacunar infarction group and a lacunar infarction group accompanied by micro hemorrhaging, with a total of 120 cases. Following the guideline opinions, after anti-platelet aggregation and anticoagulant therapy, with 12 months of follow-up, it was found that, in the 7 months of treatment, the lacunar infarction group accompanied by micro hemorrhaging had 1 case of a brain hemorrhaging incident. Additionally, it was found, after using the Kaplan-Meier product-limit method to evaluate the cumulative probability of brain hemorrhage, the two groups

Table V. Comparison of the parts and number of cerebral microbleeds before and after treatment.

Detection time	Cortex-subcortex (CSC)	CMBs number/sites basal ganglia/thalami (DGM)	Infratentorial (IT)
On admission	16	46	12
6 months	17	48	10
12 months	15	44	11

Table VI. Comparison of CMBs of the lacunar infarction with microbleeds group.

Detection time	Cortex-subcortex (CSC)	CMBs number/sites basal ganglia/thalami (DGM)	Infratentorial (IT)
On admission	315	207	83
6 months	314	209	84
12 months	312	206	82

of experimental subjects had no significant statistical differences ($p < 0.05$). Concurrently, the follow-up of patients found that neither antiplatelet aggregation nor anticoagulation therapy had an obvious impact on the number of lesions caused by CMBs. Before and after treatment, the lesions of the two groups of patients had no statistical difference ($p < 0.05$). This showed that the patients with CMBs, who were undergoing antiplatelet aggregation or anticoagulant therapy, were not affected by the occurrence of cerebral hemorrhaging. However, an extension of the observation time of these patients is likely necessary to better determine their long-term prognosis.

Conclusions

SWI sequence scanning for the detection of CMBs was better than that of other conventional sequence scanning. This type of scanning had an obvious sensitivity to the detection of the site, quantity, and range of lesions caused by CMBs. However, other regular scans in the diagnosis and identification of other lesions could be performed as a reference to the SWI sequence[20]. Concurrently, in patients suffering from lacunar infarction accompanied by CMBs, who are also undergoing antiplatelet aggregation or anticoagulant therapy, there would not be an increased risk of cerebral hemorrhaging. However, additional observation time would enable the number and characteristics of the lesions to be more fully observed.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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