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Opinion paper

Evaluation of the role of susceptibility-weighted imaging in thrombolytic therapy for acute ischemic stroke

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ABSTRACT

We inspected low-intensity venous signals and microbleeds in patients with acute ischemic stroke (AIS) using susceptibility-weighted imaging (SWI) before and after administration of within-thrombolytic-time-window thrombolytic therapies, and observed their prognosis and safety, in order to guide individualized thrombolytic therapies. Patients with AIS were divided into groups A or B according to the presence of symmetric or asymmetric veins on SWI, and were re-inspected by SWI after intravenous thrombolysis using recombinant tissue plasminogen activator (rt-PA). The National Institutes of Health stroke scale (NIHSS) score before treatment and at 1-h and 24-h posttreatment in the two groups were 11.9, 7.3, and 7.1 in group A, 12.4, 8.2, and 7.9 in group B, significant difference was detected between the two groups after treatment. The 90-day mortality rate was 0, and the incidences of cerebral microbleeds (CMBs) and symptomatic cerebral hemorrhage (SCH) were 17.6%, and 0% in group A, 25.6% and 0% in group B, respectively. The incidences of CMBs and SCH in group A were lower than those in group B, but the intergroup differences were not statistically significant ($P > 0.05$). The 90-day neurological improvement rates in the two groups were 70.2% and 58.1%, respectively, and group A showed a significantly better prognosis than group B ($P < 0.05$). Thus, low-intensity venous signals in SWI can be used to evaluate a low level of perfusion, post-thrombolytic prognosis, and bleeding indexes, and can therefore be used to guide individualized thrombolytic therapies.

1. Introduction

Acute ischemic stroke (AIS) is a common cerebrovascular condition that has a high incidence, morbidity, and recurrence rate, severely affecting patients' quality of life, in addition to having a high mortality rate [1–3]. Administration of intravenous thrombolysis with recombinant tissue plasminogen activator (rt-PA) within the treatment time-window is the only treatment proven to reduce disability rates in patients with AIS [4,5]. Currently, intravenous thrombolytic rates during the acute phase of cerebral infarction are low, worldwide, mainly due to the extremely strict treatment time-window and concerns about the potential for fatal intracranial bleeding complications [6]. Factors related to rt-PA thrombolytic therapy, such as extending the time-window of thrombolytic therapies, patient selection, and therapeutic efficacy and safety, have been the focus of clinical research. Methods for improving thrombolytic recanalization rates and clinical outcomes within a limited time-window are of particular interest. Susceptibility-weighted imaging (SWI) is a magnetic resonance imaging (MRI) technology [7,8] that exploits susceptibility differences among organs, including veins. A variety of blood products, such as deoxyhemoglobin and hemosiderin, have more susceptibility effect, and therefore small veins appear as low-intensity signals in SWI. Using the differences in the content of deoxyhemoglobin between perfusion-insufficient regions and normal tissues, SWI could indirectly reflect oxygen metabolism in tissues. After cerebral infarction, ischemic tissues exhibit a compensatory increase in the oxygen-uptake fraction, resulting in an increased proportion of deoxyhemoglobin flowing back to the veins; thus, SWI may reveal increased low-intensity signals on the ischemic side in veins, seen as asymmetrical veins between ischemic and normal brain tissues [9]. Increasing numbers of studies have shown that SWI plays an important role in the rapid detection of ischemic penumbra. Cerebral microbleeds (CMBs), small bleeding lesions in intracranial microvessels (<5 mm), represent a type of subclinical damage to the brain parenchyma, and have an incidence rate ranging from 26% to 68% in ischemic stroke patients; however,

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conventional computed tomography (CT) is often unable to detect CMBs effectively. CMBs often occur in the infarction zone of patients with AIS, and thrombolytic therapy for treatment of cerebral infarction in patients with multiple CMBs may increase the risk of diffuse intracranial hemorrhage [10–12]. We used SWI to inspect low-intensity venous signals and CMBs in patient with AIS in order to assess the prognosis of rt-PA thrombolysis performed within the intravenous thrombolytic time-window, and to guide individualized thrombolytic therapies.

2. Methods

2.1. Subjects

This study retrospectively analyzed the clinical data of 60 patients with AIS who were admitted and treated in the emergency department of our hospital from January 2015 to January 2016. The inclusion criteria were as follows: (1) patients aged 18–80 years; (2) clinical diagnosis of AIS and treatment administered within 4.5 h of onset; (3) cranial CT imaging indicating absence of early massive cerebral infarction (e.g., sulcus effacement) or other non-stroke diseases, except for intracranial hemorrhage; (4) National Institutes of Health stroke scale (NIHSS) score <25 points; (5) normal activated partial thromboplastin time (APTT), prothrombin time (PT), and fibrinogen level; (6) informed consent provided by the patient or family. This study was approved by the hospital's ethics committee.

The exclusion criteria included: (1) signs of intracranial or subarachnoid hemorrhage; (2) severe hypertension (systolic blood pressure [SBP] $\geqslant$185 mmHg or diastolic blood pressure [DBP] $\geqslant$110 mmHg), or an inability to achieve the target value after treatment; (3) association with epilepsy; (4) arterial puncture within the previous 7 days; (5) administration of heparin or oral anticoagulants within the previous 14 days, prolonged bleeding time (>15 s), or platelet count $<100 \times 10^9$/L; (6) blood glucose concentration <2.7 mmol/L or >22.2 mmol/L, or an inability to meet these standards after treatment; (7) abdominal dialysis or hemodialysis; (8) association with severe heart, liver, or kidney dysfunction; (9) history of malignant cancer or anti-tumor therapy.

2.2. Research methods and grouping

The enrolled patients first underwent head CT within the time-window from onset to exclude cerebral hemorrhage or massive cerebral infarction; patients then underwent SWI while awaiting the results of routine blood, blood clotting, and other laboratory tests (all completed within 15 min to avoid delay in administration of thrombolytic therapy). The inspection sequences included conventional sequences (T1-weighted imaging [T1WI], T2-weighted imaging [T2WI], fluid-attenuated inversion recovery [FLAIR]), MRI angiography [MRA], diffusion-weighted imaging [DWI], perfusion-weighted imaging [PWI], and SWI. The patients were administered 0.9 mg/kg rt-PA intravenous thrombolytic therapy (highest dosage: 90 mg) within 4.5 h of onset, and underwent re-inspection by SWI within 24 h of administration of thrombolytic therapy. Symptomatic cerebral hemorrhage (SCH) was defined as intracranial hemorrhage confirmed by CT or MRI within 24 h after administration of thrombolytic therapy, combined with an NIHSS score increase of four points or more. Microbleeding in SWI was defined by circular and quasi-circular low-intensity signals with a diameter of 2–5 mm, if no edema and brain calcification were detected. Uniform low-intensity signals may be present in the globus pallidus due to reasons other than calcification and vascular continuity in empty vessels, based on minimum-intensity projection. CT images could be performed to identify these effectively, and simultaneously exclude deposition of hemosiderin in the pia mater. CMB was categorized according to the level of bleeding: grade 0 (none), grade 1 (1–4 CMBs), grade 2 (5–8 CMBs), and grade 3 (>8 CMBs).

Based on the pre-treatment SWI sequence data, differences in low-intensity venous signals between the diseased and normal cerebral sides were observed. A total of five lateral ventricle levels above the basal ganglia (main distribution regions of intracranial deep veins) were collected, and MRIcroN software was used to estimate the total number of intravenous pixels on the infarction side and on the unaffected side after tracing and automatic segmentation of the shallow and deep veins. Vein asymmetry was defined when the number of venous pixels on the diseased side were $\geqslant$20% than that on the unaffected side. The patients were then divided into group A (with symmetrical veins) and group B (with asymmetrical veins).

The pretreatment and 1-h and 24-h posttreatment NIHSS scores, clinical efficacies, incidences of CMBs and SCH within 24 h after thrombolytic therapy, and 90-day mortalities of the two groups were observed and compared. The 90-day modified Rankin scale (mRS) scores were used to evaluate prognosis, with 0–1 and 2–5 points considered good and poor prognosis, respectively.

2.3. MRI parameters

A MAGNETOM Verio 3.0T MRI (Siemens) instrument was used in the current study, which involved fast spin echo (FSE), T1-(T1WI) and T2-weighted imaging (T2WI), diffusion weighted imaging (DWI), and magnetic resonance angiography (MRA). The parameters for T1WI were as follows: repetition time (TR) 2000 ms, echo time (TE) 9 ms, matrix 512×512, field-of-view [FOV] 230 mm $\times$ 230 mm, thickness 5 mm, layer interval 0.3 mm, layer number 19, and scanning time of 1 min 38 s. For T2WI, the parameters were: TR 6000 ms, TE 95 ms, matrix 512×512, FOV 230 mm $\times$ 230 mm, thickness 5 mm, layer interval 0.3 mm, layer number 19, and scanning time of 1 min 2 s. DWI used single excitation spin echo−echo planar imaging technology, with the following parameters: TR 5900 ms, TE 95 ms, FOV 230 mm $\times$ 220 mm, thickness 5 mm, matrix 512×512, and scanning time of 1 min 6 s. The MRA parameters included: TR 21 ms, TE 3.6 ms, matrix 512×512, FOV 230 mm $\times$ 230 mm, layer interval 0.7 mm, and a scanning time of 5 min 6 s.

Perfusion weighted imaging (PWI) used T2*-weighted dynamic susceptibility contrast (DSC) imaging. Each patient was first administered a rapid bolus injection of 0.2 mL/kg gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA) into the intravenous access in the antecubital fossa, by means of a high-pressure syringe, at a flow rate of 5 mL/s. The single excitation spin echo–echo planar sequence was then used for continuous scanning, 60 times. The contrast solution was injected at the beginning of the fourth scanning, followed by flushing with 15 mL normal saline (flow rate: 5.0 mL/s): transverse view T2WI (TR 1500 ms, TE 30 ms, FOV 230 mm $\times$ 220 mm, matrix 128×128, single excitation, flip angle 90°, 16 layers on each scanning plain [total of 960 images], and a scanning time of 1 min 38 s).

SWI used a standard 8-channel phased-array head coil, with the following main parameters: TR 27 ms, TE 20 ms, FOV 230 mm, thickness 1.5 mm, and scanning time of 2 min 35 s. The original images were acquired for automated reconstruction of SWIminP images.

2.4. Statistical analysis

PASW Statistics for Windows, version 18.0, was used to analyze clinical data. Normally distributed measurement data were