Official Title: Early neurological deterioration in recent small subcortical infarction：a multicenter prospective study

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Informed consent form and informed page of the First Affiliated Hospital of Zhengzhou University

research topic	Early neurological deterioration in recent small subcortical infarction: a multicenter prospective study.
Proponent	Department of Neurology, First Affiliated Hospital of Zhengzhou University
Name of research institution	First affiliated hospital of Zhengzhou university
Address of research institution	**No.1 Jianshe East Road, Erqi District, Zhengzhou City, Henan Province**
contact number	**0371-66862134**
Patient's initials	
Patient screening number	

Subjects must know

Dear subject:

We invite you to participate in this clinical study. Before you decide whether to participate in this research, it is important for you to know the purpose of this research and its impact on you in detail. Please read the following information carefully. If you feel it necessary, you can discuss with your relatives, friends and family doctors about your participation in this research. Once all your questions have been answered, you are satisfied with the explanation about this research, and you decide to participate, you will be asked to sign this informed consent form. Participating in this clinical trial is your voluntary behavior. You can agree to participate or disagree, and you can voluntarily withdraw from this clinical trial at any time.

The clinical study is "Early deterioration of neurological function in recent small subcortical infarction: a multi-center prospective study". This study was approved by the Scientific Research Department of the First Affiliated Hospital of Zhengzhou University, and has passed the audit of the Ethics Committee of the First Affiliated Hospital of Zhengzhou University, and agreed to carry out the clinical study.

1. Why do you want to participate in this research?

Recent small subcortical infarction (RSSI) is defined as a small deep infarction in the territory of a perforating artery with maximum axial diameters (MAD) of less than 20 mm. Although RSSI is generally considered to be of a relatively favorable prognosis, about 13.5% to 43% of RSSI patients experience early neurological deterioration (END) in the acute phase, which often bring adverse effects on long-term outcomes. Although a number of risk factors for END have been identified previously, however, the risk factors of END and the underlying etiological mechanism are still ambiguous, and also the relevant intervention measures lack sufficient evidences, which is a thorny problem that clinicians have to face. In this multicenter, large-sample prospective registry study, the primary objective is to investigate the natural course of END in patients with RSSI. Exploring the risk factors and potential mechanism of its development, and trying to establish a comprehensive predictive model for END that integrates multi-dimensional information including clinical symptom, demographic data, biochemical biomarker and image data, and so as to provide a valuable tool for clinical evaluation and early management. Secondary objective is to figure the long term outcome of the patients with RSSI and its risk factors.

2. How many people will participate in this research?

In this study, all districts and counties in the whole province were finally included in about 1000 cases of new subcortical infarction.

3. How long does it last to participate in this research?

This study will be followed up for 1 year.

4. What is the difference between this study and previous treatment methods? What are the advantages and disadvantages?

This project is a registered study, and whether you participate in this study or not will not affect your treatment plan.

5. How is this research conducted?

Source of patients: Prospective consecutive patients with acute RSSI from June 2022 to June 2024 in Henan province within 72 hours of onset.
Registration: This study plans to collect the current status, clinical features, diagnosis and treatment information of SI patients who visited the hospital within 72 hours of onset.
Prospective: From the time when the patient sees a doctor in the hospital, all information needs to be filled out prospectively (except the past history);
Continuity: Once the project is started, each center shall not stop itself before it is announced to be finished. At the same time, in order to ensure the continuity of data, each center needs to arrange special scientific research secretaries to continuously collect qualified inpatient clinical cases, so as to ensure that every inpatient who meets the admission criteria and does not meet the exclusion criteria receives continuous registration.

6. What do the subjects need to do in this study?

① Baseline information registration (during hospitalization)

A. Demography (including: age, sex, education, nationality, marriage/residence status, occupation)

B. Pre-hospital first aid (date of onset, first aid transport mode, hospital arrival, intravenous thrombolysis, endovascular treatment)

C. Past history/family history (smoking; Drinking; Hypertension; Diabetes; Dyslipidemia; Lifestyle; History of cerebrovascular disease; Heart disease; Acute infection; Other diseases; Family history)

D. Past medication: including whether the drug application is regular (antiplatelet therapy; Lipid-lowering treatment; Anticoagulant; Antihypertensive drugs; Hypoglycemic drugs; Other;)

E. previous disability (mRS);

F. Admission assessment: admission for physical examination;

G. preliminary diagnosis: cerebral infarction /TIA;

H. Evaluation of risk factors for admission (blood pressure: the average blood pressure within 24 hours after admission, other factors should be excluded)

I. Admission score: at the time of admission (mRS score; NIHSS score)

J. Laboratory examination: completed within 24 hours of admission (blood routine/biochemical/renal function), and collection of biological specimens.

② Cerebrovascular events during hospitalization

A. Ischemic stroke: Ischemic stroke is defined as the occurrence of the following two situations during hospitalization: 1. The occurrence of new symptoms or aggravation of the original symptoms (NIHSS score increased by 2 points or more than before), with symptoms lasting for more than 24 hours. 2. New symptoms or aggravation of original symptoms (NIHSS score increased by 4 points or more than before), symptoms lasting for less than 24 hours, and imaging confirmed (CT or MR) that new infarct or original infarct was enlarged. In both cases, fever, drug action and infection should be excluded. Besides, imaging (CT or MR) is required to exclude brain edema, hemorrhage and hemorrhagic transformation.

B. Transient ischemic attack: the neurological deficit caused by sudden focal cerebral or retinal ischemia caused by various reasons, and the duration of neurological deficit is less than 24 hours. Imaging examination (CT or MR) showed no evidence of new cerebral infarction.

C. Hemorrhagic stroke: Hemorrhagic stroke is defined as acute focal or whole brain or spinal cord neurological dysfunction caused by non-traumatic intracerebral hemorrhage, intraventricular hemorrhage and subarachnoid hemorrhage.

D. Intracerebral hemorrhage: Hemorrhage caused by rupture of blood vessels in brain parenchyma, confirmed by imaging (CT or MR). This mainly refers to non-traumatic cerebral hemorrhage, including primary and secondary cerebral hemorrhage.

E. subarachnoid hemorrhage: refers to the spontaneous subarachnoid hemorrhage caused by the rupture of intracranial blood vessels and confirmed by imaging (CT or MR).

F. Post-infarction hemorrhage transformation: any non-traumatic extravascular hemorrhage in the infarction focus of known ischemic stroke.

③ Cerebrovascular events during hospitalization

Treatment (antiplatelet/anticoagulation/lipid lowering/blood sugar lowering/blood pressure lowering/volume expansion/dehydration/anti-infection): including administration time and dosage;

Vascular related procedures and surgical procedures (carotid artery stenting/carotid endarterectomy/intracranial artery stenting/decompressive craniectomy)

Other KPIs: evaluation of swallowing function/deep vein thrombosis/rehabilitation training

④ Evaluation at discharge.

Final diagnosis: cerebral infarction (TOAST classification) transient ischemic attack.

Other diagnosis: hypertension; Abnormal blood sugar; Disorder of lipid metabolism; Heart disease; Respiratory diseases; Liver diseases; Urinary system diseases; Peripheral vascular diseases; Bleeding; epilepsy

⑤ Follow-up information (3 months)

MRS score; All-cause death, cardiovascular death, non-vascular death; Recurrence of stroke; Cardiovascular events; Systemic embolism events; Endovascular operation or surgery; Compliance of secondary preventive drugs; Control of risk factors.

7. After participating in this research, do you have the right to withdraw from it? When can I withdraw from the study? And how to settle or handle matters related to withdrawal?

Participation in this study is completely voluntary. You can refuse to participate in the study or withdraw from this study at any time during the study. It will not affect the doctor's treatment for you. If you decide to withdraw from this study, please contact your doctor in advance. In order to protect your safety, you may be asked to do some related checks.

8、What are the side effects or risks of joining this research? What will be the impact of overlapping with other treatment methods? What trial group may the patient be assigned to?

This study is a registered study, that is, recording your disease status, related risk factors, medication and examination results, which will not affect your treatment measures, so it will not bring you additional risks.

9、Besides participating in this study (or if not participating in this study), do the subjects have any other medical options? What are the alternative treatments outside this experiment?

This project is a registered study, and whether you participate in this study or not will not affect your treatment plan. You only need to receive routine clinical treatment, no research medication. All the examinations you receive are routine clinical examinations.

10. What if the subject or the subject's spouse is pregnant?

This project belongs to the registered study, and only carries out routine clinical examination, but the annual return visit will take up your time and need your cooperation to complete it, so as to better evaluate your health status.

1. What are the free medical treatment programs and other related subsidies that may be obtained during the trial?

During the research process, the research doctor will pay close attention to your physical condition, evaluate your neurological function related scores and quality of life scores for free, and make other clinical evaluations in time based on your physical condition.

If necessary, you can learn more about your illness from your image and blood test results obtained in this study.

12. What if the subject is damaged during the research? What are the treatments and financial compensations for injuries related to trials? And whether to buy insurance for the subjects, and what kind of insurance?

This study is a registered study, that is, recording your disease status, related risk factors, medication and examination results, which will not affect your treatment measures, so it will not bring you additional risks. This project belongs to the registered research, and only records your disease status, related risk factors, medication and examination results. No additional damage will occur if you participate in this research.

13、Do I have to pay an extra fee to participate in the study?

This study doesn't require you to spend extra money.

During hospitalization, the cost of clinical examination is not free of charge. If you combine the treatment and examination required for other diseases at the same time, it will not be covered for free.

14. Will you get timely information that may affect your continued participation in the research?

The information obtained from this study will be helpful to evaluate the etiology and prognosis of acute cerebral vascular occlusive stroke and formulate more effective treatment strategies. This will help you and other patients. If necessary, you can learn more about your illness from your image and blood test results obtained in this study.

15. According to relevant laws and regulations, the subjects' personal privacy should be kept fully confidential. Can the privacy be kept completely confidential in this experiment? What is the confidentiality of medical records? Who has the right to obtain the medical and personal information of the subjects participating in this study? How to deal with the obtained information?

We will make every effort to protect the privacy of your personal medical data within the scope permitted by law. In the project, your identity (such as your name and all information that can identify you) will be replaced by the project code, and your personal identity will not be disclosed in any public report of the results

of this research. The research data related to you will be kept in the hospital, and only researchers, research authorities and ethics committees are allowed to consult your medical records.

The first affiliated hospital of Zhengzhou University

informed consent and consent signature page

I have carefully read the early neurological deterioration of recent small subcortical infarction: the informed consent form of a multicenter prospective study. I have the opportunity to ask questions and all questions have been answered. I understand that taking part in this experiment is voluntary. I can choose not to take part in this experiment, or quit after informing the researcher at any time without being discriminated against or retaliated. My medical treatment and rights will not be affected by this. If I need other diagnosis/treatment, or I don't follow the trial plan, or there are other reasonable reasons, the researcher can terminate my participation in this clinical trial. I voluntarily agree to participate in this clinical trial, and I will receive a signed copy of the ″informed consent form″.

Please copy: **"I have read and understood this clinical trial, and volunteered to participate in this clinical trial".**

Subject name:

Subject's signature:

Subject ID number:

Tel:

Date:

(When the subject's informed consent ability is lacking or insufficient, add or replace the

Guardian's name:

Signature of guardian:

Guardian ID number:

Relationship with the subject:

Tel:

Date:

I have accurately informed the subjects of the informed consent form and answered their questions, and the subjects volunteered to participate in this clinical trial. And give it a copy of the signed informed consent form.

Name of study doctor:

Signature of research doctor:

Tel:

Date: