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Use of various CT imaging methods for diagnosis of acute ischemic cerebrovascular disease★

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Abstract

Thirty-four patients with cerebral infarction and 18 patients with transient ischemic attack were examined by multi-slice spiral CT scan, CT perfusion imaging, and CT angiography within 6 hours after onset. By CT perfusion imaging, 29 cases in the cerebral infarction group and 10 cases in the transient ischemic attack group presented with abnormal blood flow perfusion, which corresponded to the clinical symptoms. By CT angiography, various degrees of vascular stenosis could be detected in 41 patients, including 33 in the cerebral infarction group and eight in the transient ischemic attack group. The incidence of intracranial artery stenosis was higher than that of extracranial artery stenosis. The intracranial artery stenosis was located predominantly in the middle cerebral artery and carotid artery siphon, while the extracranial artery stenosis occurred mainly in the bifurcation of the common carotid artery and the opening of the vertebral artery. There were 34 cases (83%) with convict vascular stenosis and perfusion abnormalities, and five cases (45%) with perfusion abnormalities but without convict vascular stenosis. The incidence of cerebral infarction in patients with National Institutes of Health Stroke Scale scores ≥ 5 points during onset was significantly higher than that in patients with National Institutes of Health Stroke Scale scores < 5 points. These experimental findings indicate that the combined application of various CT imaging methods allows early diagnosis of acute ischemic cerebrovascular disease, which can comprehensively analyze the pathogenesis and severity of acute ischemic cerebrovascular disease at the morphological and functional levels.

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Key Words

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Research Highlights

(1) A combined application of various CT examinations, neurological deficit score, and location and severity of vascular stenosis allows evaluation of the cause and severity of ischemic cerebrovascular disease.
(2) A combined application of CT scan, CT perfusion imaging, and CT angiography provides rapid, comprehensive, and accurate diagnosis of ischemic cerebrovascular disease.

INTRODUCTION

Early diagnosis and treatment of acute ischemic cerebral vascular disease is an important topic in medical research. At present, CT perfusion imaging and digital subtraction angiography are frequently applied to evaluate hemodynamic changes and to visualize lesions in patients with acute cerebral vascular disease[1]. With the development of CT software and hardware technology, multi-slice spiral CT has become an important diagnostic method for ischemic cerebral stroke because of its low cost, high accuracy, and ease of operation[2]. However, CT perfusion imaging alone has some deficiencies in the diagnosis of acute ischemic cerebrovascular diseases[3]. In this study, we employed multi-slice spiral CT scan, CT perfusion imaging, and CT angiography as detection methods in a broader attempt to explore the application prospect of “one-stop” multi-slice spiral CT examination in the diagnosis of acute ischemic cerebrovascular disease.

RESULTS

Quantitative analysis of participants

Fifty-two patients with acute ischemic cerebrovascular disease were included in this study and were involved in the final analysis.

Baseline information

The 52 patients with acute ischemic cerebrovascular disease detected by clinical observation and brain CT findings were divided into cerebral infarction (n = 34) and transient ischemic attack (n = 18) groups. The baseline information of patients is shown in Table 1. There were no significant differences in the sex, age, body mass index, and time of onset between the two groups (P > 0.05).

Table 1 Baseline information of the 52 patients

Item	Cerebral infarction group	Transient ischemic attack group	χ^2	t	P
n	34	18			
Sex (M/F, n)	19/15	10/8	0.001		0.982
Age (year)	60.3±7.9	58.2±6.3		0.852	0.386
Body mass index (kg/m^2)	28.2±0.9	27.8±0.6		1.439	0.195
Time of onset (hour)	4.9±0.8	4.7±0.8		0.738	0.427

Measurement data are expressed as mean ± SD. There were no significant differences in the sex, age, body mass index, and time of onset between the two groups (P > 0.05). M: Male; F: female.

Multi-slice spiral CT scan results of cerebral infarction and transient ischemic attack patients

No patients in the two groups showed imaging abnormalities at the first CT scan. The included patients were rechecked by brain CT findings at 1–8 days after onset. Over this time the transient ischemic attack patients still had no abnormal imaging findings (Figure 1A), while cerebral infarction patients presented patchy hypodense lesions, with an unclear boundary, compression of the adjacent tissue, and a midline tissue shift to the contralateral side (Figure 2E).

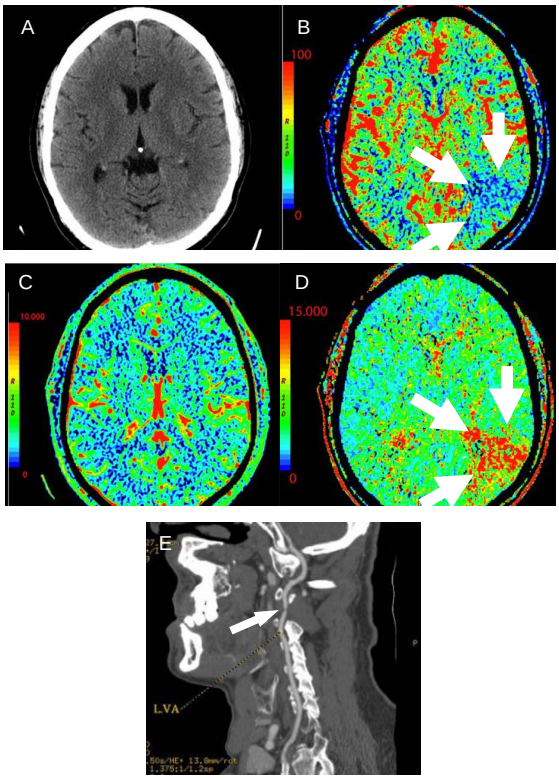

Figure 1 Imaging manifestations of cerebral vessels in transient ischemic attack patients.

(A) CT scan showed no signs of acute cerebral infarction. (B) CT perfusion imaging showed a low perfusion of cerebral blood flow in the posterior segment area of the left middle cerebral artery (arrows). (C) CT perfusion imaging showed no abnormal signs of cerebral blood volume. (D) CT perfusion imaging showed a low perfusion area of cerebral blood flow (arrows), and a prolonged mean transit time. (E) CT angiography revealed apparent stenosis in the left vertebral artery (LVA; arrow).

Hemodynamic parameter change of cerebral infarction and transient ischemic attack patients

CT perfusion imaging revealed blood flow perfusion abnormalities that corresponded to clinical symptoms in 29 cases in the cerebral infarction group and 10 cases in the transient ischemic attack group. Compared with the contralateral side, the cerebral blood flow and

cerebral blood volume of cerebral infarction patients were significantly decreased ($P < 0.05$), and the mean transit time and time to peak of contrast agent were significantly prolonged ($P < 0.05$; Figures 2A–C). By contrast, in the transient ischemic attack group only the mean transit time and time to peak of contrast agent were longer than that on the contralateral side ($P < 0.05$), and the time to peak was significantly shorter than that of cerebral infarction group ($P < 0.05$; Figures 1B–E, Table 2).

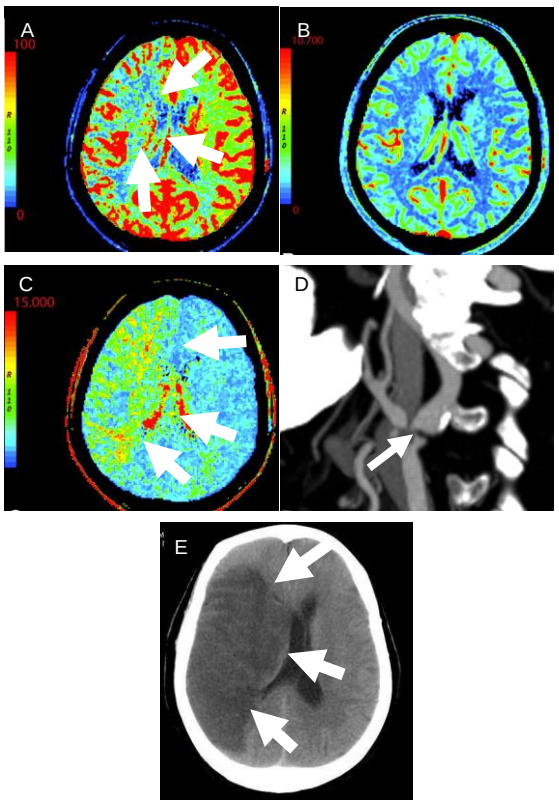

Figure 2 Imaging manifestations of cerebral vessels in cerebral infarction patients.

(A) CT perfusion imaging at admission showed low cerebral flow perfusion in the right middle cerebral artery and anterior artery (arrows). (B) CT perfusion imaging showed no abnormal signs of cerebral blood volume. (C) CT perfusion imaging showed that the mean transit time was prolonged (arrows). (D) CT angiography revealed apparent stenosis in the right internal carotid artery (arrow). (E) After 3 days, brain CT showed a large scale of cerebral infarction in the right temporal lobe (arrows).

Cerebral vascular stenosis of cerebral infarction and transient ischemic attack patients

CT angiography results showed that 41 cases presented with vascular stenosis, which corresponded to clinical symptoms, including 33 cases in the cerebral infarction group and eight cases in the transient ischemic attack group. Extracranial artery stenosis occurred in 11 cases (27%), intracranial artery stenosis in 21 cases (51%), and both intracranial and extracranial stenosis in nine cases (22%). There were 97 lesions exhibiting various degrees of stenosis or occlusion, including 39 extracranial stenosis lesions (40%) that consisted of 32 mild to moderate stenosis, six severe stenosis, and one occlusion segment, and another 58 intracranial stenosis lesions (60%) that consisted of 46 mild to moderate stenosis, nine severe stenosis, and three occlusion segments. Intracranial stenosis was mainly located in the middle cerebral artery (total 28 lesions; 29%) and the internal carotid artery siphon. Extracranial stenosis was mainly located in the carotid artery bifurcation (total 17 lesions, 18%) and in the vertebral artery openings. The stenosis location and severity of patients in two groups are shown in Table 3 and Figure 2D.

Table 2 Changes of hemodynamic parameters of cerebral infarction and transient ischemic attack patients as detected by CT perfusion imaging

Group	Cerebral blood flow (mL/min per 100 g)	Cerebral blood volume (mL/100 g)	Mean transit time (second)	Time to peak (second)
Lesion side in cerebral infarction group	26.9±4.0[a]	2.6±1.3[a]	6.0±1.2[a]	17.8±3.2[a]
Lesion side in transient ischemic attack group	54.2±3.7[b]	5.1±1.2[b]	5.5±2.4[a]	11.6±4.0[ab]
Contralateral control	55.0±5.5	5.5±1.4	3.5±0.8	8.8±2.6

Data are expressed as mean ± SD, there are 34 cases in cerebral infarction group and 18 cases in transient ischemia attach group. [a]$P < 0.05$, *vs*. contralateral control (paired *t*-test); [b]$P < 0.05$, *vs*. lesion side in cerebral infarction group (two sample *t*-test).

Correlation between neurological function score and patient's onset

The results of National Institutes of Health Stroke Scale scores showed that 31 patients were scored ≥ 5 points, including seven transient ischemia attack patients and 24 cerebral infarction patients, while 21 patients were scored < 5 points, including 11 transient ischemia attack patients and 10 cerebral infarction patients. The incidence rate of cerebral infarction in patients with National Institutes of Health Stroke Scale scores ≥ 5 points was significantly higher than that of National Institutes of Health Stroke Scale score < 5 points (24/31 *vs*. 10/21, respectively; 77% *vs*. 48%, respectively; $X^2 = 4.912$, $P < 0.05$). These data suggest that the severer the neurological deficits, the greater the susceptibility to cerebral infarction.

Table 3 Severity and location of intracranial and extracranial vascular stenosis (*n*) in cerebral infarction and transient ischemic attack patients by CT angiography

Group	Stenosis severity	Extracranial stenosis (*n* = 39)			Intracranial vascular stenosis (*n* = 58)						Total (*n* =97)
		CCA (*n* =17)	ICAE (*n* =10)	VAE (*n* =12)	ICAI (*n* =14)	MAC (*n* =28)	ACA (*n* =2)	VAI (*n* =2)	BA (*n* =3)	PCA (*n* =9)	
Transient ischemic attack (*n* = 18)	Mild to moderate	4	2	2	2	7	1	0	0	0	18
	Severe	0	0	0	0	2	0	0	1	0	3
	Occlusion	0	0	0	0	0	0	0	0	0	0
Cerebral infarction (*n* = 34)	Mild to moderate	11	5	8	10	15	1	0	2	8	60
	Severe	2	3	1	2	3	0	1	0	0	12
	Occlusion	0	0	1	0	1	0	1	0	1	4

CCA: Common carotid artery; ICAE: internal carotid artery extracranial segment; VAE: vertebral artery extracranial segment; ICAI: internal carotid artery intracranial segment; MCA: middle cerebral artery; ACA: Anterior cerebral artery; VAI: vertebral artery intracranial segment; BA: basilar artery; PCA: posterior cerebral artery.

Correlation between the positive rate of CT perfusion imaging and CT angiography vascular stenosis

By CT angiography, among the involved 52 patients there were 34 cases (83%) with convict vascular stenosis and perfusion abnormalities, and five cases (45%) with perfusion abnormalities but without convict vascular stenosis. Statistical analysis showed a significant difference between the two groups ($X^2 = 6.495$, $P < 0.05$; Table 4, Figures 2A–D), suggesting that the CT perfusion imaging positive rate of patients with stenotic vessels was significantly higher than that with no convict vascular stenosis.

Table 4 Correlation between the positive rates of CT perfusion imaging and CT angiography vascular stenosis (*n* = 52)

CT angiography	CT perfusion imaging (+) (*n*)	CT perfusion imaging (–) (*n*)	Positive rate (%)	X^2	*P*
Stenosis	34	7	83	6.495	0.019
No stenosis	5	6	45		

DISCUSSION

Cerebral ischemia may induce a series of pathological and physiological changes in local brain tissue that are closely related to hemodynamic changes. CT and MRI techniques can be used to detect lesions when sustained, severe, ischemia and hypoxia leads to infarction and morphological changes[4]. CT perfusion imaging provides a quantitative assessment for early cerebral infarction, which is characterized by low perfusion resulting from cerebral hemodynamic changes; at this time, cerebral blood flow velocity is altered and cerebral local micro-vessels have no compensatory dilatation. Early detection of the abnormal perfusion area and distinguishing between reversible and irreversible ischemic cerebral tissue are both important for the timely treatment of patients[5]. However, hemodynamic perfusion parameters of CT perfusion imaging have different degrees of sensitivity to ischemia. Nevertheless, mean transit time is regarded as a sensitive indicator for early cerebral reperfusion injury, and can reflect cerebral ischemic changes[6]. In this study, there was no difference in cerebral blood flow and cerebral blood volume between the affected side and the contralateral side of transient ischemic attack patients, while the mean transit time and time to peak were significantly increased at the affected side; all perfusion parameters were significantly different between the affected side of cerebral infarction patients and transient ischemic attack patients. Koenig *et al* [7] demonstrated that the prolonging of time to peak is the result of slow collateral circulation or blood flow. In addition, the time to peak scheme provides information about the size of the low perfusion area. Furthermore, the mean transient time is used to measure the cerebral perfusion pressure, with a prolonged mean transient time indicating a reduced cerebral perfusion pressure and impaired perfusion reserve. In the present study the mean transient time was extremely sensitive for distinguishing between normal brain tissue and ischemic brain tissue. However, it was not as sensitive as cerebral blood flow and cerebral blood volume for evaluation of the ischemic impairment and cerebral infarction risk. Perfusion parameters such as mean transient time, cerebral blood flow, and cerebral blood volume can determine early ischemia and infarction. A comprehensive analysis of these parameters provides reliable, objective hemodynamic information for clinical practice, and is important for the diagnosis and treatment of ischemic cerebrovascular disease.

In this study, the positive rate of cerebral infarction between the cerebral infarction group and the transient ischemic attack group was compared using the 5-point threshold National Institutes of Health Stroke Scale scores. We found that the neurological impairment was severer in the cerebral infarction group than in transient ischemic attack group. A higher National Institutes of Health Stroke Scale score indicates severer clinical symptoms and a higher risk for cerebral infarction. Therefore, a combined use of National Institutes of Health Stroke Scale score and CT perfusion parameters allows a comprehensive evaluation of the severity of acute ischemic cerebral vascular disease, and is important for determining the pathogenesis and potential treatment strategies. In addition, we found that transient ischemic attack patients may relieve their clinical symptoms over an intermittent period, although 10 patients still presented abnormal perfusion in CT perfusion imaging corresponding to clinical symptoms. The positive rate of CT perfusion imaging was higher in patients with convict vascular stenosis, suggesting that CT perfusion imaging is an effective indicator for abnormal hemodynamic perfusion in brain tissue of patients, and can provide cerebral blood flow hemodynamic functions based on the relationships between various parameters, as well as acquire blood hemodynamic information that is absent by conventional CT. In addition, CT perfusion imaging and CT angiography can directly display abnormalities in the corresponding arteries, the location and severity of vascular stenosis, and the collateral circulation, which are thus useful for performing individualized treatment plans.

CT perfusion imaging is remarkably specific and sensitive for the diagnosis of transient ischemic attack, and can detect an abnormal perfusion area at 40 minutes after onset, accounting for 91% of ≥ 10 mm lesions and 50% of < 10 mm lesions[8-9]. This technology has been increasingly used in clinical practice because of advantages such as high spatial resolution, simple scanning equipment, low cost, no need for radioactive isotopes and xenon, high accuracy, short imaging time, and detection of several blood flow parameters. There is also increasing attention to performing neuromonitoring prior to cerebral infarction, rather than immediately after cerebral infarction onset[10-11].

The pathogenesis of ischemic cerebrovascular disease has not been fully elucidated. However, there is strong evidence that both intracranial and extracranial artery stenosis and occlusion are the key factors contributing to ischemic cerebrovascular disease[12-13]. Nevertheless, the correlation between ischemic stroke and cerebral artery stenosis remains unclear, with no clear standard for evaluation[14]. The vascular events caused by unstable atherosclerotic plaque shedding in the intracranial and extracranial arteries can directly lead to the occurrence of ischemic stroke, and severe intracranial and extracranial vascular stenosis itself can also alter hemodynamic changes and induce acute cerebral ischemia or infarction[15]. The emergence of multi-slice spiral CT angiography scanning and post-processing technology has overcome the problems of evaluation of cerebral artery stenosis and occlusion, and is regarded as the preferred method for the detection of suspicious intracranial and extracranial artery stenosis or occlusion[16].

In this study, multi-slice spiral CT showed various degrees of feeding artery stenosis or interruption of blood flow in 29 out of 34 cerebral infarction patients detected by CT angiography. The detection rate of feeding artery abnormalities at ischemic foci immediately following cerebral infarction onset was 85% by CT angiography; the remaining five cerebral infarction patients showed no abnormalities by CT angiography, but small infarction volumes were observed, which may have been induced by tiny vascular lesions unable to be detected by CT resolution[17]. Intracranial vascular stenosis was mainly located in the middle cerebral artery and the internal carotid artery siphon, while extracranial stenosis was mainly detected in the carotid artery bifurcation and internal carotid arteries, which are consistent with atherosclerosis predilection sites.

“One-stop” multi-slice spiral CT is a simple, fast, accurate, economic, and easy popularized detection method, and has no obvious adverse reaction. This method can complete three scans within 10–15 minutes, and is particularly applicable to the emergency ward. Furthermore, one examination can simultaneously obtain conventional CT plain scan, enhanced scan, cerebral blood perfusion imaging, and cerebral vessel information. CT perfusion imaging displays abnormal perfusion areas that correspond with neurological impairment, while CT angiography displays the severity of artery stenosis. The combined application of these methods allows effective evaluation of blood flow and arterial stenosis, thus providing strong technical support for clinical treatment[18]. This method also helps to elucidate the location and nature of the ischemic event, the vascular status, and the area of reversible brain tissue of stroke patients, allowing a broader evaluation of therapeutic effect and prognosis assessment.

SUBJECTS AND METHODS

Design

A clinical observation focused on the neuroimaging.

Time and setting

Experiment was performed in January 2012 at the First Affiliated Hospital of Liaoning Medical University, China.

Subjects

A total of 52 patients with acute ischemic cerebrovascular disease were recruited from the First Affiliated Hospital of Liaoning Medical University, China between August 2009 and October 2011 (29 males and 23 females). The patient age range was 45–83 years (64 ± 13 years). All cases had stroke-associated clinical symptoms and signs, and a diagnosis consistent with the *Diagnostic Criteria for Cerebrovascular Disease* formulated by the Fourth National Conference of Chinese Medical Association in 1995[19], including: (1) acute onset; (2) recurrent episodes of vertigo or dizziness in the middle-aged or elderly, due to head position or posture changes; each episode lasts for a few minutes to 1 hour, and symptoms and signs disappear within 24 hours; (3) motion and sensation disorders; (4) vision loss in single or double eyes; and (5) excluding other diseases such as otogenic vertigo.

Inclusion criteria were: (1) all patients underwent CT scan within 6 hours after acute stroke onset, followed by CT perfusion imaging. CT angiography after intracranial hemorrhage was excluded and no responsible lesions were found. Patients and their relatives gave informed consent; (2) neurological impairment was evaluated by the National Institutes of Health Stroke Scale; and (3) there were 1–8 days duration between the first CT examination and follow-up CT examination.

Exclusion criteria were: (1) intracranial hemorrhage patients; (2) patients with hemorrhage disease, hemorrhagic diathesis, cardiac insufficiency, severe liver disease, hyperthyroidism, or hypothyroidism; and (3) pregnant patients.

The study was in accordance with the ethical requirements in *Declaration of Helsinki*.

Methods

"One-stop" multi-slice spiral CT scan

One-stop detection of CT scan, CT perfusion imaging, and CT angiography was performed using the GE Light speed 16 MSCT (Bethesda, MD, USA). Scanning parameters of CT scan were: starting at canthomeatal line, 120 kV voltage, 250 mA current, slice thickness 5 mm, layer space 5 mm, matrix 512 × 512, and field of view 23 cm. Scanning parameters of CT perfusion imaging were: the basal ganglia used as region of interest, "Toggling-table" technology, cine scanning mode[20], scan speed 1 layer/s, 80 kV voltage, 200 mA current, slice thickness 5 mm, time interval 0.5 second, scanning time 50 seconds, and delay time 8 seconds. A 40 mL of nonionic contrast agent iohexol (100 mL: 35 g iodine; Hokuriku Industry, Beijing, China) was injected (4.0 mL/s) using a high-pressure syringe *via* the elbow vein, and a synchronous dynamic scanning was performed when contrast agent injection began. At 10 minutes after CT perfusion imaging scan, a CT angiography scanning was performed at 120 kV voltage and 250 mA current; 100 mL of contrast agents were injected at 4 mL/s speed, with a delay of 18–23 seconds. The scanning ranged was from the head to the carotid artery.

Data processing

Data were processed on the ADW4.2 workstation (GE Medical System, Milwaukee, WI, USA) using the Perfusion 3.0 software package. The cerebral blood flow, cerebral blood volume, contrast agent mean transit time, and time to peak at the region of interest and the contralateral side were measured. Post-processing technology including multiple planar reconstruction, curved planar reconstruction, maximum intensity projection, and volume rendering, was applied to reconstruct and analyze the head and neck arteries and to measure the stenosis diameter in the carotid artery. The measuring level was perpendicular to the vascular major axis, and the diameter of the normal blood vessels at both ends of the stenosis vessels served as controls. According to the North American Symptomatic Carotid Endarterectomy Trial, the degree of stenosis was divided into four grades: I, mild stenosis (0–29%); II, moderate stenosis (30–69%); III, severe stenosis (70–99%); and IV, occlusion (100%)[21].

National Institutes of Health Stroke Scale scores

Prior to CT examination, patients were assessed with the National Institutes of Health Stroke Scale. Patients were not forced to train, such as repeatedly performing a task. Higher scores indicated more severe neurological impairment[22] (supplementary Table 1 online).

Statistical analysis

All data were analyzed using SPSS 11.5 software (SPSS, Chicago, IL, USA). Measurement data are expressed as mean ± SD, and statistical comparisons were performed using two-sample *t*-test of a paired design and a group

design. Count data were analyzed using the chi-square test. A *P* value less than 0.05 was regarded of significantly different.

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