Original research article

What influenced the lesion patterns and hemodynamic characteristics in patients with internal carotid artery stenosis? A retrospective study

Jinjie Liu [a,b,1,*], *Hong Wang* [a], *Meiyan Zhang* [b], *Xiaowen Sui* [b], *Furong Li* [b], *Zanhua Liu* [b], *Sibo Liu* [c], *Hongling Zhao* [b,*]

[a] *General Medical Ward No.2, Dalian Municipal Central Hospital, Dalian 116000, China*
[b] *Department of Neurology, TCD Team, Dalian Municipal Central Hospital, Dalian 116000, China*
[c] *Surgical Intensive Care Unit (SICU), Dalian Municipal Central Hospital, Dalian 116000, China*

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ABSTRACT

Objectives: This study aimed to explore the dynamic changes of lesion patterns and hemodynamic characteristics in patients with internal carotid artery stenosis (ICAS).
Patients and methods: Patients who had suffered an acute ischemic stroke in the distribution of ipsilateral ICAS were included. Computed tomography (CT) and transcranial doppler ultrasound (TCD) were conducted to evaluate the degree of ICAS and the hemodynamic characteristics of the intracranial and extracranial arteries.
Result: A total of 424 patients were included in the study. With the aggravation of ICAS, blood velocity in ipsilateral ICA was increased, while blood flow in the ipsilateral middle cerebral artery (MCA) was decreased. In the same degree of ICAS, patients with opened communicating arteries showed relatively higher blood perfusion in MCA compared with those without communicating arteries. In the average stage of ICAS, small lesions ($D = 0$–1.5 cm), middle lesions (1.5 cm $< D \leq 3.0$ cm) and large lesions ($D > 3.0$ cm) commonly existed. The number of small and large lesions significantly increased when the blood flow of ipsilateral MCA decreased. In the same degree of stenosis, the number of small lesions and large lesions, and the total area of all lesions, evidently increased with the decrease of ipsilateral MCA blood velocity.
Conclusion: Hypoperfusion is an independent risk factor for ischemic lesions in patients with ICAS. Whether or not the communicating arteries are open influences the blood flow of the intracranial arteries. TCD was a convenient and rapid tool to assess intracranial perfusion and vascular compensatory status.

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* *Corresponding authors at*: Department of Neurology and General Medical Ward, TCD Team, Dalian Municipal Central Hospital, Number 826, XiNan Road, Dalian City, Liaoning Province 116000, China.
   E-mail addresses: liujinjie4581583@126.com, jinjieliu4581583@126.com (J. Liu), zhaohongling2000@126.com (H. Zhao).
 1 Joint first author: Jinjie Liu.

1.   Introduction

Ischemic stroke is one of the most common causes of acquired disability, dementia and death, with significant psychological and economic burden [1]. Two basic mechanisms are proposed to account for ischemic events in carotid artery occlusive disease: (1) emboli from carotid plaque and (2) hypoperfusion in distal arteries [2–4]. However, most of these studies mainly focused on severe stenosis (≥70%) [3–8]. Dynamic change of lesion characteristics and artery hemodynamic characteristics in all degrees of ICAS has not been demonstrated.

The hemodynamic character of the intracranial cerebral hemisphere depends predominantly on the degree of ICAS [9,10]. However, many other factors, such as individual difference, openness of communicating arteries, and forma-tion of new vessels, might also influence the blood velocity of intracranial arteries. TCD is a widely used, noninvasive method for the evaluation of hemodynamics in extracranial arteries and intracranial arteries [8]. Combined with CT angiography (CTA), TCD could more accurately reflect the blood flow of the intracranial arteries. Thus, in this study, we included patients who underwent CTA and TCD to evaluate the blood perfusion in distal cerebral arteries and communi-cating arteries, rather than the degree of ICAS itself.

Patients tend to go to the hospital mostly because of symptomatic lesions. However, from CT scanning or magnetic resonance imaging (MRI), we know that many patients have suffered asymptomatic or mild symptomatic lesions before they go to a doctor. These lesions may influence their cognitive function or other latent functions [11,12]. Therefore, we also aimed to collect all lesions detected by past medical histories, CT scanning, MRI and diffusion-weighted imaging (DWI) to get a more detailed description of these lesions.

2.   Patients and methods

2.1.   Inclusion and exclusion criteria

We retrospectively reviewed 2801 patients who had suffered acute cerebral ischemia confirmed by DWI scanning from 2010 to 2016. Inclusion criteria: patients with unilateral ICAS (0%–99%) or complete occlusion of internal carotid artery (ICA) (100%), as confirmed by CTA. Exclusion criteria: patients with other brain pathology (such as tumors, idiopathic or hereditary artery diseases, or multiple sclerosis), bilateral ICAS, carotid endarterectomy, internal carotid artery stent implantation, intracranial artery stenosis, potential cardiac sources of embolism, heart failure, nonatherosclerotic vasculopathies, and hematologic diseases. Patients were divided into 4 groups according to the degree of ICAS (0%–49%, 50%–69%, 70%–99%, and 100%). This study was approved by the ethics committee of the Dalian Central Municipal Hospital. Written or tele-phoned informed consent was obtained from all patients.

2.2.   Data collection

A total of 424 patients were included in the study. All patients had undergone both DWI examination (Philips Achieva 3.0 T magnetic resonance system, Philips Healthcare, USA, 5 mm-thick slices) and CT scanning (Discovery HD750, GE Medical Systems, USA, 5 mm-thick slices) to find the responsible foci of acute stroke. The number of ischemic lesions (lesions that were not distributed in the same branch artery or were isolated from each other were counted as two or more) and the diameter of lesions were analyzed by two professional investigators blinded to both clinical and image data. Ischemic lesions were divided into small lesions (≤1.5 cm in diameter, according to the Adams classification [13]), middle lesions (1.5–3.0 cm in diameter), and large area infarcts (>3.0 cm). The area of every lesion was estimated as (major axis multiply by minor axis)/2 cm^2. The total area of all lesions was also calculated to present the degree of brain damage. Lesions were also divided into acute lesions and old lesions as well as symptomatic lesions and asymptomatic lesions.

CTA was conducted by contrast-enhanced, high-speed CT (Discovery HD750, GE Medical Systems, USA). The image of CTA was evaluated by professional investigators blinded to clinical and image data. The degree of stenosis was evaluated as mild stenosis (0%–49%), moderate stenosis (50%–69%), severe stenosis (70%–99%) and complete occlusion (100%) according to the North American Symptomatic Carotid Endarterectomy Trial method [14]. From the image of CTA, we also assessed the opening of the anterior communicating artery or posterior communicating artery.

Among the 424 patients, 374 had undergone a detailed TCD examination to evaluate the hemodynamic status of the bilateral intracarotid artery, bilateral MCA, bilateral anterior cerebral artery (ACA), Willis circle, and supratrochlear artery using the GE Vivid 3 Ultrasound system (GE Medical Systems, USA), equipped with a 2 and 4-MHz probe. Sixty patients failed to receive a complete result because of an unsatisfactory transtemporal and transorbital window. The M1 segment of MCA was detected through the transtemporal window, while the A1 segment of ACA was measured through the transorbital or transtemporal window. An opened, closed or congenital defective Willis circle was evaluated through the blood direction of the ipsilateral A1 segment of ACA, blood velocity of the contralateral A1 segment of ACA, blood velocity of the P1 segment and P2 segment of the bilateral posterior cerebral artery, and the pressing test of the carotid artery. Blood direction of the supratrochlear artery was also examined to estimate the openness of the ophthalmic artery and traffic between the internal and external carotid artery. We calculat-ed the difference of bilateral MCA blood velocity to evaluate the degree of hypoperfusion in ipsilateral intracranial arteries.

2.3.   Assessment of baseline characteristics

Baseline data including age, sex, diabetes, hypertension, hyperlipemia, and smoking history were collected to analyze the risk factors of ICAS.

2.4.   Statistical analyses

Statistical analyses were performed with IBM SPSS Statistics version 20 (SPSS Inc., Chicago, Illinois). Values were expressed as the means ± SD. Analysis of variance was used to compare continuous variables between groups. Correlation analysis was

used to check the relationship between the total area of lesions and the difference in the value of bilateral MCA blood velocity.

3. Result

3.1. Baseline analysis

Baseline data are shown in Table 1. This study involved 424 patients, and the mean age was 66.19 years old (range 31–90 y); 84% were males (Table 1). The ratio of patients with hypertension, diabetes mellitus, hyperlipemia, hyperhomocysteinemia and smoking seemed to be higher in severe ICAS (≥50%) compared with mild ICAS (<50%), but the difference was not significant.

3.2. The relationship between the degree of ICAS and lesion patterns

Small lesions ($D = 0$–1.5 cm, Fig. 1a) existed in patients of all groups. The average number of small lesions did not increase with the aggravation of ICAS overall (Fig. 1a, $P = 0.455$), but did increase with the aggravation of ICAS in patients without large-area infarcts (Fig. 1d, $P = 0.041$). These small lesions were mainly distributed in the basal ganglia and periventricular region and then the cortex (Fig. 1e). The average number of middle lesions ($D = 1.5$–3.0 cm) increased nonsignificantly in patients with ICAS ≥ 70% compared to those with ICAS < 70% (Fig. 1b, $P = 0.089$). The average number of large-area lesions ($D > 0.3$ cm) significantly increased with the aggravation of ICAS (Fig. 1c, $P < 0.01$). The number of old symptomatic lesions (Fig. 1f, $P < 0.001$), old asymptomatic lesions (Fig. 1f, $P < 0.001$), and the history rate of transient ischemic attack (TIA) (Fig. 1f, $P = 0.037$) significantly increased with the aggravation of ICAS (>50%) (Fig. 1f).

3.3. The relationship between lesion patterns and bilateral hypodynamic characteristics of MCA

With the increase of bilateral MCA blood velocity difference, the number of small lesions (Fig. 2a, $P < 0.05$) and large-area lesions ($P < 0.05$) showed a significant increase in the same

Characteristics	0%–49% ($n = 130$)	50%–69% ($n = 72$)	70%–99% ($n = 118$)	100% ($n = 104$)	P (between groups)
Age, y	62.31 ± 9.89	66.12 ± 9.47	66.64 ± 9.56	66.29 ± 10.87	$P = 0.59$
Male/Female	110/20	66/6	108/10	100/4	$P = 0.76$
HYN (yes/no)	86/44	56/16	86/32	74/30	$P = 0.12$
DM (yes/no)	38/92	12/60	40/78	34/70	$P = 0.12$
HLP (yes/no)	68/62	37/35	64/54	57/47	$P = 0.91$
HHCY (yes/no)	24/106	18/53	28/90	18/86	$P = 0.33$
Smoking (yes/no)	62/68	34/38	60/58	57/47	$P = 0.69$

Table 1 – Baseline characteristics of study patients (total number: $n = 424$).

HYN: hypertension; DM: diabetes mellitus; HLP: hyperlipemia; ACI: acute cerebral infarction; HHCY: hyperhomocysteinemia.
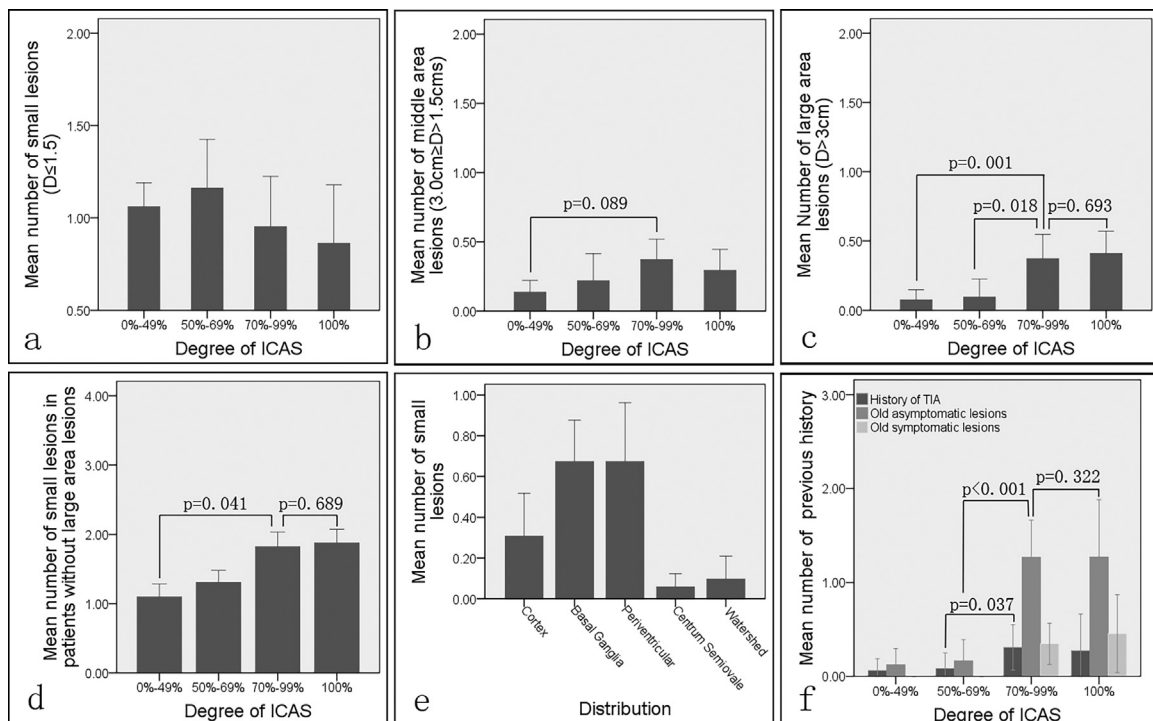

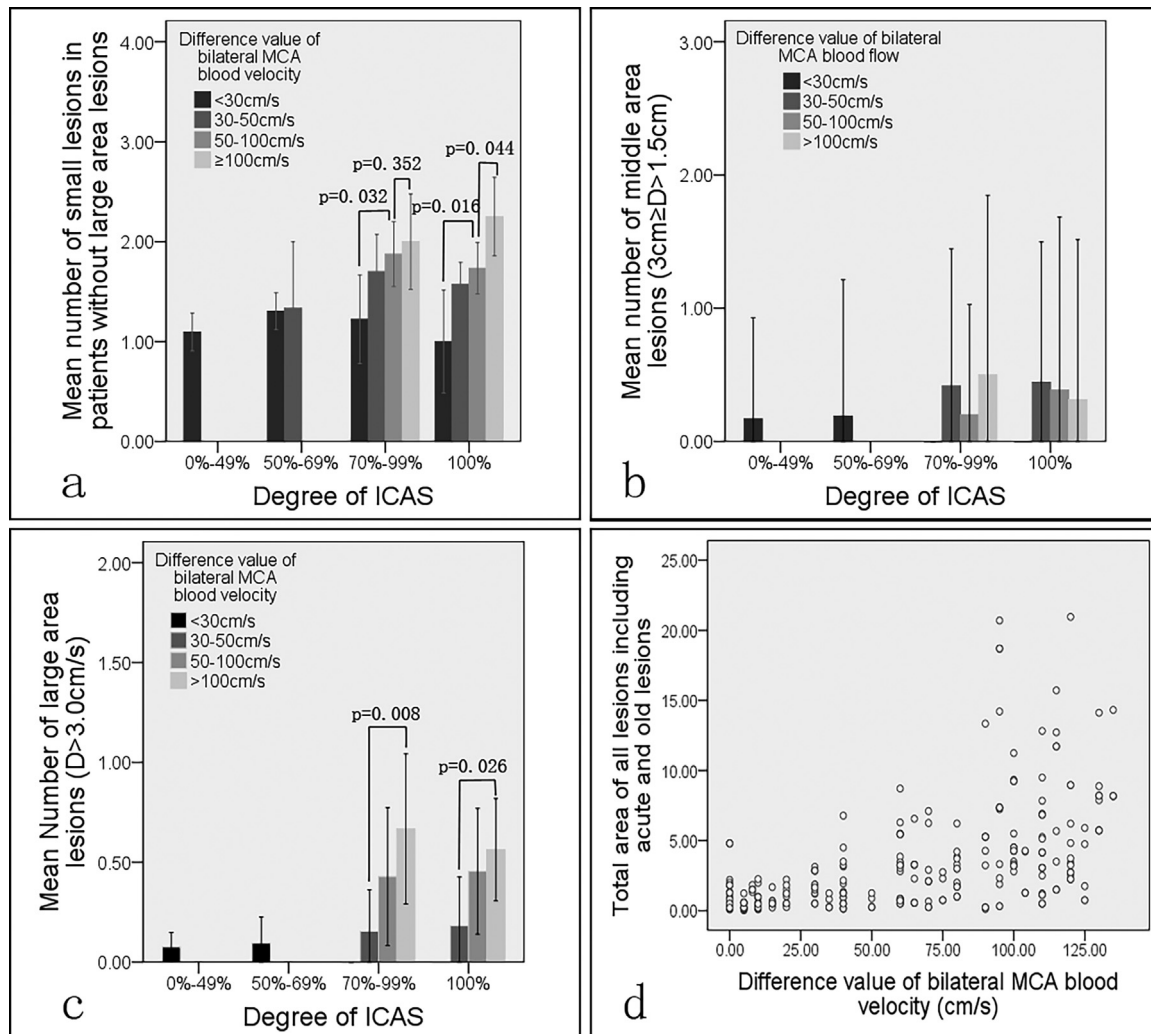Fig. 1 – The relation between the stage of ICAS and lesion patterns.

Fig. 2 – The relation between lesion patterns and bilateral hypodynamic characters of MCA. *p: comparison between patients with and without open of ACOA in the same degree of ICAS.

degree of ICAS (≥70%). The number of middle lesions was not increased with the aggravation of bilateral MCA blood velocity difference in the same degree of ICAS (Fig. 2b). The total area of all lesions was positively correlated with the aggravation of bilateral MCA blood velocity difference (Fig. 1d, $P < 0.001$). (The direction and blood flow of ACA were very complex when the origin of ACA was anomalous or when communicating arteries were opened, so only the blood flow of MCA is presented as it better reflects the blood flow of intracranial arteries.)

3.4. Hypodynamic characteristics in every stage of ICAS

With the aggravation of ICAS, the peak systolic velocity (PSV) of ipsilateral ICA increased significantly (Fig. 3a, $P < 0.001$). No blood flow was detected in patients with completely occluded ICA (Fig. 3a). When the anterior communicating artery aneurysm (ACOA) was open, the PSV of contralateral ICA increased correspondingly, especially in the complete occlusion group (Fig. 3b, $P = 0.028$). PSV of ipsilateral MCA evidently decreased in patients with severe ICAS (≥50%). The difference in the value of PSV between bilateral MCA showed a significant

increase with the aggravation of ICAS (Fig. 3c, $P < 0.001$). The openness of communicating branches (one or more communicating arteries) significantly improved the blood flow of ipsilateral MCA (Fig. 3c, $P < 0.001$).

4. Discussion

Embolism and low blood flow are the two primary mechanisms of cerebral infarction. Although previous studies have demonstrated some characteristics of lesion patterns in severe ICAS, the relationship between detailed characteristics and distal artery hemodynamics in all stages of ICAS has not been demonstrated. It is necessary to further explore which mechanisms played important roles during the attack of these lesions to make the best protocols for further treatment.

Consistent with recent studies [15,16], multiple lesions were detected in this study. Small lesions ($D \leq 1.5$ cm) existed in patients with all degrees of ICAS. These lesions primarily included subcortical ischemic infarcts distributed in the basal ganglia and periventricular regions. A second distribution of
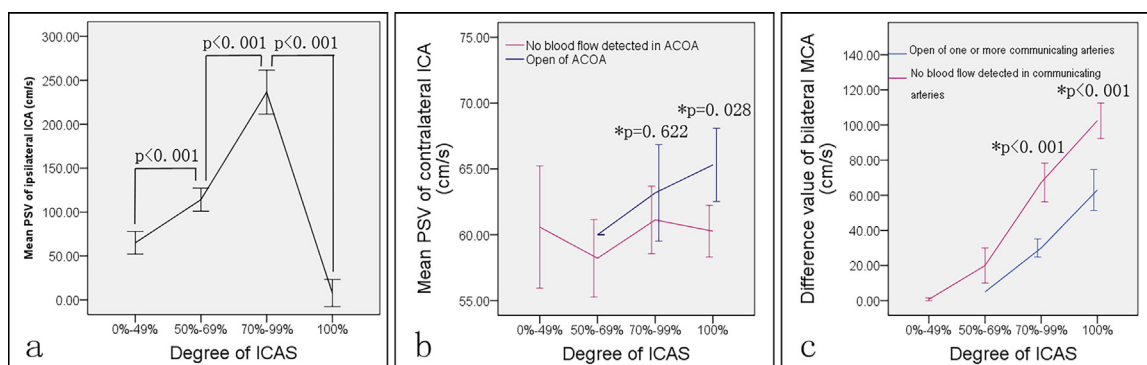
Fig. 3 – Hypodynamic characters in every stage of ICAS.

these small lesions was found in the cortex. This distribution may be because the perforating artery was more easily involved in atherosclerosis and was more easily influenced by hypoperfusion compared to the cortical arteries. This possibility is consistent with the result of several recent studies that show that cortical arteries possess higher flow velocity and collateral circulation than perforating arteries, especially in the periventricular region [17,18]. In this study, the average number of small lesions did not increase with aggravation of ICAS but increased in patients without large-area infarcts, indicating that aggravation of ICAS contributed to the occurrence and development of small lesions, and these small lesions were probably covered by large-area infarcts in patients with large-area lesions. Unexpectedly, the number of middle lesions showed nonsignificant change with the aggravation of ICAS. The number of large infarcts ($D > 3.0$ cm) increased significantly with the aggravation of ICAS. In the same degree of ICAS, the number of small lesions and large lesions increased with the aggravation of bilateral MCA blood velocity difference, especially when the difference of the bilateral MCA blood velocity exceeded 50 cm/s. Correlation analysis showed that the total area of all lesions detected by DWI and CT scanning was positively correlated with bilateral MCA blood velocity difference. These results indicated that hypoperfusion in ipsilateral MCA was a primary risk factor for small lesions, large infarcts, and the severity of brain damage. This finding was consistent with a recent study showing that MCA wave forms seemed to be an independent risk factor for cerebral ischemia in carotid stenosis [19].

With the aggravation of ICAS, the history of TIA and the number of old asymptomatic lesions showed significant increases in patients with ICAS ≥ 70% compared to those with ICAS < 70%. The number of old symptomatic lesions also increased with the aggravation of ICAS, but without significant difference. These lesions should also raise our attention, as they might influence patients' cognitive function or other latent functions [11,12].

To further explore the cause of hemodynamic change in ipsilateral MCA, we analyzed the data of CTA and TCD. The results showed that the decrease of PSV in ipsilateral MCA started in the 50%–69% ICAS group, and very few started from the <50% ICAS group. The difference in bilateral MCA blood velocity was correspondingly increased. In the same degree of ICAS, whether or not the communicating arteries are open is

an independent factor of MCA blood velocity. Once the communicating artery (which in this study included the Willis circle and communicating artery between the internal and external carotid arteries) opened, the difference in the bilateral MCA blood velocity was significantly decreased compared to those with unopened communicating arteries. The blood velocity of the compensatory artery, such as contralateral ICA, also increased with the openness of the ACOA. Thus, compared with the degree of ICAS and the area of acute infarcts, direct measurement of intracranial artery blood flow using TCD was more accurate to assess cerebral perfusion.

There are also limitations to our study: patients involved in this study only accepted CUS to detect the carotid plaques, and these data were not strong enough to evaluate the plaque characteristics. Further studies are still needed.

5.   Conclusion

Hypoperfusion resulting from ICAS was an independent risk factor for ischemic brain injury, especially for small infarcts and large-area infarcts. Whether or not the communicating arteries were open was an important issue influencing the blood flow of intracranial arteries in the same degree of ICAS. TCD was a convenient and rapid tool to assess intracranial perfusion and vascular compensatory status.

Conflict of interest

None declared.

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