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# Evaluation of Cranial and Cervical Arteries and Brain Tissue in Transient Ischemic Attack Patients with Magnetic Resonance Angiography and Diffusion-Weighted Imaging

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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**Background:** Magnetic resonance angiography (MRA) and diffusion-weighted imaging (DWI) have been widely used in the prediction of ischemic stroke; however, the differences of the 2 methods in detection the artery lesion differences between transient ischemic attack (TIA) and infarction patients have been long neglected. We performed the present study to investigate the differences between vessel characteristics detected by MRA and DWI in acute stroke and TIA patients.

**Material/Methods:** We classified 110 subjects into 2 groups and all the patients underwent both MRA and DWI. The degree of stenosis of cranial and cervical arteries, the distribution of the stenosis, the development and changes of the vessels, and the DWI scanning results of the brain tissue were all analyzed.

**Results:** We detected a significant difference in the number and the degree of stenosis of cranial and cervical arteries among the 3 groups ($P$=0.006). Compared with health controls, patients with TIA and cerebral infraction had much more severe stenosis and occlusive arteries ($P$<0.05). However, no significant difference was detected between TIA and cerebral infraction patients ($P$=0.148). Moreover, a higher rate of unilateral vertebral artery dysplasia was found in the vertebrobasilar TIA patients. Higher lesion signals were also observed by DWI in TIA patients of internal carotid artery system (4/8, 50%).

**Conclusions:** Vessel characteristics were not significantly different between TIA and infarction patients. Unilateral vertebral artery hypoplasia was a predisposing factor for vertebrobasilar TIA and ischemic focus in DWI detection was always caused by severe artery lesions.

**MeSH Keywords:** **Carotid Artery Diseases • Ischemic Attack, Transient • Magnetic Resonance Angiography**

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## Background

Transient ischemic attack (TIA) has long time been one of the most important risk factors for severe ischemic stroke, the incidence of which is dramatically high during the early stage of ischemic stroke [1–3]. Thus, advanced evaluation and management of TIA is imperative. With the development of new neuroimaging modalities, such as CTA, MRA, and DSA, increasing imaging records on TIA can be found, especially with the application of MRA, which can be used to improve the determination of patients with high risk of having recurrent stroke or TIA [4]. Application of neuroimaging modalities have revealed that stenosis or occlusion of a large proximal intracranial or extracranial symptomatic artery were significantly associated with recurrent stroke/TIA [4–8]. Most previous studies concentrated on the imaging results of brain tissues and vascular lesions, and the degree of artery stenosis and plaques, but few researchers have paid attention to the difference of vascular characteristics between TIA and infarction patients. A hypoplastic vertebrobasilar system can lead to posterior circulation ischemia [9–11]. The mechanism underlying occurrence of TIA in vertebral artery lesions, such as hypoplasia should be studied. In the current study, we present a heuristic model of determination of TIA patients by utilizing MRA, CE-MRA, and DWI. The contributing factors of TIA attack are explained in terms of the entire circulatory system.

## Material and Methods

### Patients

Thirty-four healthy subjects (18 males and 16 females, average age 55.24±13.84) with no history of hypertension, hyperlipoidemia, diabetes mellitus, heart or cerebrovascular disease, or abnormal CT/MRI results were randomly selected as the control group (Group A) in the present study. Forty TIA patients (30 males and 16 females, average age 60.53±10.39) were enrolled from September 2009 to August 2012 in the Rizhao City People's Hospital (Group B). The TIA patients were diagnosed based on the criteria of Easton et al. [12] and had transient ischemic symptoms with a mean attack time of 0.932±0.665 h (range, 1 min to 9 h). Eight patients in Group B had TIA of the internal carotid artery (ICA) system and 32 patients had TIA of the vertebral artery system. Group C consisted of 36 cerebral infarction patients (21 males and 15 females, average age 56.58±8.21). Patients were diagnosed as having cerebral infarction when infarct size was larger than 2 cm$^2$ as illustrated by CT or MRI. There was no significant difference in age or sex between the 3 groups ($\chi^2$=4.267, P=0.118). The project was approved by the Rizhao City People's Hospital. The ethics committee of Rizhao City People's Hospital approved the relating screening, inspection, and data collection of the patients, and all subjects signed a written informed consent form. All works were undertaken following the provisions of the Declaration of Helsinki.

### MRA and DWI detection

MRA and DWI detection was conducted on all subjects using a 1.5-T MR scanner (Twin-Speed Infinity with Excite I, GE, USA) following standard procedure: intracranial 3D TOF (time of flight) (TR/TE=32/3.3 ms, FOV=18×18 cm, flip angle=20°, section thickness=1.5 mm, matrix=288×128, band width=15.6 kHz, total acquisition time=5 min) and a Cervical 3D CE-MRA (TR/TE=6 ms/minimum, FOV=24–28 cm, flip angle=45°, section thickness=1.8 mm, slab thickness=65 mm, matrix=256×256, total acquisition time=55 s, from aorta to circle of Willis) with intravenous administration of Gd-DTPA (2 mL/s of 0.1 mmol/Kg Gd, 20 mL saline flash). DWI was also performed using 3 sensitive gradients for brain tissue (TR/TE=10000/107 ms, matrix=128×128, FOV =24×24cm, section thickness=6 mm with a gap of 1.5 mm, b value=0 s/mm$^2$ and 1000 s/mm$^2$, acquisition time=40 s). The head entered first and the patient was in supine position. MRA range was from the aortic arch to top of skull, and DWI was from the skull base to top of skull. Tortuous lesion of artery was also considered as a factor affecting blood flow. The inner diameter of vertebral artery was measured at the level between C6 and C2. Vertebral artery hypoplasia (VAH) was defined as that the diameter of vertebral artery (VA) was less than 2–3 mm by 3D TOF MRA [13,14]. All patients were evaluated by the same 2 senior vascular radiology physicians.

### Statistical analysis

According to the standard of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) [15], lesions were classified as mild (0–29%), moderate (30–69%), severe (70–99%), and occlusion (100%). Arterial stenosis was graded by comparing the diameter of the maximally stenosed artery with the diameter of the more proximal normal segment of the same vessel [1,3]. All data are expressed as mean ±SD. Least significant difference (LSD) and chi-square analyses were performed with a significant level of 0.05 using SPSS version 16.0 (IBM, Armonk, NY, USA).

## Results

### The stenosis degree and lesion distribution

Both observers came to agreement in interpreting 3D TOF, DWI, and CE-MRA images for more than 97% of patients. If there was any disagreement between the 2 readers, the results were evaluated in a joint session. The number and degree of stenoses of cranial and cervical arteries are provided in Table





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**Table 1.** The number and degree of stenosis of cranial and cervical arteries.

| Group | Degree of stenosis | | | | Total |
|---|---|---|---|---|---|
| | Tortuosity | Mild | Moderate | Severe and occlusion | |
| Group A | 9 | 4 | 2 | 1 | 16 |
| Group B | 12 | 21 | 14 | 29 | 76 |
| Group C | 17 | 12 | 21 | 23 | 73 |
| Total | 38 | 37 | 37 | 53 | 165 |

**Table 2.** The results of maldevelopment of vertebral artery in group A and TIA of internal carotid artery (ICA) system.

| Group | Maldevelopment | Normal development | Total |
|---|---|---|---|
| Control A | 6 | 28 | 34 |
| TIA of internal carotid artery (ICA) system | 13 | 19 | 32 |
| Total | 19 | 47 | 66 |

1. Seventy-six arteries in 35 TIA patients (87.5%) had different severities of artery tortuosity and stenosis, of which 43 affected arteries (56.58%) were intracranial lesions, 24 (31.58%) were extracranial lesions, and 9 (11.84%) were extracranial-intracranial lesions. The number of the lesions in Group A was significantly less than in Group B and Group C. The major types of lesions were tortuosity and mild stenosis (16 arteries), which were common in the middle-aged population. Severe stenoses and occlusions were more frequently in Group B and Group C. Chi-square test showed that the difference between the 2 groups was significant ($\chi^2$=18.02, *P*=0.006). After $\chi^2$ partition, there was significant difference between the 3 groups ($\chi^2$=13.524, *P*=0.004; $\chi^2$=10.407, *P*=0.015) but no significant difference was detected between Group B and Group C ($\chi^2$=5.351, *P*=0.148). Twenty-one brain infarction patients were followed up; we found there were 13 patients (61.9%) had suffered from transient ischemia symptom in the last 2 years. Multiple artery lesions were more common in Group B and Group C compared with Group A ($\chi^2$=25.921, *P*<0.001; $\chi^2$=29.179, *P*<0.001), but no significant difference was found between Group B and Group C ($\chi^2$=1.194, *P*=0.755).

### Maldevelopment of vertebral artery

The 8 patients with TIA of the internal carotid artery (ICA) system had no maldevelopment of the vertebral artery but 13 patients with TIA of the vertebral artery system (40.63%) were found to have unilateral maldevelopment. Moreover, 6 cases (17.65%) in healthy controls were found to have maldevelopment of the vertebral artery (Table 2). The HVAs had a mean inner diameter of 1.72±0.89 mm and the mean diameter of the opposite side vertebral arteries was 3.90±0. 84 mm. Arthrosclerosis was common in the HVA patients in Group B, characterized by low signal intensity, irregularity of the artery wall, stenosis, and occlusion. The opposite side always showed dilatation of the lumen and tortuosity, but 6 (46.15%) of them had focal stenosis (Figure 1).

### The results of DWI

Eight patients in Group B had high signal intensity in DWI images, 4 of which were attacked by TIA of the ICA system. The focus was 1–2 cm in area, most of them were solitary but a few were multiple. One had focus in the brain stem, but no obvious lesion was found in the VA system. The others were consistent with the corresponding artery lesions. In the 8 patients, 12 were found to have severe stenosis and occlusion. Compared with the 32 patients (17 arteries) who had no high DWI signal intensity, it was significantly different ($\chi^2$=8.869, *P*=0.003). One patient with TIA of the ICA system showed large area of abnormal signal intensity on apparent diffusion coefficient (ADC) image in the right temporal and occipital lobe (Figure 2.). The ADC value was 27.26% lower than in the contralateral area. However, no abnormal ADC value was found in other patients.

## Discussion

### The degree and distribution of stenosis in TIA patients

It is reported that more than 90% TIA patients had lesions in brain-feeding arteries, which was confirmed by our study (87.5%). However, 31.58% of TIA patients in our study had



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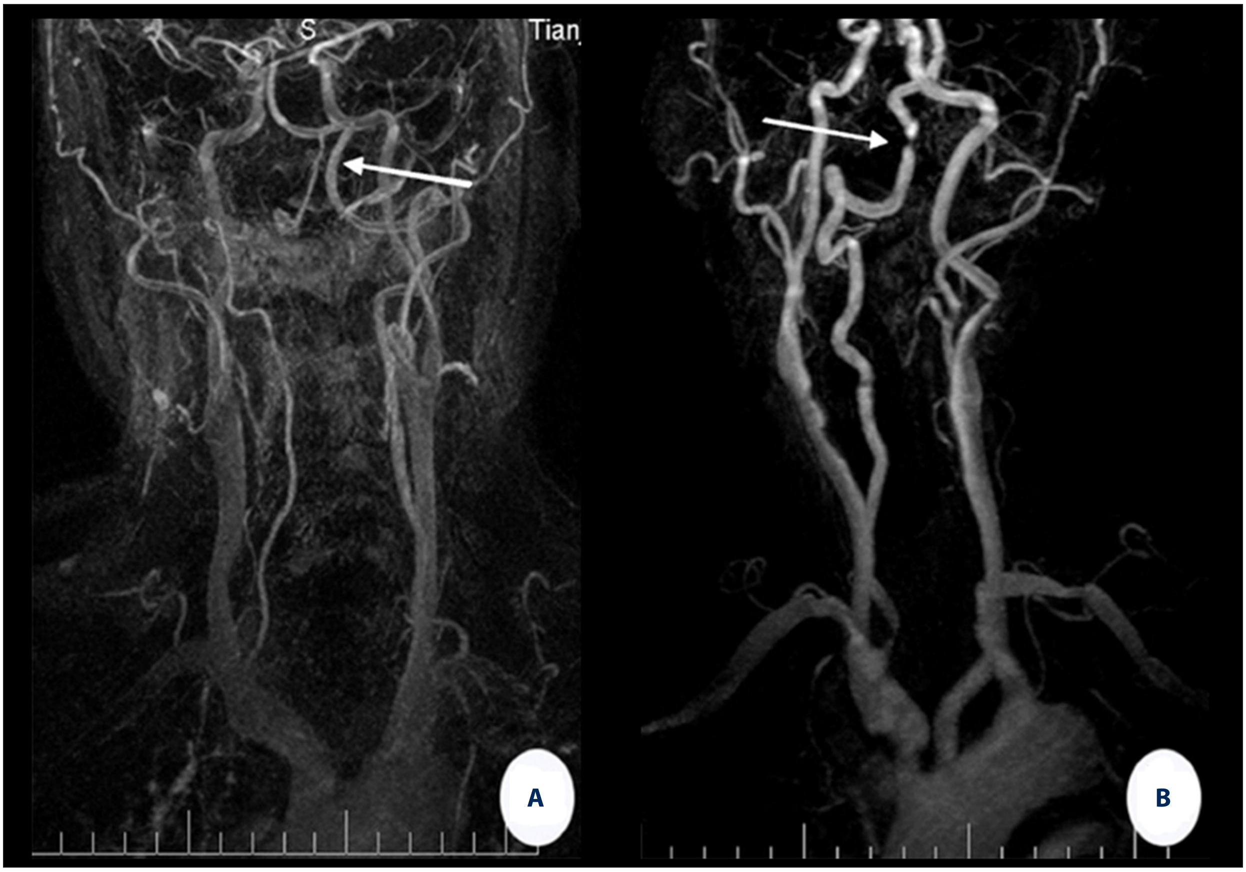


**Figure 1.** (**A**) A 36-year-old man had dizziness and vomiting several times, but the symptoms disappeared after 8 h. MRA showed the right VA was leptons, but the contralateral VA was pyknic and circuity (arrow). (**B**) A 55-year-old man had paroxysm dizziness and blurred vision for 3 years, which aggravated in the last 2 months. MRA showed the left VA was occluded; the contralateral VA was pyknic and circuity, with stenosis at the distal end (arrow).

lesions at the extracranial part of the cervical arteries and the result was inconsistent with previous studies [16,17]. This high percentage of lesions at cervical arteries might be due to the improved living standard of Chinese or the higher sensitivity of the CE-MRA in the diagnosis of cervical disease.

The number and degree of stenoses of cranial and cervical arteries was not significantly different between Group B and Group C in our study. No large infarcted area was found as in multiple artery stenosis and occlusions in most TIA patients, but these lesions might have the same pathological basis, with large area of the infarcted lesion. Brain infarction may happen at any time because of the shedding of the existing embolism or the impairment of the compensating path. The recurrence of transient ischemia symptoms suggests that artery stenosis and thrombus might already exist and the severe stenosis and irregular filling defect might be one of the most important risk factors for severe ischemia stroke [18], which makes it necessary for TIA patients to have accurate assessment of artery lesions as early as possible.

### The meaning of unilateral VA maldevelopment for TIA patients

VA maldevelopment is a congenital variation, most of which is unilateral. According to George's study [19], 5.7% of patients have left-side VA maldevelopment, 8.8% have right-side VA maldevelopment, and 0.6% have it on both sides. Almost all the VA maldevelopment patients have non-homogenous signal intensity and irregularity of the artery wall, causing most maldevelopment VA patients to have atherosclerosis, and the contralateral VA compensates by enlarging. Self-compensation always occurs when 1 side of the VA is compromised. With the compensation of the contralateral VA being enhanced and more dominant, the contralateral VA has a high incidence rate of maldevelopment VA, in which case, even small atherosclerosis will cause decompensation and lead to ischemic brain artery disease. In the present study, a much higher percentage of unilateral VA maldevelopment was detected compared with previous ones (40.63%) and 6 of the 13 (46.15%) TIA patients who had unilateral VA maldevelopment suffered from contralateral VA stenosis. Although other compensatory mechanisms of VA insufficiency, such as circle





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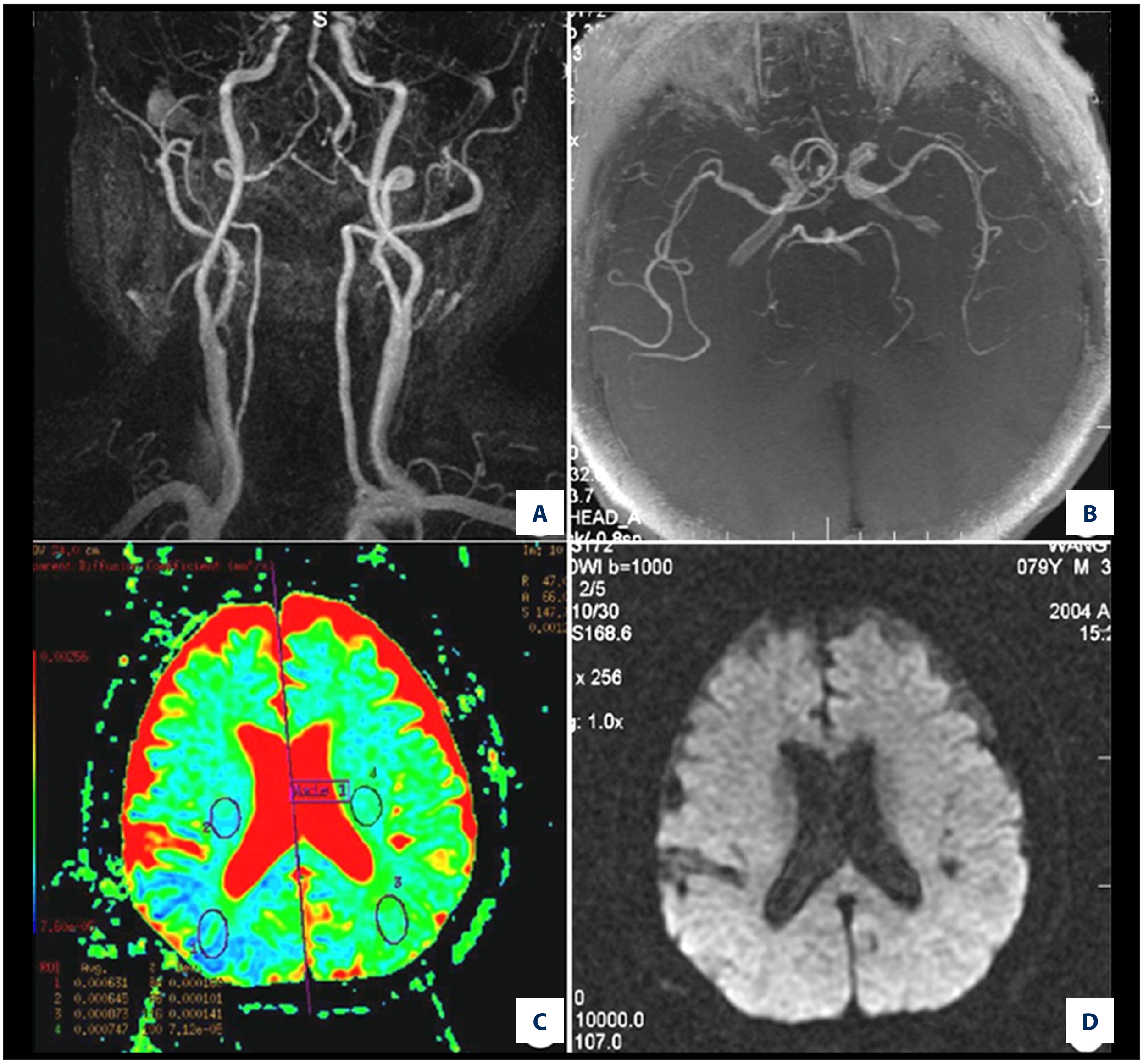


**Figure 2.** (**A**) A 79-year-old man had from paroxysm dizziness, aphasia, and numbness of the left leg several times. (**A, B**). MRA showed there were multiple plaques in the bulb of the right CCA, left ICA, and the distal end of left VA. The walls were irregular (arrow), and the bilateral PCA were very dark. (**C**) ADC images showed there was large ischemic area in the right temporal and occipital lobe (arrow). (**D**) No abnormality was found on DWI image.

of Willis, were also important, the maldevelopment of posterior communicating arteries was more frequent. We have thought that unilateral VA maldevelopment could be a predisposing factor for vertebrobasilar TIA because this vulnerable compensatory mechanism would promote the incidence rate of the disease. It is quite important to determine the situation and give an accurate assessment for normal people and asymptomatic patients.

### DWI findings of TIA patients

High DWI signal intensity is commonly detected in TIA patients, which involves the swelling of neurons and possibility of infarction [20]. In the present study, 22.5% (9/40) of TIA patients had high DWI signal intensity or ADC value abnormality and the patients with high DWI signal intensity had more severe artery stenosis than those with negative DWI detection. High DWI signal intensity was associated with severe artery lesions. In addition, only 12.5% of VB TIA patients had high DWI signal intensity, suggesting that the incidence of infarction of TIA patients is very low, which might be caused by the perfect compensatory mechanism.

Kamal et al. [21] analyzed the images of TIA patients when attack occurred within 6 h and demonstrated that the affected





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area that seemed normal had lower ADC value (9% to 26%) than the contralateral side. However, the change was only detected clearly on ADC images, while it was negative with DWI detection. In the present study, ADC value abnormality with negative DWI finding was found in only 1 patient, which was obviously inconsistent with the result of Kamal's study. This might have been due to the inappropriate examination time. The nerve system damages could be quantitatively evaluated by the measurement of ADC value, and it would be of great help for the diagnosis of this slight but measurable abnormality during the evaluation of brain damage in TIA patients.

There were several limitations of our study: 1) the sample size was small; 2) because of limitations on obtaining research sequences in acute TIA patients, we covered only 1 imaging modality (MRI); 3) the nature of the lesions was unrevealed, generally, and stenosis is usually attributed to intracranial atherosclerosis but can also result from angiospasm. However, the incidence of angiospasm should be similar between groups.

## Conclusions

The severe stenosis and filling defect of cranial and cervical arteries of TIA patients might be one of the most important risk factors of severe stroke. The patients with unilateral VA malformation were prone to have atherosclerosis, which might cause decompensation and be a predisposing factor for TIA. The fresh ischemia foci on DWI were correlated with severe artery lesions. It would help to reveal the pathologic mechanism of TIA patients to detect the variation of ADC value. All these findings suggest that imaging of cranial and cervical arteries should be included in the initial evaluation of TIA to prevent severe stroke.

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**Disclosure of conflict of interest**

The authors declare that have no conflicts of interest in relation to the research and the publication.

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