

Original Article

Magnetic resonance angiography (MRA) study of morphology and hemodynamics of circle of Willis in patients with transient ischemic attack (TIA)

Jianlong Li^{1,2}, Yunpeng Kong², Yuefeng Pan², Rui Xu², Wenjian Xu¹, Chao Wang²

¹Department of Radiology, The Affiliated Hospital of Qingdao University, Qingdao 266071, China; ²Department of Imaging Radiology, Rizhao People's Hospital, Rizhao, China

Received August 15, 2017; Accepted February 23, 2018; Epub June 15, 2018; Published June 30, 2018

Abstract: *Objective:* To evaluate the magnetic resonance angiography (MRA) features of the circle of Willis in transient ischemic attack (TIA) patients. *Methods:* The MRA features of 40 TIA patients (TIA), 34 normal controls (CON), and 36 patients with large cerebral infarction (LCI) were compared. *Results:* The proportion of A1 dysplasia or absence in the patients with TIA in the internal carotid arterial system (TIA-ICA) was significantly higher than that in the patients with TIA in the vertebrobasilar arterial system (TIA-VBA) ($P < 0.05$). The comparison between Group TIA and CON showed significant difference in the detection rate of embryonic posterior cerebral artery (PCA) ($P = 0.008$). The display rate of posterior communicating artery (PCOA) in patients with TIA-VBA was lower than that in Group CON ($P = 0.002$). When the carotid arterial stenosis was severe, the directions of blood flow in the anterior and posterior communicating arteries (ACOA and PCOA) of TIA patients tended to incline toward the lesion side. *Conclusions:* A1 dysplasia or absence may be the predisposing factors of TIA-ICA; PCOA dysplasia or absence may be the predisposing factors of TIA-VBA; embryonic PCOA has protective effect toward the blood supply of posterior circulation.

Keywords: Transient ischemic attack, magnetic resonance angiography, circle of Willis

Introduction

The circle of Willis is located at the bottom of the brain, between internal carotid arterial system (ICA) and vertebrobasilar arterial system (VBA), and between the bilateral intracranial ICA. As the main pathway of forming the collateral circulation, when the ICA or VBA occurs occlusive diseases, the circle of Willis will become very important as the collateral circulation so as to provide compensatory blood supply [1-3]. The existence of a complete collateral circulation can reduce the incidence of transient ischemic attack (TIA) and stroke [4]. Magnetic resonance angiography (MRA) is a valuable non-invasive technique for evaluating the circle of Willis. With the development of MR techniques, more and more scholars have used new magnetic resonance imaging (MRI) techniques to study the morphology of the circle of Willis and its relationship with ischemic diseases [5-8]. However, in recent years, studies in China and abroad focusing on the morphology

of the circle of Willis in normal controls and using MRI-combined techniques to study TIA are rare [5-7, 9, 10]. Comprehensively diagnosing and assessing the cerebral ischemic lesions in the TIA stage is very important for the prognosis of such patients [11, 12]. We applied a variety of MRA techniques for evaluating the morphology and hemodynamics of circle of Willis in TIA patients, aiming to investigate the pathogenesis of TIA from the angles of morphology and hemodynamics and to preliminarily analyze its hemodynamic features.

Materials and methods

General information

A total of 40 TIA patients with good head-and-neck MRA image quality and complete examination sequences (examined in our hospital from January 2012 to March 2015) were enrolled into this study and compared with the data of 34 normal healthy controls and 36 LCI

MRA study of circle of Willis

patients. Group CON included 18 males and 16 females with an average age as 55.24 ± 13.84 years. Group TIA included 30 males and 10 females with an average age as 60.53 ± 10.39 years. All the patients exhibited transient neurological symptoms on admission, and the majority of the patients suffered from multiple seizures with the shortest seizure duration as 1 minute while the longest as up to 9 h (averagely 0.932 ± 0.665 h). Seventeen patients had previous history of hypertension, 12 patients had previous history of hyperlipidemia, 4 patients had previous history of diabetes, and 10 patients had previous history of cervical spondylosis. This study included 32 TIA-VBA cases, 8 TIA-ICA cases. Group LCI included 21 males and 15 females with an average age as 56.58 ± 8.21 years, including 12 cases with previous history of hypertension, 6 cases with previous history of hyperlipidemia, and 2 cases with previous history of diabetes. There was no significant difference in the average age among the above groups ($F=2.365$, $P=0.099$), as well as in the gender composition ($\chi^2=4.267$, $P=0.118$). This study was conducted in accordance with the declaration of Helsinki. This study was conducted with the approval from the Ethics Committee of Qingdao University. Written informed consent was obtained from all participants.

MRA scanning

All the scans were performed on an 1.5T Superconduction MR system (Twin-Speed Infinity with Excite I, GE, USA).

Intracalvarial artery imaging

3D TOF sequence, time of repeat/time of echo (TR/TE): 32/3.3 ms, field of view (FOV): 18 cm \times 18 cm, flip angle: 20°, layer thickness: 1.5 mm, matrix: 288 \times 128, bandwidth: 15.6 kHz, acquisition time: ~5 min.

Blood flow direction detection

3D PC (GRE) sequence, TR/TE: 25 ms/6 ms, flip angle: 25°, layer thickness: 1.0 mm, matrix: 256 \times 128, layer mass thickness: 30 mm, FOV: 22 cm, acquisition time: ~2 min and 40 s. One single direction flow coding gradient was applied onto the front, rear, left and right direction, respectively, so as to detect the blood flow direction in ACOA and PCOA; the flow coding speed was 40 cm/s.

Cervical artery imaging

3D CE-MRA, TR/TE: 6 ms/min, flip angle: 45°, matrix: 256 \times 256, layer thickness: 1.8 mm, layer mass thickness: 65 mm, FOV: 24~28 cm, acquisition time: up to 55 s. Using agent of Gd-DTPA (Bayer, Germany, 15 ml: 7.4 g).

Image analysis

The 3D TOF images were used to evaluate the morphology of circle of Willis by the tracer method. Blood-vessel linkage between bilateral ACA can be defined as the existence of ACOA, as well as bilateral fusion can also be used for this definition; if the starting and end points of PCOA can be confirmed or continued and formed PCA, it can be considered as its existence. The condition of embryonic PCA was defined as the diameter of PCOA greater than the ipsilateral P1 segment and continued to for PCA. The condition in which the diameter of the communicating artery <0.8 mm was considered as dysplasia [2].

From the aspect of human body development, the circle of Willis is divided into the anterior and posterior circles. The anterior circle includes the bilateral ICA, ACOA, and A1 segment of bilateral ACA; the posterior circle includes the bilateral PCOA, as well as the P1 segment and BA of bilateral PCA. If certain related vessels exhibited dysplasia (less than 8 mm) or absence, they were considered as incomplete.

The vascular integrity of the circle of Willis was observed and recorded by two experienced diagnostic radiographers according to the above-mentioned uniform standards; meanwhile, the diameter of partial PCOA was measured, and the blood flow directions in the ACOA and PCOA were observed, and the accordant results should be obtained through negotiation if the diagnostic results were inconsistent.

Statistical analysis

SPSS11.0 software was used for the statistical processing, with the significance level $\alpha=0.05$.

Results

Distribution features of stenotic lesions

In order to discuss the importance of the compensation by the circle of Willis, the craniocerebral artery stenosis was divided into two parts:

MRA study of circle of Willis

Table 1. Distribution of craniocerebral stenotic lesions (with the circle of Willis as the boundary)

Group	Branches anterior to the circle of Willis (n)	Branches posterior to the circle of Willis (n)	Sum (n)
CON	12	4	16
TIA	54	21	75
LCI	29	41	70
Sum (n)	95	66	161

Note: There was no significant difference between Group CON and TIA ($\chi^2=0.060$, $P=0.807$), but there was significant difference between Group LCI and CON/TIA ($\chi^2=5.884$, $P=0.015$; $\chi^2=13.826$, $P<0.001$).

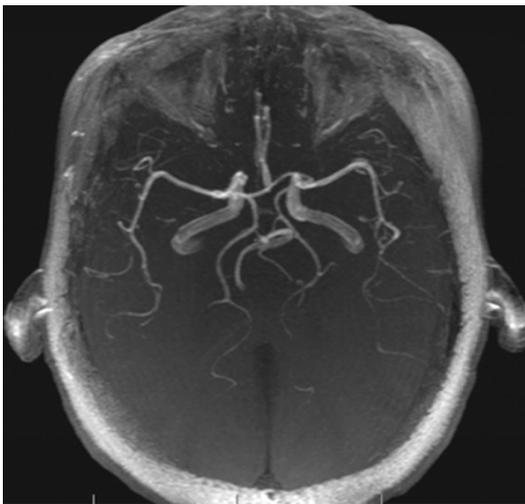


Figure 1. A normal people with bilateral embryonic PCOA. The bilateral PCOA thickened, but the bilateral A1 segment become thinner; the blood supply area in bilateral PCA comes mostly from ICA while few from BA, thus forming a dual blood supply mechanism.

anterior and posterior stenosis of the circle of Willis (**Table 1**). There was no significant difference between Group CON and TIA ($\chi^2=0.060$, $P=0.807$), but there was significant difference between Group LCI and CON/TIA ($\chi^2=5.884$, $P=0.015$ and $\chi^2=13.826$, $P<0.001$, respectively).

Morphology of circle of Willis

A1 dysplasia was more common in Group TIA (8 cases, 20%) and Group LCI (8 cases, 22.2%), but there was no significant difference when compared with Group CON (4 cases, 11.76%) ($\chi^2=1.425$, $P=0.490$). Among the 8 cases in Group TIA-ICA, 5 cases were A1 dysplasia or absence; among the 32 cases in Group TIA-VBA, only 6 cases were A1 dysplasia or absence (both unilateral), and there was a significant dif-

ference between the two groups ($\chi^2=4.146$, $P=0.042$). There were significant differences in embryonic PCA combined with P1 dysplasia among the three groups ($\chi^2=6.853$, $P=0.033$). After c2 subdivision, there were significant differences between Group CON (12 cases, 35.29%, including 2 cases of bilateral embryonic PCA) and Group TIA (4 cases, 10.00%, **Figure 1**, $\chi^2=6.938$, $P=0.008$), while there was no significant difference between Group LCI and the other two groups ($P>0.05$). Among the 32 patients in Group TIA-VBA, only one case (3.13%) occurred embryonic PCA combined with P1 dysplasia, showing a significant difference when compared with Group CON ($\chi^2=10.785$, $P=0.001$). Among the 8 patients in Group TIA-ICA, 3 cases (37.50%) were embryonic PCA, while there were no significant difference than Group CON ($\chi^2=0.014$, $P=0.907$). There was no significant difference in A1, P1, PCOA, or ACOA absence among the three groups (**Table 2**).

The display rate of PCOA in Group TIA-VBA (18/64, 28.125%) was significantly lower than that of Group CON (37/68, 54.41%) ($\chi^2=9.373$, $P=0.002$) (**Figure 2**). The average diameter of the 18 PCOA in Group TIA-VBA was 2.013 ± 0.629 mm, which was slightly thicker than the latter (1.836 ± 0.538 mm), but there was no significant difference between the two groups ($u=1.555$, $P=0.128$). The display rate of PCOA in Group TIA-ICA was 68.75% (11/16), which was significantly different from Group TIA-VBA ($\chi^2=9.141$, $P=0.002$). There was no significant difference in the display rate of PCOA between the 12 TIA patients with severe arterial stenosis or occlusion and the rest 28 TIA patients ($\chi^2=2.805$, $P=0.094$).

There was no significant difference in the type of the circle of Willis among the three groups ($\chi^2=1.836$, $P=0.934$), in which type II and IV were common in the three groups (**Table 3**). There was no significant difference in the integrity of anterior and posterior circle among the three groups ($\chi^2=1.030$, $P=0.597$; $\chi^2=0.229$, $P=0.892$).

Blood flow directions in ACOA and PCOA in the circle of Willis

There was no significant difference in the blood flow directions in ACOA and PCOA among the three groups ($\chi^2=3.305$, $P=0.192$ and $\chi^2=5.363$, $P=0.068$, respectively). Among the 11 PCOA with clear display in the 8 patients

MRA study of circle of Willis

Table 2. Morphology of circle of Willis in Group TIA and CON

Group	A1	A1	P1	P1	Embryonic PCA	PCOA absence	ACOA absence
	dysplasia	absence	dysplasia	absence			
CON	4	2	12 (14)	0	12 (14)	19 (31)	5
TIA	8	3	4	2	4	29 (51)	6
LCI	8	4	8	4	9	24 (39)	4

Note: (1) A1 was the first segment of ACA, starting from the beginning to the ACOA part; P1 was the first segment of PCA, starting from the beginning to the intersection with the PCOA; (2) the values in the table without parentheses were cases, and the numbers in parentheses were the number of lesion sides. There were significant differences in embryonic PCA combined with P1 dysplasia among the three groups ($\chi^2=6.853$, $P=0.033$).

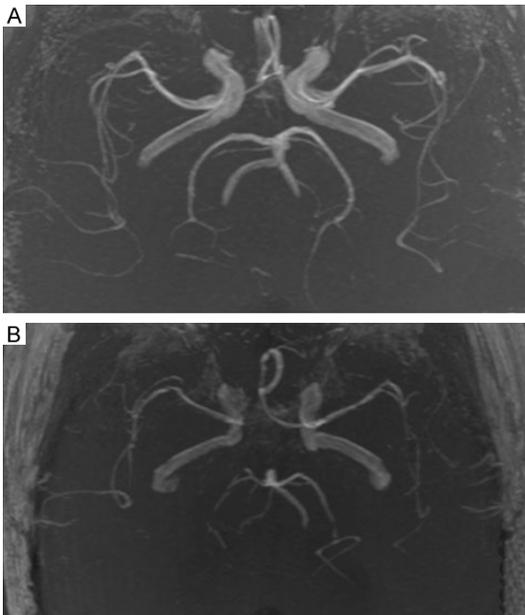


Figure 2. (A and B) Two patients with TIA-VBA (A and B). The absence of both sides PCOA was common in such patients.

Table 3. Comparison of circle of Willis between Group TIA and CON

Group	Type				Sum (n)
	I	II	III	IV	
CON (n=34)	5	18	4	7	34
TIA (n=40)	4	19	4	13	40
LCI (n=36)	4	20	3	9	36
Sun (n)	13	57	11	29	110

Note: There was no significant difference in the type of the circle of Willis among the three groups ($\chi^2=1.836$, $P=0.934$), in which type II and IV were common in the three groups.

with TIA-ICA, the blood flow directions were retrogressive in 9 branches and prorsal in 2 branches. The blood flow directions in three

cases of ACOA were left to right (1 case with severe right ICA stenosis and 2 cases with bilateral moderate stenosis), from right to left in five cases (1 case with left ICA occlusion, 2 cases with moderate left ICA stenosis, and 2 cases without obvious stenosis); among the

32 patients with TIA-VBA, the blood flow directions were retrogressive in 15 PCOA cases and prorsal in three cases. Among all the TIA patients, 5 patients exhibited severe anterior carotid artery stenosis (3 cases) and/or occlusion (1 case with unilateral ICA occlusion, 1 case with bilateral occlusion) (Figure 3). The blood flow direction in ACOA was clear (Figure 4), including flowing toward the lesion side in 4 cases (Figure 4), flowing toward the A1 absence side in one case, and appearing reverse blood flow in the A1 segment in one case. The diameters showed no significant thickening (Table 4).

Discussion

Morphological remodeling of circle of Willis in TIA patients caused by stenotic lesions: The morphological changes occurring in the circle of Willis due to different pressure gradients in the both arterial ends are called the remodeling of circle of Willis [13]. When arterial stenosis or occlusion occurs, the blood pressure in the distal arterial end decreases, and if there is no effective blood flow compensation from collateral branches at this time, it is prone to cerebral infarction. Therefore, stroke in TIA and cerebral hemisphere can be significantly reduced when collateral circulation exists. In patients with severe ICA occlusive diseases, the presence of collateral vessels in the circle of Willis can not only maintain the perfusion pressure required for the brain tissues but also attenuate damages caused by emboli [14, 15]. This study revealed that TIA patients and normal controls mainly occur lesions in the anterior circle of Willis, but LCI patients mainly occur lesions in the posterior circle of Willis. Although the display rate of PCOA in Group TIA was low (29/80, 36.25%), the display rate of PCOA in 12

MRA study of circle of Willis

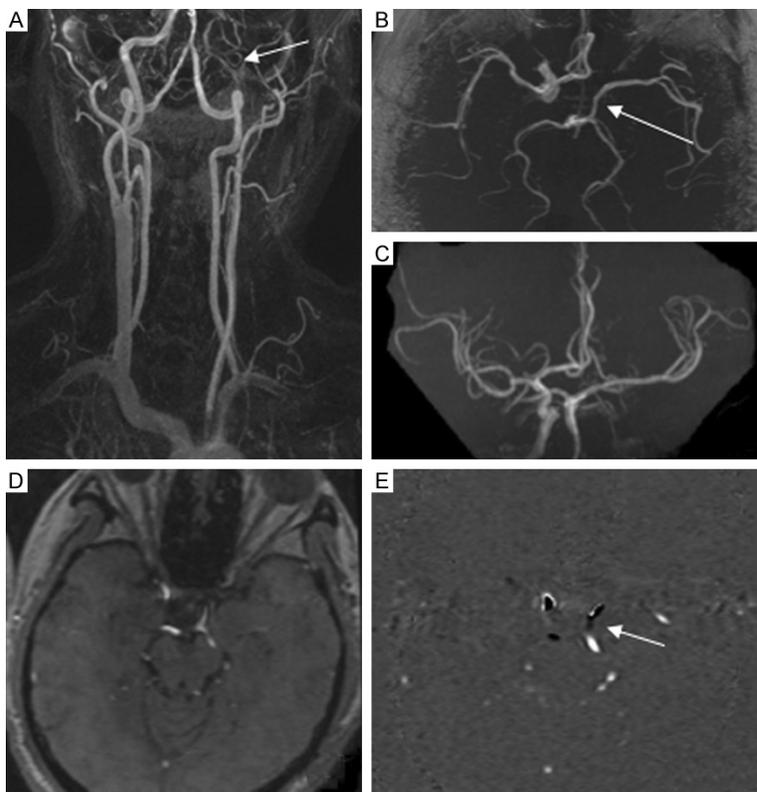


Figure 3. Male, 47 years old. Main complaint: paroxysmal left lower limb numbness for more than 10 days, system increase when doing activities together with headache; the systems can alleviate within 1 h. A. CE-MRA reveals left ICA occlusion (arrow), thinner CCA, contralateral CCA thickening, and bilateral VA thickening; B, C. TOF MRA reveals the left MCA supplies blood through the thickened PCOA (arrow), but the A1 segment absences in the left ACA, so the distal A2 segment obtains the blood supply from the opposite side of ACOA; D, E. 3D PC reveals the blood flow direction in left PCOA is prorsal (arrow).

patients with severe anterior carotid artery stenosis or occlusion was slightly higher than that in the patients with mild and moderate stenosis, suggesting that the remodeling of circle of Willis already exists, and collateral circulation mainly in the circle of Willis effectively prevents the occurrence of stroke in some patients. Rappeport *et al.* [16] reported that with the age increasing in TIA patients, arterial stenosis increases, which is similar to the results of this study. Although the number and extent of stenotic lesions increase, some patients still remain in the TIA state, indicating that with the increase of the degree of arterial lesions, the remodeling of collateral circulation is also enhanced.

In this study, the display rate of ACOA in TIA patients was 85.0%, namely that the ACOA in these patients had the collateral circulation function; the patients with A1 absence or dys-

plasia accounted for 27.5% (11/40), including 62.5% cases with TIA-ICA (5/8) and 18.75% cases of TIA-VBA (6/32), exhibiting significance between the two groups, $P=0.002$), suggesting that TIA-ICA is related to A1 absence or dysplasia, and the presence of this variation increases the risk of disease in TIA-ICA. However, TIA-VBA is not related to A1 absence or dysplasia.

Morphology and variation of posterior circle: the bilateral PCOA is responsible for the compensatory functions of the anterior- and posterior circles, while the P1 segment in the bilateral PCA is related to balancing the blood flow pressures in the bilateral PCA, so the morphological variations of these two are the main reason causing variations in the posterior circle. As the vertebral artery is affected by the direction or development, its blood supply capacity may easily disease due to external factors and internal diseases, thus resulting in blood supply insufficiency in the vertebro-

basilar artery. At this time, complete posterior cycle will be necessarily required so as to play the collateral compensation function. In this study, the display rate of PCIA in the TIA patients was low, especially only 28.125% in the 32 patients with TIA-VBA, significantly lower than the normal controls, suggesting that the incomplete posterior circle may be one of the important predisposing factors toward TIA-ICA. The display rate of PCIA in the TIA-ICA patients was higher (68.75%), which may be related to the compensation.

The study also reveals that 35.29% (12/34) of the normal controls exist embryonic PCA, including 2 cases of bilateral embryonic PCA. At the same time, only 1 patient (3.125%) in Group TIA-VBA is embryonic PCA. Embryonic PCA is often associated with ipsilateral P1 dysplasia or absence, at which time the blood supply area toward the ipsilateral P1 segment

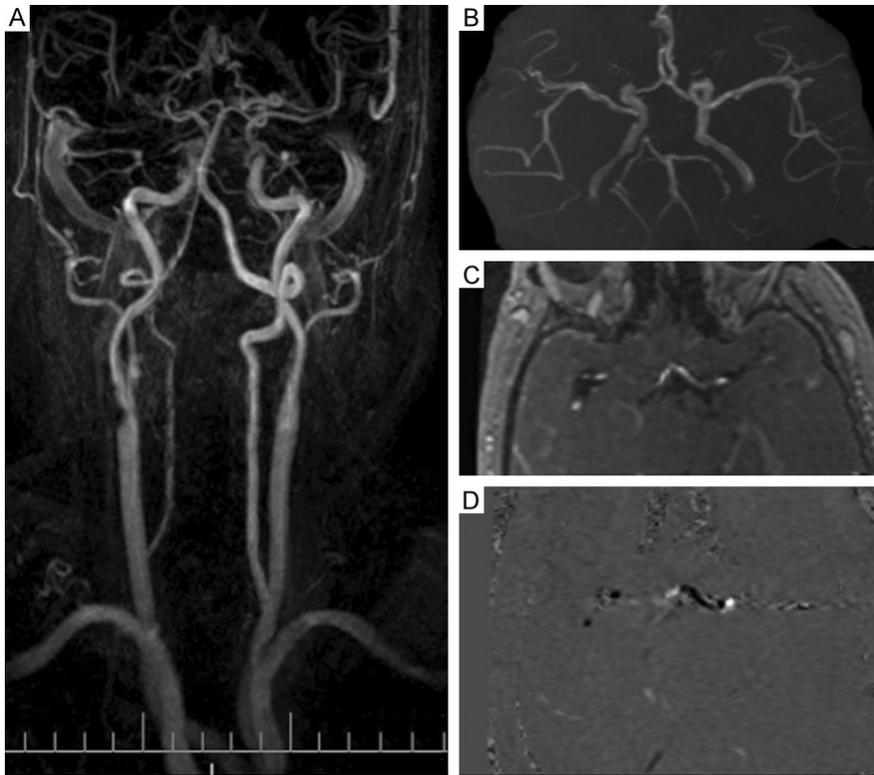


Figure 4. Female, 55 years old. Main complaint: intermittent left limb numbness for 20 days, time interval: 5 h. A. CE-MRA reveals localized stenosis in the bulbar zone of right internal carotid artery and ICA starting segment (arrow); B. Intracranial 3D TOF reveals slimmer right A1 segment, left A1 and ACOA thickening (short arrow), rightward compensatory blood supply; right ICA petrous bone exhibits localized stenosis (long arrow); C, D. 3D PC reveals rightward blood flow in the left A1 and ACOA, while leftward in the right A1 segment (arrow).

Table 4. Blood flow directions in ACOA and PCOA in 40 TIA patients

Group	ACOA		Left PCOA		Right PCOA	
	Left→right	Right→left	Front→back	Back→front	Front→back	Back→front
CON	10	6	15	1	18	0
TIA	12	8	10	3	12	2
LCI	4	7	12	1	8	3
Sum	26	21	37	5	38	5

Note: There was no significant difference in the blood flow directions in ACOA and PCOA among the three groups ($\chi^2=3.305$, $P=0.192$; $\chi^2=5.363$, $P=0.068$). But the blood flow direction of ACOA tends to the lesion side.

is mainly by the internal carotid artery system; if the internal carotid artery system occurs arteriosclerotic lesions, the ischemic symptoms of posterior circle also appear [17]. However, we believe that this situation is not easy to occur. First, the blood supply amount by the internal carotid artery system is large (accounting for 85% of the brain requirement), so the protection mechanisms are relatively sound, only severe or worse stenosis can affect the perfusion pressure of brain tissues, so the chances

of ischemia compared with the VBA system are rare; second, the majority of embryonic PCA is associated with ipsilateral P1 dysplasia, but absence is rare, so in fact, this PCA blood supply area can form dual blood supply through the poor developed P1 segment and embryonic PCA, while the contralateral PCA actually can receive the most blood supply from the bilateral VA. In this way, the blood supply of the entire posterior circle has been strengthened. Therefore, when the carotid artery has severe stenosis or occlusive diseases, embryonic PCA has important protective effect toward the posterior circle, and can reduce the vertebrobasilar arterial blood supply insufficiency. The increase in embryonic PCA in normal controls also supports this view.

Blood flow direction of the circle of Willis: When lesions in lateral internal carotid artery cause TIA, the ACOA and PCOA can both form collateral circulation, but the compensatory effect of ACOA toward the vertebrobasilar system is not big. In this study, the ACOA flow in 8 patients with TIA-ICA did not show regularity, which may be due to the too small patient number and the lesions mainly distributing in the circle of Willis. The display rate of PCOA was significantly increased in the TIA-IVA patients, but the blood

flow direction in most cases was retrogressive, and only two branches exhibited the blood flow direction as prorsal; the diameter also showed no significant thickening. Therefore, the clinical significance of the high display rate of PCOA in patients with TIA-ICA needs further studies. The display rate of PCOA in the 32 TIA-VBA patients was very low, and the detected PCOA diameter was similar to the normal controls, suggesting that some such patients have limited compensatory capacity of PCOA branches, when the vertebrobasilar system is damaged to a certain degree, they can't obtain the reserve collateral blood flow like that previously restored in normal people, so blood supply insufficiency is prone to occurrence and causes TIA.

In this study, the collateral blood flow in the 5 TIA patients with severe stenosis and occlusion in unilateral anterior cervical artery system is more representative. The ACOA blood flow tended toward the lesioned side, and the healthy A1 segment and ACOA were thickened, suggesting the importance of ACOA in the anterior compensation. The reverse flow in the A1 segment and the retrogressive flow in PCOA were more common in the patients with ICA occlusion, consistent with Hartkamp, indicating that there would be greater chances of prorsal blood flow in PCOA of the patients with anterior ICA occlusion [13], but as for those with stenosis, when the degree of stenosis has not changed the superior blood supply in the internal carotid artery system (the pressure is higher than the posterior circle), there will be no enough pressure gradient to force the PCOA blood flow to change prorsally.

Conclusions

The remodeling of circle of Willis in TIA patients progresses with the severity of stenosis in a non-linear relationship, which only becomes significant in severe stenosis or occlusion and may also be affected by factors such as individual differences. A1 dysplasia or absence is associated with TIA-ICA while not with TIA-VBA; PCOA dysplasia or absence may be a predisposing factor of TIA-VBA, and embryonic PCA has protective effect of maintaining the blood supply toward the posterior circle. The flow of ACOA in patients with TIA-ICA is variable due to the impact of pressure gradient, distribution of stenotic lesions, or anterior circle variations, and the compensatory ability of PCOA toward TIA-ICA is limited. The compensatory ability of

PCOA is insufficient, and the function of PCOA collateral branches in TIA-VBA is insufficient, suggesting that the incidence of TIA is related to this phenomenon. When the blood supply area in lateral carotid artery system is ischemic, the blood flow direction of ACOA tends to the lesion side, and the reverse blood flow in the A1 segment only appears in patients with ICA occlusion.

Acknowledgements

This study was supported by research support fund in Jining Medical School (No. JY2016-KJ017Z and JY2015KJ046).

Disclosure of conflict of interest

None.

Address correspondence to: Wenjian Xu, Department of Radiology, The Affiliated Hospital of Qingdao University, 16 Jiangsu Road, Qingdao 266071, China. Tel: +86 532 82911842; Fax: +86 532 82911841; E-mail: docwenjianxu@126.com

References

- [1] Zhou H, Sun J, Ji X, Lin J, Tang S, Zeng J and Fan YH. Correlation between the integrity of the circle of Willis and the severity of initial noncardiac cerebral infarction and clinical prognosis. *Medicine (Baltimore)* 2016; 95: e2892.
- [2] Goerlitz J, Wenz H, Al-Zghloul M, Kerl HU, Groden C and Förster A. Anatomical variations in the posterior circle of Willis and vascular pathologies in isolated unilateral thalamic infarction. *J Neuroimaging* 2015; 25: 983-988.
- [3] Sallustio F, Kern R, Günther M, Szabo K, Griebel M, Meairs S, Hennerici M and Gass A. Assessment of intracranial collateral flow by using dynamic arterial spin labeling mra and transcranial color-coded duplex ultrasound. *Stroke* 2008; 39: 1894-1897.
- [4] Henderson RD, Eliasziw M, Fox AJ, Rothwell PM and Barnett HJ. Angiographically defined collateral circulation and risk of stroke in patients with severe carotid artery stenosis. North American symptomatic carotid endarterectomy trial (NASCET) group. *Stroke* 2000; 31: 128-132.
- [5] Jalali Kondori B, Azemati F and Dadseresht S. Magnetic resonance angiographic study of anatomic variations of the circle of Willis in a population in Tehran. *Arch Iran Med* 2017; 20: 235-239.
- [6] Yeniçeri İÖ, Çullu N, Deveer M and Yeniçeri EN. Circle of Willis variations and artery diameter

MRA study of circle of Willis

- measurements in the Turkish population. *Folia Morphol (Warsz)* 2017; 76: 420-425.
- [7] Naveen SR, Bhat V and Karthik GA. Magnetic resonance angiographic evaluation of circle of Willis: a morphologic study in a tertiary hospital set up. *Ann Indian Acad Neurol* 2015; 18: 391-397.
- [8] Iryo Y, Hirai T, Nakamura M, Inoue Y, Watanabe M, Ando Y, Azuma M, Nishimura S, Shigematsu Y, Kitajima M and Yamashita Y. Collateral circulation via the circle of Willis in patients with carotid artery steno-occlusive disease: evaluation on 3-T 4D MRA using arterial spin labeling. *Clin Radiol* 2015; 70: 960-965.
- [9] Qiu C, Zhang Y, Xue C, Jiang S and Zhang W. MRA study on variation of the circle of willis in healthy Chinese male adults. *Biomed Res Int* 2015; 2015: 976340.
- [10] Klimek-Piotrowska W, Rybicka M, Wojnarska A, Wójtowicz A, Koziej M and Hołda MK. A multitude of variations in the configuration of the circle of Willis: an autopsy study. *Anat Sci Int* 2016; 91: 325-333.
- [11] Giles MF and Rothwell PM. Systematic review and pooled analysis of published and unpublished validations of the ABCD and ABCD2 transient ischemic attack risk scores. *Stroke* 2010; 41: 667-673.
- [12] Ssi-Yan-Kai G, Nasr N, Faury A, Catalaa I, Cognard C, Larrue V and Bonneville F. Intracranial artery stenosis or occlusion predicts ischemic recurrence after transient ischemic attack. *AJNR Am J Neuroradiol* 2013; 34: 185-190.
- [13] Hartkamp MJ, van Der Grond J, van Everdingen KJ, Hillen B and Mali WP. Circle of Willis collateral flow investigated by magnetic resonance angiography. *Stroke* 1999; 30: 2671-2678.
- [14] Caplan LR and Hennerici M. Impaired clearance of emboli (washout) is an important link between hypoperfusion, embolism, and ischemic stroke. *Arch Neurol* 1998; 55: 1475-1482.
- [15] Powers WJ, Press GA, Grubb RL Jr, Gado M and Raichle ME. The effect of hemodynamically significant carotid artery disease on the hemodynamic status of the cerebral circulation. *Ann Intern Med* 1987; 106: 27-34.
- [16] Rappeport Y, Simonsen L, Christiansen H and Boysen G. Prevalence of significant carotid artery stenosis in patients with transient ischaemic attack. *Med Sci Monit* 2002; 8: CR317-320.
- [17] Edelman RR, Mattle HP, O'Reilly GV, Wentz KU, Liu C and Zhao B. Magnetic resonance imaging of flow dynamics in the circle of Willis. *Stroke* 1990; 21: 56-65.