Neurology Asia 2015; 20(1) : 7 – 14

ORIGINAL ARTICLES

Pattern of circle of Willis between normal subject and patients with carotid atherosclerotic plaque

Hyo Sung Kwak *MD PhD*, Seung Bae Hwang *MD*, Gyung Ho Chung *MD PhD*, Sang Yong Lee *MD PhD*

Department of Radiology and Research Institute of Clinical Medicine of Chonbuk National University-Biomedical Research Institute of Chonbuk National University Hospital, Chonbuk National University Medical School and Hospital, Chonbuk, South Korea

Abstract

Objective: We investigated whether circle of Willis (COW) morphology on 3D time-of-flight (TOF) MR angiography differs between young normal subjects, older normal subjects, and patients with carotid atherosclerotic plaques. *Methods:* One hundred seventy-seven subjects were grouped according to age into a young group (20 – 40 years; n = 91) and an older group (> 60 years; n = 86). Subjects underwent brain MR examination as part of a health check-up. Fifty-three patients with carotid atherosclerotic plaque were also included for evaluation in this study. COW morphology on 3D TOF MR angiography was analyzed in terms of completeness or incompleteness of the anterior and posterior components of the circle and completeness of the circle. *Results:* An incomplete pattern of anterior circulation was significantly more common in carotid atherosclerotic plaque patients (20.7%) than normal older subjects (5.5%) ($p < 0.01$). A complete posterior circulation pattern was more frequent in normal young subjects (46.5%) than in normal older subjects (16.5%) or the patient group (18.9%) ($p < 0.01$). Of patients with carotid artery stenosis, 18.9% had a bilateral incomplete connection and were significantly more likely to have an incomplete pattern than normal young (2.3%) or normal older subjects (2.2%) ($p < 0.001$).
Conclusion: Young, healthy subjects were significantly more likely to have a complete pattern of posterior circulation than older subjects. Patients with carotid atherosclerotic plaques were significantly more likely to have incomplete anterior circulation and an incomplete circle than young, normal subjects.

INTRODUCTION

The circle of Willis (COW) plays a critical role in maintaining adequate cerebral perfusion should blood flow in one of the major feeding arteries to the brain be compromised. An intact COW can compensate for occlusion of one of the four feeding arteries by flow in the circle.[1-3] In patients with carotid artery stenosis, cerebral perfusion is dependent not only on the degree of stenosis, but also on the collateral pathways.[4-7] Although several collateral pathways may contribute to cerebral perfusion, primary collateral vessels are part of the COW, which can respond quickly to low perfusion pressure with simple reversal of flow. COW shows considerable morphologic variation among relatively healthy individuals, and authors of various studies[6-11] have concluded that anatomic variations may affect outcomes in patients with carotid artery disease.

Conventional angiography, transcranial Doppler ultrasonography, MR angiography, and CT angiography have been used to evaluate collateral cerebral blood flow through the anterior and posterior communicating arteries in normal volunteers or patients with carotid artery disease.[6-14] Three-dimensional (3D) time-of-flight (TOF) MR angiography is a noninvasive and sensitive technique for detecting the anatomy of the COW in patients[6,7] and healthy volunteers.[8,14]

However, to the best of our knowledge, COW morphology as determined using 3D TOF MR angiography has not previously been compared between normal subjects and patients with carotid artery disease. Therefore, in this study, we investigated whether COW morphology

Address correspondence to: Hyo-Sung Kwak, M.D., Department of Radiology and Research Institute of Medical Science, Chonbuk National University Medical School and Hospital, 567 Baekje-daero, Jeonju-si, Jeollabuk-do 561-756, South Korea, Tel: 82-63-250-2582, Fax: 82-63-272-0481. E-mail: kwak8140@jbnu.ac.kr

on 3D TOF MR angiography differs between normal subjects and patients with carotid artery disease.

METHODS

Study subjects

This retrospective analysis was conducted with Institutional Review Board approval. Informed consent was obtained from all participants. Normal subjects were randomly recruited from a database of individuals who underwent brain MR angiography with carotid angiography as part of a health check-up from January 2011 to May 2012. We divided subjects into young subjects (20 – 40 years) and older subjects (60 years and older), and randomly selected 95 subjects per each group. All brain MR angiography and related carotid angiography were evaluated by two neuroradiologist (H.S.K and S.Y.L). Exclusion criteria for normal subjects were as follows: 1) >5% stenosis of intracranial or extracranial artery by atherosclerosis; 2) no visualization of bilateral vertebral artery; 3) vasculitis such as Moyamoya disease; and 4) MR examination with poor image quality. Furthermore, patients with proximal internal carotid artery (ICA) stenosis who underwent carotid artery stenting (CAS) were recruited to accurately measure ICA stenosis on cerebral angiography. Seventy-seven patients with proximal internal carotid artery (ICA) stenosis diagnosed at our institution from 2009 to 2011 were included. Inclusion criteria for this group were: 1) preprocedural 3D TOF MR angiography and 2) >50% ICA stenosis in patients with symptomatic lesions or >70% ICA stenosis in patients with asymptomatic lesions. Symptomatic carotid artery stenosis was defined as the onset of focal neurologic symptoms (TIA or nonfatal stroke) occurring within 6 months before CAS and attributable to an ipsilateral carotid artery vascular distribution. Exclusion criteria were 1) >5% stenosis of intracranial artery by atherosclerosis; 2) no visualization or >50% stenosis of bilateral vertebral artery; 3) vascular disease such as Moyamoya disease; and 4) MR examination with poor image quality.

MR angiography

All subjects underwent routine brain MRI including 3D TOF MR angiography of the COW and contrast-enhanced carotid MR angiography at 3.0-T (Verio; Siemens, Erlangen, Germany and Achieva; Philips Medical System, Best, Netherlands). We obtained 3D multislab TOF MR angiography from the petrous portion of the ICA to the whole brain using the following imaging parameters: repetition time (TR)/echo time (TE) = 23/3.45 msec, flip angle = 20^0, field of view (FOV) = 200 x 200 mm, matrix size = 488 x 249, sensitivity encoding (SENSE) factor = 2.5, slice thickness = 1.2 mm, echo train length (ETL) = 1, and number of averages (NEX) = 1. TOF-MRA scan time was 4.11 min. Angiographic images were reconstructed with a maximum intensity projection (MIP) algorithm. Two sets of 15 MIP images were obtained by rotation of the stacked images along the vertical axis and horizontal axis. We also performed contrast-enhanced carotid MR angiography from the aortic arch to the whole brain by using coronal planes with a 3D spoiled gradient echo sequence optimized for high spatial resolution and intravenous bolus injection of 0.03 mmol/kg gadofosveset trisodium (Vasovist, Schering, Berlin, Germany), which was administered with an automatic injector at a rate of 1 ml/s through an 18-gauge cannula placed in the antecubital vein of the right arm, followed by 15 ml of saline solution. The following imaging parameters were used: TR/TE = 4.9/1.7 ms, flip angle = 27°, slice thickness = 1.0 mm, matrix size = 384×384, voxel size = 1×1×0.7 mm. Optimal delay between injection and acquisition of flip angles was evaluated using the bolus tracking technique. Angiographic images of proximal cervical arteries were reconstructed with the MIP algorithm. Percentage stenosis of the ICA was determined from contrast-enhanced carotid MR angiography per NASCET criteria.

Image analysis

COW morphology was analyzed by two experienced reviewers (G.H.C and S.B.H) blinded to the clinical and demographic details of the subjects using personal computer-based software (Rapidia, Infinitt, Seoul, Korea). We initially analyzed COW morphology using axial source images obtained from 3D TOF MR angiography followed by volume rendering reconstruction. Features of the anterior and posterior parts of the COW were evaluated separately and categorized into several patterns (Figure 1). The aim of image assessment was to confirm the completeness or incompleteness of the COW and to identify and record the prevalence of different anatomic variations. We defined the anterior posterior section as A1, A2, and the anterior communicating artery, while we defined the

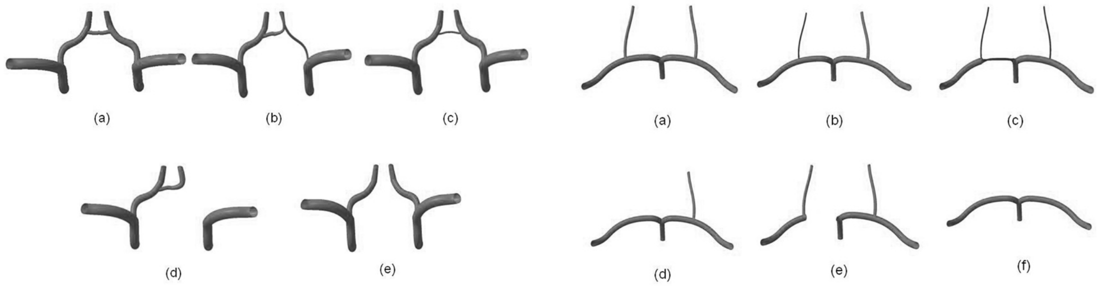

Figure 1. Schematic views of anatomic variations of the anterior (A) and posterior (B) circulation of the circle of Willis.

A. Demonstrable anterior communicating artery (a), hypoplastic A1 segment (b), hypoplastic anterior communicating artery (c), widely separated A1 segments with no demonstrable anterior communicating artery (d), absence of A1 segment (e). The anterior part of the circle of Willis was considered complete in type a, indeterminate in types b and c, and incomplete in types d and e.

B. Demonstrable posterior communicating artery and P1 segment (a), hypoplastic posterior communicating artery or P1 segment (b and c), no demonstrable posterior communicating artery (d), no demonstrable P1 segment (e), and absence of bilateral posterior communicating artery (f). The posterior part of the circle of Willis was considered complete in type a, indeterminate in types b and c, and incomplete in types d, e, and f.

posterior circulation as P1, P2, and the posterior communicating artery. Based on the vessel size seen on 3D TOF MR angiography, the component vessels of COW were classified as normal, hypoplastic, or absent. We considered the anterior communicating artery to be normally patent if the anterior communicating artery was clearly visualized or junctions of the A1 and A2 segments were in close contact and were not separable from each other on 3D TOF MR angiography. Hypoplasia of the anterior communicating artery and posterior communicating artery was defined as an artery diameter of less than 1 mm. If one of the components of the anterior or posterior circulation was hypoplastic and not absent, its role as a collateral pathway for cerebral blood flow was considered indeterminate. If one of the components of the COW was absent, it was considered to be incomplete. If all components of the COW were intact, the COW was considered complete. Morphology of the anterior and posterior circulation of the COW was classified as bilateral incomplete, bilateral complete, incomplete – complete + indeterminate, or other.

Statistical analysis

Continuous values are expressed as medians [inter-quartile ranges (IQR)] and/or ranges and categorical data as counts and percentages. Subjects were classified as young normal, older normal, or carotid artery disease. Continuous and categorical variables were compared among these groups using the Mann-Whitney test and Fisher's exact test, respectively. Statistical significance was defined as $p < 0.05$. All statistical analyses were performed using R 2.14.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patients

Of 95 young subjects, five had diffuse or focal luminal narrowing of the middle cerebral artery. These patients were diagnosed with Moyamoya's disease. Two had stenosis of the proximal carotid artery and two had MR angiographs of poor image quality. Of 95 older subjects, two had atherosclerotic plaques in the proximal carotid artery and two had stenosis of the middle cerebral artery. Therefore, 177 normal subjects (91 older subjects; 86 young subjects) were included in this study. Also, of 77 patients who underwent CAS, 16 did not undergo MR angiography and eight had stenosis of the middle cerebral artery or basilar artery. We therefore recruited 53 patients with carotid artery disease who had available preprocedural 3D TOF MR angiography results.

Demographic data of normal subjects and patients with carotid artery disease are presented in Table 1. The proportion of males in the carotid disease group was significantly higher than the proportion of males in the normal subject groups ($p < 0.001$).

Table 1: Demographic data of normal subjects and patients with carotid artery disease

	Total (n = 230)	Young normal subjects (n = 86)	Old normal subjects (n = 91)	Patients (n = 53)
Age (years) [Median]	64	36 [31 – 39]	69 [65 – 77]	73 [66 – 78]
Male (%)	122 (53.0)	39 (45.3)	37 (40.7)	46 (86.8)*

*: Significant difference between normal old subjects and carotid disease patients ($p < 0.05$).

Anterior circulation

Table 2 lists the prevalence of each morphological variant of the anterior circulation corresponding to the schematic variants illustrated in Figure 1A. The prevalence of a normal circulation was significantly lower in the patient group (62.3%) than in the normal young group (84.9%) or normal older group (87.9%) ($p < 0.01$). Patients had a significantly higher incidence of incomplete anterior circulation (20.7%) than normal older subjects (5.5%) ($p < 0.01$). A1 absence was found only in the patient group (7.5%).

Posterior circulation

Table 3 lists the prevalence of each of the morphological variants of the posterior circulation corresponding to the schematic variants illustrated in Figure 1B. A complete posterior circulation pattern was more frequent in normal young subjects (46.5%) than in normal older subjects (16.5%) or the patient group (18.9%) ($p < 0.01$). Patients showed a significantly higher prevalence of bilateral absence of the posterior circulation (17.0%) than normal older subjects (5.5%) ($p < 0.05$).

General morphology of the circle of Willis

Of patients with carotid artery stenosis, 18.9% had a bilateral incomplete connection and were significantly more likely to have an incomplete pattern than normal young (2.3%) or normal older subjects (2.2%) ($p < 0.001$) (Table 4). Conversely, younger subjects were more likely to have bilateral complete connections (41.9%) than normal older subjects (15.4%) or the patient group (17.0%) ($p < 0.01$).

DISCUSSION

The major finding of the current study is a significantly lower prevalence of a complete anterior circulation pattern in patients with carotid atherosclerotic stenosis than normal subjects. Normal younger subjects were significantly more likely to have a complete posterior circulation pattern than older subjects and patients, while patients with carotid atherosclerotic stenosis were more likely to show bilateral absence of the posterior circulation. Patients with carotid

Table 2: Comparison of the morphology of the anterior circulation between normal subjects and patients

Patterns	Total, n = 230 (%)	Young normal subjects, n = 86 (%)	Old normal subjects, n = 91 (%)	Patients, n = 53 (%)
Complete	186 (80.9)	73 (84.9)	80 (87.9)	33 (62.3)*
Indeterminate	21 (9.1)	6 (7.0)	6 (6.6)	9 (17.0)
Acom hypoplasia	19 (8.3)	5 (5.8)	6 (6.6)	8 (15.1)
AI hypoplasia	2 (0.9)	1 (1.2)	0 (0.0)	1 (1.9)
Incomplete	23 (10.0)	7 (8.1)	5 (5.5)	11 (20.7)**
Acom absence	19 (8.3)	7 (8.1)	5 (5.5)	7 (13.2)
A1 absence	4 (1.7)	0 (0.0)	0 (0.0)	4 (7.5)*

*: Significant difference between normal subject and carotid disease groups ($p < 0.05$).
**: Significant difference between normal old subject and carotid disease groups ($p < 0.05$).
Acom: anterior communicating artery, Hypoplasia: artery diameter < 1 mm on TOF MR angiography. Absence: no visualization of artery on TOF MR angiographs

Table 3: Comparison of the morphology of the posterior circulation between normal subjects and patients

Patterns	Total, n = 230 (%)	Young normal subjects, n = 86 (%)	Old normal subjects, n = 91 (%)	Patients, n = 53 (%)
Complete 65 (28.3)	40 (46.5)*	15 (16.5)	10 (18.9)	
Indeterminate	90 (39.1)	24 (27.9)**	45 (49.5)	21 (36.9)
Unilateral hypoplasia	55 (23.9)	14 (16.3)	25 (27.5)	16 (30.2)
Bilateral hypoplasia	35 (15.2)	10 (11.6)	20 (22.0)	5 (9.4)
Incomplete	75 (32.6)	22 (25.6)	31 (34.0)	22 (41.5)
Unilateral absence	23 (10.0)	8 (9.3)	9 (9.9)	6 (11.3)
Unilateral absence and contralateral hypoplasia	32 (13.9)	8 (9.3)	17 (18.7)	7 (13.2)
Bilateral absence	20 (8.7)	6 (7.0)	5 (5.5)	9 (17.0)#

*: Significant difference between normal young subjects and normal old subjects or patients ($p < 0.05$).
**: Significant difference between normal young subjects and normal old subjects ($p < 0.05$).
#: Significant difference between normal old subjects and patients ($p < 0.05$).
Hypoplasia: artery diameter < 1 mm on TOF MR angiography. Absence: no visualization of artery on TOF MR angiography.

atherosclerotic stenosis were also significantly more likely to show incomplete bilateral connection than normal young and older subjects.

In previous studies, the reported prevalence of a complete anterior circle ranged from 74% to 90%, while the prevalence of a complete posterior circle varied from 31% to 52% in the normal population.[8,12,15] Based on an autopsy study, Alpers *et al*.[16] reported a high prevalence of a complete COW in normal brains (52%). In previous studies based on imaging modalities, the prevalence of a complete COW in normal subjects ranged from 31% to 42%. Krabbe-Hartkamp *et al*.[8] reported that a complete anterior circle showed a similar prevalence in normal younger and older subjects (86% vs. 68%, respectively), while a complete circle was more common in younger subjects than older subjects (54% of younger subjects vs. 36% of older subjects). In our study, we found a complete anterior circle in 86.4% of normal subjects, with a similar prevalence in normal younger and older subjects (84.9 vs. 87.9%, respectively). Furthermore, normal young subjects were significantly more likely to have a complete posterior circle (46.5%) than normal older subjects (16.5%), and normal young subjects were significantly more likely to have a complete bilateral connection (41.9%) than normal older subjects (15.4%).

Table 4: Comparison of the general morphology of the circle of Willis between normal subjects and patients

Patterns	Total, n = 230 (%)	Young normal subjects, n = 86 (%)	Old normal subjects, n = 91 (%)	Patients, n = 53 (%)
Bilateral complete	59 (25.7)	36 (41.9)**	14 (15.4)	9 (17.0)
Incomplete and complete	57 (24.8)	21 (24.4)	25 (27.5)	11 (20.8)
Incomplete and indeterminate	13 (5.7)	4 (4.7)	7 (7.7)	2 (3.8)
Bilateral indeterminate	11 (4.8)	3 (3.5)	1 (1.1)	7 (13.2)
Complete and indeterminate	76 (33.0)	20 (23.3)	42 (46.2)	14 (26.4)
Bilateral incomplete	14 (6.1)	2 (2.3)	2 (2.2)	10 (18.9)*

*: Significant difference between patients and normal subjects ($p < 0.05$).
**: Significant difference between normal young subjects and normal old subjects or patients ($p < 0.05$).

Krabbe-Hartkamp *et al*.[8] also reported that mean vessel diameter differed according to age and sex. Diameters of vessels in the COW tended to be smaller in normal older subjects than normal young subjects, while the diameter of the internal carotid artery and basilar artery tended to be significant larger in the normal older subjects. This might be due to compensatory enlargement of large vessels in elderly persons in reaction to decreased cardiac output, decreased vessel elasticity, or atherosclerosis, of which the prevalence is known to increase with age. Also, these factors may account for the lower velocity of blood flow in vessels of older individuals. Smaller COW vessel diameters in the elderly are likely related to 3D TOF signal intensity, which is dependent on blood flow velocity, because blood flow rate in these vessels decreases with age and decreased blood flow velocity is known to cause signal intensity loss.[14] Blood brain barrier permeability increases with normal aging and may be an important mechanism in the initiation or worsening of cerebral microvascular disease.[17] Capillary surface area decreases while capillary diameter, volume, and total length increase. This age-related degeneration of the brain vascular structure and function may lead to disruption of local perfusion.[18] In our study, normal older subjects had a lower prevalence of complete connection of the COW than normal younger subjects. This may be due to factors such as age-related low cardiac output, degeneration of brain vascular structures, or microatherosclerosis of small brain arteries.

COW is important because the prevalence of adequate collateral supply via the COW is associated with a reduced risk of recurrent stroke[19], a smaller infarct size[20], a normal response to CO_2 reactivity tests[21] and a reduced occurrence of ischemia during clamping of the carotid artery.[7] Likewise, a significant difference in the prevalence of normal circles between patients with and without cerebral infarction has been shown at autopsy (22 vs. 52%, respectively).[22] In addition, asymmetry of the A1 segment is significantly more frequent in patients with infarction than those without infarction (28 vs. 14%), and cerebral infarction is most frequently seen when asymmetric A1 segments are present in combination with an ipsilateral fetal variant of the posterior circulation. These findings indicate that compromised collateral supply by the COW is associated with an increase in occurrence of cerebral infarction.

In previous studies, the prevalence of a complete anterior circle in patients with carotid atherosclerotic stenosis ranged from 80% to 88%, while the prevalence of a complete posterior circle varied from 31% to 52% in the normal population and from 8.1% to 63% in patients with carotid atherosclerotic stenosis.[7,23,24] We found a significantly lower prevalence of complete anterior circulation in the patient group (62.3%) than the normal groups. Hypoplasia or absence of the A1 segment is uncommon. Autopsy studies revealed that hypoplastic A1 segments were present in 2 – 12% of normal brains, while A1 segments were absent in only 2 – 4% of normal brains.[16,25] Waaijer *et al*.[24] reported a prevalence of 15% nonvisualized and 17% hypoplastic A1 segments in patients using CT angiography. Some studies have reported that the anterior pathway plays an important role in the prevention of cerebral infarction in the presence of carotid artery stenosis.[4,9,26] In our study, A1 absence was found only in the patient group (7.5%).

The fetal type of posterior circulation is an important variant of the posterior COW. The reported prevalence of fetal posterior circulation varies greatly. In many cases, the ipsilateral proximal P1 segment is hypoplastic or absent. In patients with an adult configuration and an invisible or hypoplastic Pcom, the collateral circulation is also jeopardized, and this configuration is a risk factor for cerebral ischemia in patients with carotid artery occlusion.[6] In our study, bilateral absence of the Pcom or P1 in the patient group was significantly higher than in normal older subjects.

We also found that patients with carotid atherosclerotic stenosis showed a significantly higher prevalence of bilateral incomplete connection than normal younger and older subjects. Two studies reported that a complete circle was more often present in patients than controls[23,27], while other studies reported that the absence of a collateral pathway in symptomatic patients was associated with an increased risk of infarction[9,28] or that no difference in circle morphology existed between patients with symptomatic and asymptomatic carotid stenosis.[4,7] Waaijer *et al*.[24] reported a compromised anterior and posterior pathway in 26% of patients compared to only 4% of normal subjects. The presence of bilateral incomplete segments of the COW may result in a single major artery, such as the internal carotid artery, supplying several cerebral artery territories, with little collateral flow provided by other arteries. We hypothesize that patients with simultaneously bilateral incomplete segments of the COW and carotid atherosclerotic stenosis may show cerebral hypoperfusion or ischemia because of poor collateral flow.

Various imaging techniques such as digital subtraction angiography, CT angiography, TOF or contrast-enhanced MR angiography, and transcranial Doppler have been used to evaluate the COW. CT and MR angiography have been more commonly used in recent years because these are noninvasive and objective modalities. Furthermore, these imaging modalities allow visualization of the small vessels of COW using 3D programs that provide volume-rendered images. CT angiography is not dependent on flow velocity, thereby allowing accurate documentation of vessel diameters. The disadvantages of CT angiography compared to MR angiography include lack of information regarding flow direction, possible venous contamination, radiation exposure, and administration of iodinated contrast material. 3D TOF MR angiography is adequately sensitive and specific for the detection of COW patterns, but it does have its limitations. Some of the vessels cannot be seen with 3D TOF MR angiography because of turbulent flow, the saturation effect of slow flow or long in-plane flow, or slower velocity of the blood adjacent to the wall due to laminar flow.[14,29,30] In addition, laminar flow-related spin dephasing and partial volume averaging at the vessel wall may result in reduction of the vessel on source images and the MIP algorithm. This study was performed with a dedicated MRA protocol, in which the acquired resolution was 0.6 x 0.6 x 0.6 mm^3 isotropic to maximize uniform visualization of small vessels in all planes relative to 0.80 x 0.80 x 1.20 mm^3. Furthermore, we used a 3D program to volume-render images for accurate evaluation of the small vessels of the COW.

Our study had several limitations. First, hypoplastic vessels in the COW have been defined using different sets of criteria. Vessels with a diameter smaller than 0.8 mm[8,10,23] or 1 mm have been considered hypoplastic.[7,15,24] In our study, we chose a cut-off of <1 mm to define hypoplasia based on autopsy studies and flow models, which reported significant flow reduction below this diameter.[6,16] Second, we did not analyze the prevalence of fetal posterior circulation nor compare this configuration of the COW between patients and normal subjects. Fetal posterior circulation is the most important and common variant of the COW, and is an important source of collateral supply. However, the primary purpose of our study was to compare morphological variants of the COW among normal subjects and those with carotid atherosclerotic stenosis. Therefore, we did not include the prevalence of fetal posterior circulation in this study. Third, although patients showed a significantly higher prevalence of bilateral incomplete connection of the COW than normal subjects, we did not analyze the clinical significance of this. Further studies are required to evaluate the relationship between brain perfusion and morphological patterns of the COW in patients with carotid atherosclerotic stenosis.

In conclusion, we compared the morphology of the COW between normal younger and older subjects, and between normal subjects and patients with carotid atherosclerotic stenosis using 3D TOF MR angiography. Young subjects showed a significantly higher prevalence of complete posterior circulation and a bilateral complete circle than older subjects. Furthermore, patients with carotid atherosclerotic plaques had a higher prevalence of an incomplete anterior circulation or incomplete COW than normal subjects. These findings are consistent with previous studies that showed that age-related vascular diseases, such as degeneration or atherosclerosis of small arteries or collapse of small arteries due to low cardiac output, may affect the diameter of small arteries in the COW, and that incomplete collateral circulation via the COW may play an important role in the development of symptoms in patients with carotid atherosclerotic stenosis.

ACKNOWLEDGEMENT

This paper was supported by Fund of Biomedical Research Institute, Chonbuk National University Hospital in 2013.

REFERENCES

1. Harnsberger HR, Osborns AG, Ross JS, *et al*. Diagnostic and Surgical Imaging Anatomy: Brain, Head and Neck, Spine. Amirsys, Salt Lake City, 2006
2. Moore K, Agur A. Essential Clinical Anatomy, 2nd edn. Lippincott Williams & Wilkins, Baltimore, 2002
3. Sinnatamby S. Last's Anatomy: Regional and Applied, 11th edn. Churchill Livingstone, Edinburgh, 2006
4. Kluytmans M, Van der Grond J, Van Everdingen KJ, Klijn CJM, Kappelle LJ, Viergener MA. Cerebral hemodynamics in relation to patterns of collateral flow. *Stroke* 1999; 30:1432-9
5. Müller M, Schimrigk K. Vasomotor reactivity and pattern of collateral blood flow in severe occlusive carotid artery disease. *Stroke* 1996; 27:296-9
6. Schomer DF, Marks MP, Steinberg GK, *et al.* The anatomy of the posterior communicating artery as a

risk factor for ischemic cerebral infarction. *N Engl J Med* 1994; 330:1565-70

7. Lee JH, Choi CG, Kim DK, Kim GE, Lee HK, Suh DC. Relationship between Circle of Willis morphology on 3D time-of-flight MR angiograms and transient ischemia during vascular clamping of the internal carotid artery during carotid endarterectomy. *AJNR Am J Neuroradiol* 2004; 25:558-64
8. Krabbe-Hartkamp MJ, van der Grond J, de Leeuw FE, *et al*. Circle of Willis: morphologic variation of three-dimensional time-of-flight MR angiograms. *Radiology* 1998; 207:103-11
9. Miralles M, Dolz JL, Cotillas J, *et al*. The role of the circle of Willis in carotid occlusion: assessment with phase contrast MR angiography and transcranial duplex. *Eur J Vasc Endovasc Surg* 1995; 10:424-30
10. El-Barhoun EN, Gledhill SR, Pitman AG. Circle of Willis artery diameters on MR angiography: an Australian reference database. *J Med Imaging Radiat Oncol* 2009; 53:248-60
11. Tanaka H, Fujita N, Enoki T, *et al*. Relationship between variations in the Circle of Willis and flow rates in interncal carotid and basilar arteries determined by means of magnetic resonance imaging with semiautomated lumen segmentation: reference data from 125 healthy volunteers. *AJNR Am J Neuroradiol* 2006; 27:1770-5
12. Li Q, Li J, Lv F, Li K, Luo T, Xie P. A multidetector CT angiography study of variations in the circle of Willis in a Chinese population. *J Clin Neurosci* 2011; 18:379-83
13. Han A, Yoon DY, Chang SK, *et al*. Accuracy of CT angiography in the assessment of the circle of Willis: comparison of volume-rendered images and digital subtraction angiography. *Acta Radiologica* 2011; 52:889-93
14. Stock KW, Wetzel S, Kirsch E, Bongartz G, Steinbrich W, Radue EW. Anatomic evaluation of the circle of Willis: MR angiography versus intraarterial digital subtraction angiography. *AJNR Am J Neuroradiol* 1996; 17:1495-9
15. Eftekhar B, Dadmehr M, Ansari S, Ghodsi M, Nazparvar B, Ketabchi E. Are the distributions of variations of circle of Willis different in different populations? Results of an anatomical study and review of literature. *BMC Neurol* 2006; 6:22.
16. Alpers BJ, Berry RG, Paddison RM. Anatomical studies of the circle of Willis in normal brain. *AMA Arch Neurol Psychiatry* 1959; 81:409-18
17. Farrall AJ, Wardlaw JM. Blood-brain barrier: aging and microvascular disease-systematic review and meta-analysis. *Neurobiol Aging* 1009; 30:337-52
18. Sierra C, Coca A, Schiffrin EL. Vascular mechanism in the pathogenesis of stroke. *Curr Hypertens Rep* 2011; 13:200-7
19. Henderson RD, Eliasziw M, Fox AJ, Rothwell PM, 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; 31:128-32
20. Rodda RA. The arterial patterns associated with internal carotid disease and cerebral infarcts. *Stroke* 1986; 17:69-75
21. Norrving B, Nilsson B, Risberg J. rCBF in patients with carotid occlusion: resting and hypercapnic flow related to collateral pattern. *Stroke* 1982; 13:155-62
22. Kameyama M, Okinaka SH. Collateral circulation of the brain with special reference to atherosclerosis of the major cervical and cerebral arteries. *Neurology* 1963; 13:279-86
23. Hartkamp MJ, van der Grond J, van Everdingen KJ, Hillen B, Mali WPTM. Circle of Willis collateral flow investigated by magnetic resonance angiography. *Stroke* 1999;30:2671-8
24. Waaijer A, van Leeuwen MS, van der Worp HB, Verhagen HJM, Mali WPTM, Velthuis BK. Anatomic variations in the circle of Willis in patients with symptomatic carotid artery stenosis assessed with multidetector row CT angiography. *Cerebrovasc Dis* 2007; 23:267-74
25. Lazorthes G, Gouaze A. The arterial circle of the brain (circulus arteriosus cerebri). *Anat Clin* 1979; 1:241-57
26. Hendrikse J, Eikelboom BC, van der Grond J. Magnetic resonance angiography of collateral compensation in asymptomatic and symptomatic internal carotid artery stenosis. *J Vasc Surg* 2002; 36:799-805
27. Hedera P, Bujdakova J, Traubner P, Pancak J. Stroke risk factors and development of collateral flow in carotid occlusive disease. *Acta Neurol Scand* 1998; 98:182-6
28. Hoksbergen AW, Legemate DA, Csiba L, Csati G, Siro P, Fulesdi B. Absent collateral function of the circle of Willis as risk factor for ischemic stroke. *Cerebrovasc Dis* 2003; 16:191-8
29. Laub GA. Time-of-flight method of MR angiography. Magn *Reson Imaging Clin N Am* 1995; 3:391-8
30. Parker DL, Parker DJ, Blatter DD, Du YP, Goodrich KC. The effect of image resolution on vessel signal in high resolution magnetic resonance angiography. *J Magn Reson Imaging* 1996; 6:632-41