Neurological Sciences (2019) 40:509–514
https://doi.org/10.1007/s10072-018-3683-9

ORIGINAL ARTICLE

Completeness of circle of Willis and white matter hyperintensities in patients with severe internal carotid artery stenosis

Huirong Ye[1] · Xiumei Wu[1] · Jiangzhi Yan[1] · Jian Wang[1] · Jianting Qiu[1] · Yujie Wang[1]

Received: 18 August 2018 / Accepted: 10 December 2018 / Published online: 15 December 2018

Abstract

Background We investigated whether completeness of the circle of Willis (CoW) protected patients with severe internal carotid artery (ICA) stenosis against white matter hyperintensities (WMHs).

Methods We included 115 patients with unilateral ICA stenosis ≥ 70%. The completeness of CoW was assessed and WMHs were rated on a visual scale. The score of deep and periventricular WMHs was compared between patients with complete and incomplete CoW and between the two hemispheres, ipsilateral and contralateral to stenosed ICA.

Results We included 115 patients with severe ICA stenosis, 60 patients had a complete CoW (52.17%) and 55 had an incomplete CoW (47.83%). The patients with incomplete CoW had higher score of deep WMHs (OR = 1.82, 95% CI 1.08–3.06, $P = 0.023$) and periventricular WMHs (OR = 4.53, 95% CI 2.09–9.81, $P = 0.000$) than those with complete CoW. In the patients with incomplete CoW, the score of deep WMHs (OR = 4.14, 95% CI 1.33–12.93, $P = 0.014$) and periventricular WMHs (OR = 5.46, 95% CI 1.16–25.62, $P = 0.032$) was higher in the hemisphere ipsilateral to stenosed ICA than that in the contralateral hemisphere. In the patients with complete CoW, there was no significant difference in the score of deep WMHs (OR = 2.10, 95% CI 0.37–11.91, $P = 0.401$) and periventricular WMHs (OR = 2.83, 95% CI 0.99–8.05, $P = 0.051$) between the ipsilateral and contralateral hemispheres to stenosed ICA.

Conclusion The completeness of CoW protected patients with severe ICA stenosis against WMHs.

Keywords Circle of Willis · White matter hyperintensities · Internal carotid artery stenosis

Silent cerebrovascular disease is the most common incidental finding on brain imaging [1]. One of the best-defined manifestations of silent cerebrovascular disease is white matter hyperintensities (WMHs) of presumed vascular origin [2], which identifies WMHs from others relating to demyelinating diseases, such as infectious, toxic, or metabolic processes. WMHs had been studied over half a century and experts are keeping on investigating the etiopathology as WMHs could lead to increased risk of stroke, dementia, death [3], and impact on the quality of life in stroke survivors [4]. It is recognized that WMHs are associated with age, hypertension, small vascular disease [5], chronic carotid atherosclerosis [6], and carotid artery stenosis [7]. The severity of the internal carotid artery (ICA) stenosis is assumed to be an important factor for WMHs [8, 9]. It is necessary to study protective factors for WMHs further.

ICA stenosis is defined as the maximal luminal narrowing and its severity is rated according to the percentage of stenosis. The 70–99% has been termed severe ICA stenosis that is the main target of the treatment. Studies remain largely constrained to the maximal degree of ICA stenosis while ignoring the collateral blood flow status. The circle of Willis (CoW) is the main collateral system that connects the bilateral

✉ Yujie Wang
wangyujie196508@163.com

Huirong Ye
287389312@qq.com

Xiumei Wu
wxiumei123456@126.com

Jiangzhi Yan
2281889871@qq.com

Jian Wang
wangjian.1982@163.com

Jianting Qiu
562688005@qq.com

[1] Cerebrovascular Disease Center, Department of Neurology, People's Hospital, China Medical University, 33 Wenyi Road, Shenhe District, Shenyang 110016, People's Republic of China

carotid systems with the posterior circulation. In patients with severe ICA stenosis, collateral flow provided by the CoW is paramount to maintaining the cerebral perfusion pressure. Three-dimension time-of-flight magnetic resonance angiography (3D TOF MRA) is routinely used for imaging the proximal intracranial vasculature and is available for evaluating cerebral collateral with the advantages of high spatial resolution and lack of an intravenous contrast agent. It has been used for the assessment of the collateral function of the CoW [10]. We investigated whether complete CoW could protect patients with severe ICA stenosis from WMHs.

Materials and methods

Consecutive patients admitted to the Cerebrovascular Disease Center, Department of Neurology, People's Hospital, China Medical University, between April 2016 and September 2017 were included if they (1) had recordings on age, sex, and risk factors of cerebrovascular diseases including the history of smoking, hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, and previous stroke, (2) had undergone blood tests, Doppler ultrasound of carotid arteries, transcranial Doppler, electrocardiogram, echocardiography, and brain MR image, (3) had unilateral ICA stenosis ≥ 70% (including occlusion) and contralateral ICA stenosis < 50% or no contralateral stenosis. The patients were excluded if they had (1) ICA stenosis of non-atherosclerotic, (2) infarctions affecting the assessment of WMHs, (3) other possible specific causes of WMHs, (4) possible risks of cardiac embolism according to Adams et al. [11], (5) concomitant diseases like brain tumors, abscess, hydrocephalus, or severe situations such as heart, renal, or respiratory function failure. The Ethics Committee of People's Hospital, China Medical University, approved the study protocol. All patients or their guardians signed informed consent with regard to participation in our study.

Imaging analysis

The imaging protocols included the series of T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR), diffusion-weighted image, and 3D-TOF MRA using 3.0T MR imaging (Discovery 750, GE Healthcare, USA) or 1.5T (MR 355, GE BRIVO, USA).

Periventricular WMHs and deep WMHs were judged according to Kim et al. [12] and evaluated separately on the axial section of the FLAIR sequence according to King et al. [13]. Briefly, periventricular WMHs were rated according to the distance perpendicular from the ventricle in the axial plane (thickness of a continuous band or distance of an extension towards the deep white matter) in four categories: (0) < 3 mm, (1) 3 to 10 mm, (2) 10 to 20 mm, and (3) ≥ 20 mm. Deep WMHs were rated according to the largest diameter in four categories: (0) < 3 mm for all lesions, (1) 3 to 10 mm for a single lesion or < 20 mm for grouped lesions, (2) 10 to 20 mm for a single lesion or > 20 mm for grouped lesions, and (3) > 20 mm for a single or confluent lesion. According to Wardlaw et al. [14], lacunar infarction was rated according to the number in three categories: (0) none, (1) 1 to 3, (2) ≥ 4. The perivascular space was evaluated as existent or not.

The circle of Willis (CoW) comprises the A1 segments of the two anterior cerebral arteries, the anterior communicating artery, the P1 segments of the two posterior cerebral arteries and the two posterior communicating arteries. The CoW was graded as complete if all the aforementioned vessels were visible and was graded as incomplete if any of the aforementioned vessels was invisible [15]. According to the completeness of CoW, our included patients were categorized into two groups: those with complete CoW and those with incomplete CoW. Intracranial artery stenosis was evaluated using MRA [16] and extracranial artery stenosis was evaluated using Duplex ultrasound (Siemens Antares, a 6–13 MHz transducer).

All the vascular assessment was conducted with the combination of source imaging with multiplanar reconstruction on 3D-TOF MRA. All the evaluations were performed on each cerebral hemisphere and were performed by two neurologists with the software PACS. When the two neurologists were in different opinions, it was settled by a discussion. If consensus could not be reached, a more senior expertise would be consulted.

Statistical analysis

An unpaired Student *t* test, or unpaired nonparametric Mann–Whitney U or $\chi 2$ test was used to conduct the univariate analysis between patients with complete CoW and incomplete CoW. Logistic regression analysis was used to examine the independent effect of the CoW on WMHs. The covariates included age, sex, and the variables with a P value of < 0.1 in the univariate analysis. A paired nonparametric Mann–Whitney U or $\chi 2$ test was used to conduct the univariable analysis between the two sides, ipsilateral and contralateral to stenosed ICA in all included patients, in the patients with complete CoW and in those with incomplete CoW separately. Conditional regression analysis was used to examine the independent effect of the CoW on WMHs. All tests were two-tailed, and $P < 0.05$ was considered statistically significant. All analyses were performed with SPSS 24.0 software.

Results

WMHs score in patients with complete and incomplete CoW

We included 115 patients with ICA stenosis ≥70%, 60 with complete CoW (52.17%), and 55 with incomplete CoW

Table 1 Clinical and imaging data on patients with complete and incomplete CoW

	Complete CoW ($n = 60$)	Incomplete CoW (n = 55)	P value
Age, years, mean ± SD	64.42 ± 10.15	70.22 ± 10.43	0.003*
Male, *n* (%)	50 (83.33)	44 (80.00)	0.644
Risk factors, *n* (%)			
Hypertension	39 (65.00)	43 (78.18)	0.119
Diabetes mellitus	29 (48.33)	23 (41.82)	0.483
Coronary artery disease	10 (16.66)	10 (18.18)	0.830
Atrial fibrillation	5 (8.33)	7 (12.73)	0.441
Smoking	26 (43.33)	16 (29.09)	0.130
Stroke history	14 (23.33)	23 (41.82)	0.034†
BP (mmHg, mean ± SD)			
Systolic	150.22 ± 19.89	155.91 ± 20.18	0.131
Diastolic	80.67 ± 11.30	82.55 ± 14.19	0.432
WMHs, median (IQR)			
DWMHs	1 (0–2)	3 (2–3)	0.000‡
PWMHs	1 (0–1)	2 (1–2)	0.000‡
Lacunar infarction, median (IQR)	0 (0–1)	1 (0–1)	0.022‡
Perivascular space, *n* (%)	22 (36.67)	32 (58.18)	0.021†

CoW, circle of Willis; *BP*, blood pressure at admission; *WMHs*, white matter hyperintensities; *DWMHs*, deep white matter hyperintensities, *PWMHs*, periventricular white matter hyperintensities, *IQR*, interquartile range

* *t* test

† Fisher exact

‡ Mann–Whitney test

(47.83%). Compared with the patients with complete CoW, the patients with incomplete CoW were older, had a higher incidence of stroke history and perivascular space, and a higher score of deep WMHs, periventricular WMHs, and lacunar infarction (Table 1). Logistic regression analysis showed that the patients with incomplete CoW had a higher score of deep WMHs (OR = 1.82, 95% CI 1.08–3.06, $P = 0.023$) and periventricular WMHs (OR = 4.53, 95% CI 2.09–9.81, $P = 0.000$) in patients with ICA stenosis ≥ 70% (Table 2).

WMHs score in all included patients: ipsilateral and contralateral to stenosed ICA

In the included 115 patients of ICA stenosis, the score of the deep and periventricular WMHs was higher in the side ipsilateral to stenosed ICA than that in the contralateral side (Table 3). Regression analysis showed that the score of deep WMHs (OR = 3.96, 95% CI 1.61–9.75, $P = 0.003$) and periventricular WMHs (OR = 3.37, 95% CI 1.48–7.67, $P = 0.004$) was higher in the side ipsilateral to stenosed ICA than that in the contralateral side in all patients with ICA stenosis ≥ 70% (Table 4).

Table 2 The results of logistic regression analysis in patients with incomplete versus complete CoW

	OR	95% confidence interval	P value
Age	1.03	0.97–1.09	0.386
Sex	1.11	0.26–4.72	0.886
Stroke history	1.61	0.50–5.18	0.428
DWMHs	1.82	1.08–3.06	0.023
PWMHs	4.53	2.09–9.81	0.000
Lacunar infarction	1.01	0.45–2.25	0.988
perivascular space	1.62	0.55–4.72	0.378

CoW, circle of Willis, *DWMHs*, deep white matter hyperintensities, *PWMHs*, periventricular white matter hyperintensities

WMHs score in the patients with complete CoW: ipsilateral and contralateral to stenosed ICA

In the 60 patients with complete CoW, the score of periventricular WMHs was higher in the side ipsilateral to stenosed ICA than that in the contralateral side, but there was no significant difference in deep WMHs between the two sides. There was no difference in the score of lacunar infarction and the incidence of perivascular space (Table 3). Regression analysis showed that there was no difference in the score of deep (OR = 2.10, 95% CI 0.37–11.91, $P = 0.401$) and periventricular WMHs (OR = 2.83, 95% CI 0.99–8.05, $P = 0.051$) between the two sides ipsilateral and contralateral to stenosed ICA in the patients with ICA stenosis ≥ 70% with complete CoW (Table 4).

WMHs score in the patients with incomplete CoW: ipsilateral and contralateral to stenosed ICA

In the 55 patients with incomplete CoW, the score of deep and periventricular WMHs was higher in the side ipsilateral to stenosed ICA than those in the contralateral side (Table 3). Regression analysis showed that the score of deep WMHs (OR = 4.14, 95% CI 1.33–12.93, $P = 0.014$) and

Table 3 The comparison of the score of WMHs between the two sides, ipsilateral, and contralateral to stenosed ICA

	Ipsilateral to stenosed ICA	Contralateral to stenosed ICA	*P* value
All included patients, *n* = 115			
DWMHs, median, (IQR)	2 (0–3)	1 (0–2)	0.000*
PWMHs, median, (IQR)	1 (1–2)	1 (0–2)	0.000*
Lacunar infarction, median, (IQR)	1 (0–1)	1 (0–1)	0.532
Perivascular space, *n* (%)	54 (46.96)	53 (46.09)	0.895
Patients with complete CoW, *n* = 60			
DWMHs, median, (IQR)	1 (0–2)	1 (0–1)	0.096
PWMHs, median, (IQR)	1 (0–2)	1 (0–1)	0.028*
Lacunar infarction, median, (IQR)	0 (0–1)	0 (0–1)	0.124
Perivascular space, *n* (%)	22 (36.67)	20 (33.33)	0.702
Patients with incomplete CoW, *n* = 55			
DWMHs, median, (IQR)	3 (2–3)	2 (1–3)	0.000*
PWMHs, median, (IQR)	2 (1–3)	2 (1–2)	0.000*
Lacunar infarction, median, (IQR)	1 (0–1)	1 (1–1)	0.532
Perivascular space, *n* (%)	32 (58.18)	33 (60.00)	0.846

ICA, internal carotid artery, *WMHs*, white matter hyperintensities, *DWMHs*, deep white matter hyperintensities, *PWMHs*, periventricular white matter hyperintensities, *IQR*, interquartile range, *CoW*, circle of Willis

* Mann–Whitney test

periventricular WMHs (OR = 5.46, 95% CI 1.16–25.62, *P* = 0.032) was higher in the side ipsilateral to stenosed ICA than those in the contralateral side in the patients with ICA stenosis ≥ 70% with incomplete CoW (Table 4).

Discussion

In our study, the incidence of complete CoW was 52.17%, similar to the previous reports [17, 18]. In the univariate analysis, the mean age of the patients with incomplete CoW was older than that of complete CoW, which was also observed by prior experts [19]. The incidence of stroke history and the occurrence of lacunar infarction were higher in patients with incomplete CoW than in those with complete CoW, which was consistent with the results of the previous studies reporting that effective collateral circulations reduced the risk of transient ischemic attack and stroke [20], and incompleteness of CoW significantly affected the occurrence of lacunar infarction [21].

In the multivariate analysis, compared with the patients with complete CoW, the patients with incomplete CoW had a higher score of deep and periventricular WMHs, which suggested that complete CoW protected the brain from suffering the change of WMHs in the patients with severe ICA stenosis. This was consistent with the prior results [22, 23]. Another study showed that the WMHs volume and number of lesions increased when two or more segments of the CoW were missing in subjects treated with carotid endarterectomy [24]. It was also demonstrated that different variant models of the CoW have different collateral capacities in the situation of unilateral ICA stenosis [25]. The study by Ryan et al. suggested that

Table 4 The results of conditional regression analysis in the ipsilateral side versus contralateral to stenosed ICA

	OR	95% confidence interval	*P* value
All included patients, *n* = 115			
DWMHs	3.96	1.61–9.75	0.003
PWMHs	3.37	1.48–7.67	0.004
Patients with complete CoW, *n* = 60			
DWMHs	2.10	0.37–11.91	0.401
PWMHs	2.83	0.99–8.05	0.051
Patients with incomplete CoW, *n* = 55			
DWMHs	4.14	1.33–12.93	0.014
PWMHs	5.46	1.16–25.62	0.032

CoW, circle of Willis, *ICA*, internal carotid artery, *DWMHs*, deep white matter hyperintensities, *PWMHs*, periventricular white matter hyperintensities

incomplete CoW correlates with the incident of white matter disease, but the ICA stenosis of the participants was not assessed [26]. Nevertheless, our results were not consistent with those by Li et al., where the CoW and severe carotid atherosclerosis may not be related to white matter lesions. This might be caused by the different methods of rating WMHs, their exclusion of new and old infarcts which are associated with the CoW and severe carotid atherosclerosis and fewer participants, only 59 participants with unilateral stenosis [27].

Further, we compared the two sides, contralateral and ipsilateral sides to stenosed ICA. In all patients with ICA stenosis, the score of deep and periventricular WMHs was higher in the side ipsilateral to stenosis than that in the contralateral side, this was also true for patients with incomplete CoW. But in the patients with complete CoW, there was no significant difference in the score of deep and periventricular WMHs between the ipsilateral and contralateral sides to the stenosis. This further suggested that complete CoW protected the brain from suffering the change of WMHs in the patients with severe ICA stenosis. Completeness of CoW is regarded as the major source of collateral blood flow and is crucial to maintaining adequate perfusion pressure in patients with severe ICA stenosis. These were supported by the finding that in patients with asymptomatic ICA stenosis, the prevalence of collateral flow via the CoW was significantly increased compared with the symptomatic patients and control subjects. Patients with asymptomatic ICA stenosis demonstrated the largest mean diameter of the arteries of the CoW compared with patients with symptomatic ICA stenosis and control subjects. These studies suggested the importance of adequate hemodynamic compensation via the CoW in patients with ICA stenosis [28, 29]. The study by Men et al. suggested a higher prevalence of leukoaraiosis in southern Han Chinese patients with branch atheromatous disease which is a kind of atherosclerosis [30]. The proposed mechanisms that underlie the pathophysiology of WMHs in chronic atherosclerotic ICA stenosis may include artery-to-artery embolism, branch artery disease, and hypoperfusion [31].

There were some limitations to our study. We only compared CoW completeness versus incompleteness without differentiating the anterior or the posterior part of the CoW. Moreover, we only investigated the image change of WMHs without observing the changes of hemodynamics. Finally, the sample was not large and a larger sample is required for further investigation.

In conclusion, the score of WMHs was higher in patients with incomplete CoW than that in complete CoW in the setting of severe ICA stenosis. The score of WMHs was higher in the side ipsilateral to stenosed ICA than that in the contralateral side in the patients with incomplete CoW, while there was no significant difference in those with complete CoW. This suggested that complete CoW could protect the brain from suffering WMHs even in patients with severe ICA stenosis. Our results suggested that when the ICA stenosis related to brain injury is considered, the maximal degree of ICA stenosis is not the only contributor. CoW supplied collateral blood flow ought to be considered even in severe ICA stenosis. This data reminds us that the completeness of CoW might be included in the risk stratification of ICA stenosis.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Vernooij MW, Ikram MA, Tanghe HL, Vincent AJ, Hofman A, Krestin GP, Niessen WJ, Breteler MM, van der Lugt A (2007) Incidental findings on brain MRI in the general population. N Engl J Med 357:1821–1828
2. Smith EE, Saposnik G, Biessels GJ, Doubal FN, Fornage M, Gorelick PB, Greenberg SM, Higashida RT, Kasner SE, Seshadri S, American Heart Association Stroke Council; Council on Cardiovascular Radiology and Intervention; Council on Functional Genomics and Translational Biology; and Council on Hypertension (2017) Prevention of stroke in patients with silent cerebrovascular disease: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 48:e44–e71
3. Debette S, Markus HS (2010) The clinical importance of white matter hyperintensities on brain magnetic resonance imaging: systematic review and meta-analysis. BMJ 341:c3666
4. Tang WK, Liang HJ, Chen YK, Ahuja AT, Chu WCW, Mok VCT, Ungvari GS, Wong KS (2013) White matter hyperintensities and quality of life in acute lacunar stroke. Neurol Sci 34:1347–1353
5. The LADIS Study Group, Poggesi A, Pantoni L, Inzitari D, Fazekas F, Ferro J, O'Brien J, Hennerici M, Scheltens P, Erkinjuntti T, Visser M, Langhorne P, Chabriat H, Waldemar G, Wallin A, Wahlund A (2011) 2001-2011: a decade of the LADIS (Leukoaraiosis and disability) study: what have we learned about white matter changes and small-vessel disease? Cerebrovasc Dis 32:577–588
6. Ben-Assayag E, Mijajlovic M, Shenhar-Tsarfaty S, Bova I, Shopin L, Bornstein NM (2012) Leukoaraiosis is a chronic atherosclerotic disease. Sci World J 2012:6. https://doi.org/10.1100/2012/532141
7. Ye H, Wang Y, Qiu J, Wu Q, Xu M, Wang J (2018) White matter hyperintensities and their subtypes in patients with carotid artery stenosis: a systematic review and meta-analysis. BMJ Open 8:e020830
8. Saba L, Sanfilippo R, Pascalis L, Montisci R, Mallarini G (2009) Carotid artery abnormalities and leukoaraiosis in elderly patients: evaluation with MDCT. Am J Roentgenol 192:W63–W70
9. Enzinger C, Ropele S, Gattringer T, Langkammer C, Schmidt R, Fazekas F (2010) High-grade internal carotid artery stenosis and chronic brain damage: a volumetric magnetic resonance imaging study. Cerebrovasc Dis 30:540–546
10. Hoksbergen AW, Majoie CB, Hulsmans FJ, Legemate DA (2013) Assessment of the collateral function of the circle of Willis: three-dimensional time-of-flight MR angiography compared with transcranial color coded duplex sonography. Am J Neuroradiol 24:456–462

11. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, Marsh EE 3rd (1993) Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of org 10172 in acute stroke treatment. Stroke 24:35–41
12. Kim KW, MacFall JR, Payne ME (2008) Classification of white matter lesions on magnetic resonance imaging in elderly persons. Biol Psychiatry 64:273–280
13. King KS, Peshock RM, Warren MW, Alhilali L, Hulsey K, McColl R, Weiner MF, Ayers C, Whittemore A (2013) Evaluation of a practical visual MRI rating scale of brain white matter hyperintensities for clinicians based on largest lesion size regardless of location. AJNR Am J Neuroradiol 34:797–801
14. Wardlaw JM, Smith EE, Biessels GJ, Cordonnier C, Fazekas F, Frayne R, Lindley RI, O'Brien JT, Barkhof F, Benavente OR, Black SE, Brayne C, Breteler M, Chabriat H, Decarli C, de Leeuw FE, Doubal F, Duering M, Fox NC, Greenberg S, Hachinski V, Kilimann I, Mok V, Oostenbrugge R, Pantoni L, Speck O, Stephan BC, Teipel S, Viswanathan A, Werring D, Chen C, Smith C, van Buchem M, Norrving B, Gorelick PB, Dichgans M, STandards for ReportIng Vascular changes on nEuroimaging (STRIVE v1) (2013) Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration. Lancet Neurol 12:822–838
15. Stock KW, Wetzel S, Kirsch E, Bongartz G, Steinbrich W, Radue EW (1996) Anatomic evaluation of the circle of Willis: MR angiography versus intraarterial digital subtraction angiography. AJNR Am J Neuroradiol 17:1495–1499
16. Samuels OB, Joseph GJ, Lynn MJ, Smith HA, Chimowitz MI (2000) A standardized method for measuring intracranial arterial stenosis. AJNR Am J Neuroradiol 21:643–646
17. Krabbe-Hartkamp MJ, van der Grond J, de Leeuw FE, de Groot JC, Algra A, Hillen B, Breteler MM, Mali WP (1998) Circle of Willis: morphologic variation on three-dimensional time-off light MR angiograms. Radiology 207:103–111
18. Kapoor K, Singh B, Dewan LI (2008) Variations in the configuration of the circle of Willis. Anat Sci Int 83:96–106
19. Zaninovich OA, Ramey WL, Walter CM, Dumont TM (2017) Completion of the circle of Willis varies by gender, age, and indication for computed tomography angiography. World Neurosurg 106:953–963
20. Henderson RD, Eliasziw M, Fox AJ, Rothwell PM, Barnett HJ (2000) Angiographically defined collateral circulation and risk of stroke in patients with severe carotid artery stenosis. Stroke 31:128–132
21. Miyazawa N, Shinohara T, Yamagata Z (2011) Association of incompleteness of the anterior part of the circle of Willis with the occurrence of lacunes in the basal ganglia. Eur J Neurol 18:1358–1360
22. Chuang YM, Huang KL, Chang YJ, Chang CH, Chang TY, Wu TC, Lin CP, Wong HF, Liu SJ, Lee TH (2011) Associations between circle of Willis morphology and white matter lesion load in subjects with carotid artery stenosis. Eur Neurol 66:136–144
23. Saba L, Raz E, Fatterpekar G, Montisci R, di Martino M, Bassareo PP, Piga M (2015) Correlation between leukoaraiosis volume and circle of Willis variants. J Neuroimaging 25:226–231
24. Saba L, Sanfilippo R, Porcu M, Lucatelli P, Montisci R, Zaccagna F, Suri JS, Anzidei M, Wintermark M (2017) Relationship between white matter hyperintensities volume and the circle of Willis configurations in patients with carotid artery pathology. Eur J Radiol 89:111–116
25. Ren Y, Chen Q, Li ZY (2015) A 3D numerical study of the collateral capacity of the circle of Willis with anatomical variation in the posterior circulation. Biomed Eng Online 14:S11
26. Ryan DJ, Byrne S, Dunne R, Harmon M, Harbison J (2015) White matter disease and an incomplete circle of Willis. Int J Stroke 10: 547–552
27. Li H, Xiong Y, Xu G, Zhang R, Zhu W, Yin Q, Ma M, Fan X, Yang F, Liu W, Duan Z, Liu X (2015) The circle of Willis and white matter lesions in patients with carotid atherosclerosis. J Stroke Cerebrovasc Dis 24:1749–1754
28. Hartkamp MJ, van Der Grond J, van Everdingen KJ, Hillen B, Mali WP (1999) Circle of Willis collateral flow investigated by magnetic resonance angiography. Stroke 30:2671–2678
29. Hendrikse J, Eikelboom BC, van der Grond J (2002) Magnetic resonance angiography of collateral compensation in asymptomatic and symptomatic internal carotid artery stenosis. J Vasc Surg 36: 799–805
30. Men X, Wu A, Zhang B, Li H, Zhang Z, Chen S, Lin Y, Lu Z (2013) Leukoaraiosis and NIHSS score help to differentiate subtypes of intracranial branch atheromatous disease in southern Han Chinese patients with stroke. Neurol Sci 34:1727–1733
31. Wardlaw JM, Allerhand M, Doubal FN, Valdes Hernandez M, Morris Z, Gow AJ, Bastin M, Starr JM, Dennis MS, Deary IJ (2014) Vascular risk factors, large-artery atheroma, and brain white matter hyperintensities. Neurology 82:1–8