Association between Anatomical Variations of the Circle of Willis and Covert Vascular Brain Injury in the General Population

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Research Article

Keywords: Circle of Willis, White Matter Hyperintensity, Lacunes, Cerebral Microbleed, Perivascular Space

Posted Date: May 26th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1685139/v1

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Abstract

Background and Purpose: The circle of Willis (COW) is a circulatory anastomosis located at the base of the brain. Little is known about the association between covert vascular brain injury and COW configurations in the general population. We explored this relationship in a community-based Chinese sample.

Methods: A total of 1055 patients (mean age, 54.8 ± 8.9 years; 36.0% men) without intracranial arterial stenosis were included in the analysis. Magnetic resonance imaging was performed to evaluate the presence of imaging markers of covert vascular brain injury, including white matter hyperintensities (WMHs), lacunes, cerebral microbleeds (CMBs), enlarged perivascular spaces, and brain atrophy. Magnetic resonance angiography was used to classify the COW configurations according to the completeness, symmetry, and presence of the fetal posterior cerebral artery (FTP). The association between vascular lesions and variations in COW was analyzed.

Results: Among the 1055 patients, 104 (9.9%) had a complete COW. Completeness correlated with age (p=0.001). Incomplete COW was positively associated with WMH severity (OR=2.071; 95% CI, 1.004–4.270), and CMB presence (OR=1.542; 95% CI, 1.012–2.348), independent of age and sex. The presence of FTP was associated with lacunes (OR=1.878; 95% CI, 1.069–3.298), more severe WMHs (OR=1.739; 95% CI, 1.064–2.842), and less severe enlarged perivascular spaces (OR=0.562; 95% CI, 0.346–0.915).

Conclusions: COW configuration was significantly related to various covert vascular brain injury.

Introduction

The circle of Willis (COW) is a circulatory anastomosis system connecting both internal carotid and both vertebral arteries. It is located at the base of the brain and forms the primary intracranial collateral circulation. The COW is a highly variable anatomical structure [1–3]. Although anatomical variants do not directly impair brain perfusion, they may influence collateral capacity and increase the vulnerability to cerebral blood flow changes.

Magnetic resonance imaging (MRI)-detected vascular brain injury, namely white matter hyperintensities (WMHs), lacunes, cerebral microbleeds (CMBs), enlarged perivascular spaces (EPVS), and brain atrophy, is much more frequent than clinical stroke and is highly prevalent in community dwellings. Covert vascular brain injury has been proven to increase future risk of stroke, dementia, and death [4]. Although previous research has indicated that incomplete COW variants are associated with ischemic stroke [5], the relationship between COW variation and covert vascular brain injury has not been fully elucidated. Several studies have suggested that an incomplete COW is related to more severe WMHs [6–10], while others have failed to find a link [11–13]. Furthermore, few studies have investigated the association between COW variants and CMBs or EPVS [6, 12].

Aims

We determined the prevalence of COW variants in a large community-based Chinese population and assessed any association with covert vascular brain injury, including lacunes, WMH, CMBs, EPVS, and cerebral atrophy.

Methods

Population

Participants were evaluated from a prospective community-based cohort recruiting inhabitants aged 35 years or older from five villages in Shunyi, a rural district located 20 miles from Beijing, China. From June 2013 to September 2014, the Sunyi Study enrolled 1,586 individuals among the 2,237 eligible residents (response rate, 70.9%). Excluding 329 participants who refused or had contraindications to MRI, 1,257 participants completed the brain MRI. Seven subjects with low-quality MRA data and 195 subjects with intracranial arterial stenosis were excluded, while a subsample of 1,055 subjects was included for further analysis (Fig. 1). Compared with the participants in the present study, those who were excluded were older (60.4 ± 11.1 vs. 54.8 ± 8.9, p = 0.001) and more likely to be male (47.9% vs. 36.0%, p = 0.001). This study was approved by the Ethical Committee of the Peking Union Medical College Hospital (No: B-160), and informed consent in written format was obtained from all participants.

MRI Examination

MRI was performed using a single 3T Siemens Skyra scanner (Siemens, Erlangen, Germany) according to standard published criteria [14]. T1-weighted images (T1WI) were acquired using magnetization-prepared rapid gradient-echo in sagittal planes [repetition time (TR) = 2,530 ms, echo time (TE) = 3.43 ms, inversion time (TI) = 1,100 ms, field of view (FOV) = 256 × 256 mm², voxel size = 1 × 1 × 1.3 mm³, flip angle = 8°, 144 sagittal slices]. T2-weighted images (T2WI) (TR = 6,000 ms, TE = 125 ms, FOV = 230 × 230 mm², flip angle = 90°, slice thickness = 5 mm, gap = 1 mm, 20 axial slices), fluid-attenuated inversion recovery sequences (FLAIR) (TR = 8,500 ms, TE = 81 ms, FOV = 230 × 230 mm², flip angle = 150°, slice thickness = 5 mm, gap = 1 mm, 20 axial slices), and susceptibility-weighted images (SWIs) (TR = 8,500 ms, TE = 81 ms, FOV = 230 × 230 mm², slice thickness = 5 mm), susceptibility-weighted images (SWIs) were acquired in the axial plane. Magnetic resonance angiography (MRA) was utilized with three-dimensional (3D)-TOF MRA (TR = 21 ms, TE = 3.43 ms, FOV = 208 × 229 mm², flip angle = 18°, voxel size = 0.3 × 0.3 × 0.6 mm³), and 136 axial slices were obtained for each participant.

Image Analysis

The COW involves the anterior communicating artery (AcomA), right and left pre-communicating anterior cerebral arteries (ACA-A1 segment), posterior communicating artery (PcomA), and right and left pre-communicating posterior cerebral arteries (PCA-P1 segment). The morphology of the COW shown in MRA images was analyzed and evaluated by two experienced neurologists, according to the existence and developmental state of the aforementioned blood
vessels (Fig. 2). Consensus was reached after discussion when there were any disagreements. We defined the COW as typical when all the aforementioned arteries were present with their normal origin, course, and diameter (type I of anterior circulation and type A of posterior circulation). Cases that did not satisfy these conditions were considered atypical. The diameter of a hypoplastic vessel was less than 50% of the width of the contralateral vessel. A vessel was considered absent if it was invisible or non-consecutive on MR images.

For further analysis, we classified these variants according to the completeness and symmetry of the configuration and the presence of a fetal-type posterior cerebral artery (FTP). Complete anterior circulation refers to the presence of AcomA and bilateral ACA-A1s (types I and II), complete posterior circulation refers to the presence of bilateral PcomAs and PCA-P1s (types A, B, and C). Symmetric anterior circulation describes the presence of two balanced ACA-A1s (types I and IV). In cases of FTP, PCA-P1 was absent (type J) or its diameter was smaller than that of the ipsilateral PcomA (type B). Both single- and double-sided FTPs were included in the group.

Lacunes were defined as focal deep infarcts 3–15 mm in size on T1WI. WMH, including periventricular hyperintensity (PVH) and deep white matter hyperintensity (DWMH), was graded according to the Fazekas scale on FLAIR. Severe PVH or DWMH was defined as a Fazekas scale score ≥ 2. The WMH volume was computed using the lesion segmentation toolbox (http://www.statistical-modeling.de/lst.html) for statistical parametric mapping at κ = 0.15. We defined CMB as a round or ovoid area 2–10 mm in size that lost homogeneous signal on SWI. CMBs were classified into three categories, according to anatomical location: deep (deep gray matter: basal ganglia and thalamus; white matter of the corpus callosum; internal, external, and extreme capsules), infratentorial (cerebellum and brainstem), and lobar (cortical gray and subcortical or periventricular white matter). EPVS in the basal ganglia and white matter was evaluated according to a 4-level score [14]. Severe EPVS was defined as degrees 3 and 4. The brain parenchymal fraction (BPF) was defined as the ratio of the brain parenchymal volume (grey matter + white matter) to the total intracranial volume. The total intracranial volume was computed as the sum of the volumes of gray matter, white matter, and cerebrospinal fluid, which were automatically segmented on T1WI using Statistical Parametric Mapping 12 (http://www.fil.ion.ucl.ac.uk/spm/) and the CAT12 toolbox (http://www.neuro.uni-jena.de/vbm/). Four well-trained neurologists independently rated these imaging markers with the κ value listed earlier [15, 16].

**Assessment of Covariates**

Current smoking status was defined as smoking at least once within the previous month. Hypertension was defined as self-reported hypertension, treatment with antihypertensive medication, systolic blood pressure ≥ 140 mmHg, or diastolic blood pressure ≥ 90 mmHg. Diabetes mellitus was defined as self-reported diabetes, treatment with oral antidiabetic drugs or insulin, fasting serum glucose level ≥ 7.0 mmol/L, or hemoglobin A1c level ≥ 6.5%. Hyperlipidemia was defined as treatment with lipid-lowering drugs, fasting serum total cholesterol > 5.2 mmol/L, or low-density lipoprotein cholesterol > 3.62 mmol/L.

**Statistical Analysis**

Continuous variables were expressed as means with standard deviations (SD), and categorical variables were expressed as frequencies and proportions. T-tests were used to compare continuous variables, and the chi-squared and rank-sum tests were used for categorical variables. To assess the relationship between the COW and covert vascular brain injury, a binary logistic regression analysis with adjustment for age and sex was performed with COW variants (symmetry, completeness, and FTP) as determinants and imaging markers of lesions (lacunes, WMH, CMBs, and EPVS) as outcome variables. Statistical significance was set at p < 0.05. All analyses were performed using SPSS version 25.0.0.0 (IBM Co., Armonk, NY, USA).

**Results**

A total of 1055 subjects without intracranial arterial stenosis were included in the analysis. The baseline characteristics of the study population are presented in Table 1. The mean ± standard deviation for age was 54.8 ± 8.9 years, and 36.0% were men. A total of 131 (12.4%) participants had lacunes. Severe PVH and DWMH (Fazekas scales 2 and 3) were observed in 16.7% and 9.5% of the subjects, respectively. One hundred and three (9.8%) subjects had at least one CMB. The overall prevalence of severe EPVS (degrees 3 and 4) in the basal ganglia was 12.3% and in the white matter, 13.7%. 


Table 1
Baseline Characteristics of the Study Population and the Prevalence of Covert Vascular Brain Injury

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>54.8 (8.9)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>380 (36.0)</td>
</tr>
<tr>
<td>Body mass index, mean (SD), kg/m²</td>
<td>26.4 (3.8)</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>231 (21.9)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>484 (45.9)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>144 (13.6)</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>477 (45.2)</td>
</tr>
</tbody>
</table>

Covert Vascular Brain Injury

| Lacunes, n (%)                      | 131 (12.4)             |
| WMH volume, ml, median (IQR) *      | 0.7 (0.2, 2.3)         |
| PVH                                 |
| Degree 0                            | 314 (29.8)             |
| Degree 1                            | 565 (53.6)             |
| Degree 2                            | 131 (12.4)             |
| Degree 3                            | 45 (4.3)               |
| DWMH                                |
| Degree 0                            | 381 (36.1)             |
| Degree 1                            | 574 (54.4)             |
| Degree 2                            | 81 (7.7)               |
| Degree 3                            | 19 (1.8)               |
| CMB, n (%)                          | 103 (9.8)              |
| EPVS-BG †                           |
| Degree 1                            | 289 (27.5)             |
| Degree 2                            | 633 (60.2)             |
| Degree 3                            | 127 (12.1)             |
| Degree 4                            | 2 (0.2)                |
| EPVS-WM †                           |
| Degree 1                            | 404 (38.4)             |
| Degree 2                            | 503 (47.9)             |
| Degree 3                            | 122 (11.6)             |
| Degree 4                            | 22 (2.1)               |
| Brain parenchymal fraction ‡        | 0.77 (0.03)            |

Abbreviations: WMH = white matter hyperintensity; PVH = periventricular hyperintensity; DWMH = deep white matter hyperintensity; CMB = cerebral microbleed; EPVS = enlarged perivascular space; BG = basal ganglia; WM = white matter; SD = standard deviation

* Ninety-eight participants had missing WMH volume due to inadequate image quality for automatic WMH segmentation
† Four participants had missing EPVS scores due to inadequate imaging quality for visual assessment
‡ Seventy-three participants had missing BPF data due to inadequate image quality for automatic structural segmentation

Variations of the COW and Risk Factors

Among the participants, 104 (9.9%) had a complete COW. Within these 104 patients, 53 patients had the typical configuration and the other 51 had at least one hypoplastic artery. The most common COW variations were type IV (343 cases, 32.5%) of anterior circulation, in which AcomA was absent, and type D
(421 cases, 39.9%) of posterior circulation, in which both PcomAs were absent (Supplemental Table 1). When considering the common risk factors of vascular disease, patients who had an incomplete COW tended to be older (t = 3.228, p = 0.001). There were no significant associations between COW completeness and sex or vascular risk factors.

After classification of all variants, we found that the completeness ratio was 60.4% in the anterior circulation and 17.8% in the posterior circulation. The symmetry ratio of the anterior circulation was 83.3%. In total, 252 (23.9%) patients developed FTPs. Among 218 participants with unilateral FTPs, FTPs on the right side were more common (136 vs. 82, χ² = 13.38, p = 0.001). A significant imbalance was found in the distribution of hypoplastic/absent ACA-A1 and PCA-P1, with more present on the right side (ACA: Z = -4.503, p = 0.001; PCA: Z = -3.448, p = 0.001) (Supplemental Table 2).

**Relationship between COW Variations and Covert Vascular Brain Injury**

WMH and Lacunes. Univariate analysis showed that asymmetric anterior circulation and incomplete posterior circulation were both associated with severe PVH and severe DWMH (Supplemental Table 3). The volume of the WMH was also higher in patients with incomplete posterior circulation (t = 4.995, p = 0.03). The presence of FTP was related to severe DWMH and lacunes in white matter. After adjusting for age and sex, severity of DWMH increased in patients with severe EPVS in the white matter; incomplete posterior circulation was associated with severe EPVS in the basal ganglia (Supplemental Table 3). After adjusting for age and sex, presence of CMBs was significantly associated with completeness of the anterior circulation (OR = 1.542; 95% CI, 1.012–2.348; p = 0.049). Lacunes in white matter were positively associated with the presence of FTP (OR = 1.878; 95% CI, 1.069–3.298; p = 0.028) (Table 2).

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Symmetric</th>
<th>Asymmetric</th>
<th>Complete</th>
<th>Incomplete</th>
<th>No FTP</th>
<th>FTP</th>
<th>Complete</th>
<th>Incomplete</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lacune</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Any lacune</td>
<td>1(Ref)</td>
<td>1.205(0.727–1.996)</td>
<td>0.469</td>
<td>1(Ref)</td>
<td>1.246(0.837–1.855)</td>
<td>0.278</td>
<td>1(Ref)</td>
<td>1.221(0.767–1.943)</td>
</tr>
<tr>
<td>Lacune-BG</td>
<td>1(Ref)</td>
<td>1.322(0.752–2.327)</td>
<td>0.332</td>
<td>1(Ref)</td>
<td>1.243(0.788–1.962)</td>
<td>0.349</td>
<td>1(Ref)</td>
<td>1.015(0.589–1.750)</td>
</tr>
<tr>
<td>Lacune-WM</td>
<td>1(Ref)</td>
<td>0.891(0.462–1.718)</td>
<td>0.729</td>
<td>1(Ref)</td>
<td>1.282(0.775–2.121)</td>
<td>0.332</td>
<td>1(Ref)</td>
<td>1.878(1.069–3.298)</td>
</tr>
<tr>
<td>WMH</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Severe PVH</td>
<td>1(Ref)</td>
<td>1.394(0.886–2.193)</td>
<td>0.151</td>
<td>1(Ref)</td>
<td>1.110(0.771–1.599)</td>
<td>0.574</td>
<td>1(Ref)</td>
<td>1.348(0.881–2.061)</td>
</tr>
<tr>
<td>Severe DWMH</td>
<td>1(Ref)</td>
<td>1.291(0.757–2.202)</td>
<td>0.348</td>
<td>1(Ref)</td>
<td>0.862(0.551–1.347)</td>
<td>0.514</td>
<td>1(Ref)</td>
<td>1.739(1.064–2.842)</td>
</tr>
<tr>
<td>CMB</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Any CMB</td>
<td>1(Ref)</td>
<td>0.718(0.399–1.295)</td>
<td>0.271</td>
<td>1(Ref)</td>
<td>1.542(1.012–2.348)</td>
<td>0.044</td>
<td>1(Ref)</td>
<td>1.285(0.781–2.116)</td>
</tr>
<tr>
<td>Deep or infratentorial CMB</td>
<td>1(Ref)</td>
<td>0.393(0.150–1.027)</td>
<td>0.057</td>
<td>1(Ref)</td>
<td>1.567(0.900–2.730)</td>
<td>0.113</td>
<td>1(Ref)</td>
<td>1.279(0.658–2.485)</td>
</tr>
<tr>
<td>Strictly lobar CMB</td>
<td>1(Ref)</td>
<td>1.180(0.571–2.440)</td>
<td>0.655</td>
<td>1(Ref)</td>
<td>1.499(0.826–2.721)</td>
<td>0.183</td>
<td>1(Ref)</td>
<td>1.271(0.635–2.546)</td>
</tr>
<tr>
<td>EPVS</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe EPVS-BG</td>
<td>1(Ref)</td>
<td>0.958(0.577–1.593)</td>
<td>0.870</td>
<td>1(Ref)</td>
<td>0.952(0.648–1.399)</td>
<td>0.802</td>
<td>1(Ref)</td>
<td>0.734(0.449–1.200)</td>
</tr>
<tr>
<td>Severe EPVS-WM</td>
<td>1(Ref)</td>
<td>1.040(0.639–1.694)</td>
<td>0.873</td>
<td>1(Ref)</td>
<td>0.682(0.468–0.996)</td>
<td>0.048</td>
<td>1(Ref)</td>
<td>0.562(0.346–0.915)</td>
</tr>
</tbody>
</table>

Models are adjusted for age and sex

Abbreviations: OR = odds ratio; CI = confidence interval; Ref = reference; FTP = fetal-type posterior cerebral artery; WMH = white matter hyperintensity; PVH = periventricular hyperintensity; DWMH = deep white matter hyperintensity; CMB = cerebral microbleed; EPVS = enlarged perivascular space; BG = basal ganglia; WM = white matter

CMBs and EPVS. Univariate analysis showed that incomplete anterior circulation increased the risk of CMs. In addition, absence of FTPs was associated with severe EPVs in the white matter; incomplete posterior circulation was associated with severe EPVS in the basal ganglia (Supplemental Table 3). After adjusting for age and sex, presence of CMs was significantly associated with completeness of the anterior circulation (OR = 1.542; 95% CI, 1.012–2.348; p = 0.044). Severe EPV in the white matter was negatively associated with the presence of FTPs (OR = 0.562; 95% CI, 0.346–0.915; p = 0.020) (Table 2).

Cerebral Atrophy. A positive correlation was found between asymmetric ACA-A1 (t = 2.835, p = 0.005), incomplete anterior circulation (t = 2.345, p = 0.02), and lower BPF. However, after adjustment for age and sex, these associations were no longer significant (β ± SE = -0.288 ± 0.188, p = 0.127 for symmetry; β ± SE = -0.127 ± 0.143, p = 0.375 for completeness).
Discussion

In this community-based Chinese population, we identified 55 types of COW variants using MRA. Nearly 10% of the participants had complete COW, and they were likely to have fewer ischemic lesions (WMHs), fewer hemorrhagic lesions (CMBs), and less severe cerebral atrophy. Furthermore, more than 80% of the population had symmetric anterior circulation, and those with asymmetric circulation were more vulnerable to cerebral atrophy. Finally, FTP was found in over 20% of the subjects and was associated with more ischemic lesions (lacunes and WMHs).

COW Variations

We observed that a complete COW on MRA in 9.9% of participants, whereas the remaining 90.1% had at least one missing segment. The prevalence of COW anomalies varies greatly [1], due to limited sample sizes of a few hundred individuals. Two studies involving more than 1000 participants were conducted in Norwegian and male Chinese populations, with complete COW prevalence rates of 11.9% [2], and 12.24% [3], respectively. Our study indicated that a complete COW was negatively associated with increasing age, consistent with previous studies [2, 17]. The most common COW variant was type IV of anterior circulation, in which AcomA was absent, and type D of posterior circulation, in which two PcomAs were absent. These findings are in agreement with the two large-scale studies mentioned above [2, 3]. Although the COW configuration varies greatly in the general population, the prevalence of a complete COW and the most common variant were similar across populations.

Furthermore, we found that the distribution of hypoplastic/absent ACA-A1 and PCA-P1 was unbalanced, with more cases being observed on the right side. Several researchers have determined the same left-dominant asymmetry in the distributions of ACA-A1 [2, 3] and PCA-P1 [3]. One possible reason for the asymmetry is that the left hemisphere is better perfused in people who are right-handed (i.e. the majority of the population). Additionally, FTPs were unevenly distributed and more prevalent on the right side, congruent with earlier findings [3, 18].

Relationship between COW Variations and Covert Vascular Brain Injury

For symptomatic ischemic brain injury, a meta-analysis involving 2718 participants showed that any variation in the COW made patients 1.38 times more likely to develop ischemic stroke [5]. However, when looking at WMH and lacunes, which are generally considered to be asymptomatic ischemic lesions [19, 20], prior reports on the general population showed conflicting results (Table 3). Miyazawa et al. [21] found significant correlations between lacunes and COW completeness, while Del Brutto et al. [12] failed to find this relationship. Unlike our findings on WMH, both Hindenes et al. [22] and Del Brutto et al. [12] found that WMH may not be related to the completeness or specific variants of the COW. This might be caused by the classification method of the COW, wherein we distinguished the completeness of the anterior and posterior parts of the COW and found that the latter was related to WMH.
Our findings provide new evidence for susceptibility to silent ischemic brain lesions in people with an incomplete COW. The COW could possibly influence the development of vascular brain injury via collateral circulation. Most COW variants are generally thought not to directly reduce cerebral perfusion. However, the hypoplastic/absent vessels of COW variants can impair the hemodynamic balance [23], making it difficult to establish rapid collateral compensation after changes in cerebral blood flow [24]. This may contribute to ischemic brain injury over time.

We distinguished the completeness of the anterior and posterior proportions of the COW and found that the anterior was significantly related to brain atrophy, and the posterior was related to WMH. Further studies are warranted to explain the different impacts of anterior and posterior circulation on vascular brain injury. Most previous studies on COW configuration have focused on the completeness rather than symmetry. However, mathematical models showed that asymmetry of paired vessels in the COW correlated with higher resistance to flow [23], and may therefore affect brain perfusion and wall shear stress [25]. Our findings on asymmetric anterior circulation and brain atrophy imply the significance of symmetry considerations in further studies.

Few studies have investigated the relationship between COW variants and CMB. In this study, the presence of CMBs was higher in patients with incomplete anterior circulation. In a population-based study led by Del Brutto et al. [12], the severity of deep CMB was not related to completeness of the entire COW. This inconsistency might be caused by their exclusion of lobar CMBs, their COW classification method, or limited sample size. The majority of CMBs reflect microhemorrhages of small cerebral blood vessels after their disorganization [19]. The incomplete configuration in some COW variants can predispose blood vessels to higher wall shear stress [23, 26, 27], further damaging the downstream vessel wall and causing microbleeds.

One interesting result of our study was the negative correlation between severe EPVS in the white matter and the presence of FTP. Evidence indicates that the PVS plays an important role in the movement and drainage of fluid in the brain, and the EPVS is a marker of blood-brain barrier breakdown and microvascular functional impairment [28]. FTP is formed during embryogenesis. After the internal carotid arteries give rise to each arterial segment of the COW, the blood of
PCA-P2 is equally supplied by PCA-P1 and PcomA. Later, when the occipital lobe develops rapidly, either PCA-P1 or PcomA enlarges to maintain its blood supply, and FTP refers to the configuration in which PcomA outsizes the ipsilateral PCA-P1 [29]. Our result showed that the presence of FTP, with the blood of the PCA mainly supplied by the internal carotid system rather than the vertebrobasilar system, can protect individuals from severe EPVS. However, underlying pathogeneses require further investigations.

In this large population-based study, we comprehensively explored the relationship between various imaging markers of covert vascular brain injury and COW variants. Our study had some limitations. First, we used MRA as a noninvasive method that can be applied to the general population. Although it is sensitive to blood flow, the figure resolution is limited, making it difficult to reliably identify vessels < 1 mm on MRI. Second, in this community-based sample, we excluded subjects with intracranial arterial stenosis because of possible misleading hypoplasia of the vessel. However, the excluded patients were more likely to depend on collateral perfusion by the COW as their cerebral blood flow was reduced. Furthermore, we did not distinguish lesions of covert vascular brain injury ipsilateral and contralateral to COW variants because of the limited total number of lesions, which might have missed potential side-specific findings.

Conclusions

This study showed a positive association between specific variations in the COW and susceptibility to silent vascular brain lesions. Therefore, close monitoring may be necessary for people who are found to carry COW variants identified through imaging examinations.

Declarations

Acknowledgments

The authors are grateful to the study participants and the staff of the Shunyi Study.

Competing Interests The authors declare that there is no conflict of interest.

Sources of Funding The study was funded by the National Natural Science Foundation of China (grant number: 62072045), the Fundamental Research Funds for the Central Universities (grant number: 33320120006), and the Research Foundation for Young Scholars of Peking Union Medical College Hospital (grant number: PUMCH201911275).

Ethics Approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethical Committee of the Peking Union Medical College Hospital (No: B-160).

Consent to participate Informed consent in written format was obtained from all participants.

Data Availability Statement

The data are available upon reasonable request. Researchers interested in collaborations should contact the corresponding author, Fei Han (fourohan@163.com) or Yi-Cheng Zhu (zhuych910@163.com).

References


Figures
Figure 1
Participant Selection Flow Chart

Figure 2
Variants of the Circle of Willis in Anterior and Posterior Circulation
A. Variants in anterior circulation. Type I, two normal A1+AcomA; type II, normal A1+hypoplastic A1+AcomA; type III, normal A1+missing A1+AcomA; type IV, two normal A1; type V, normal A1+hypoplastic A1

B. Variants in posterior circulation. Type A, two normal P1+two PcomA; type B, two hypoplastic P1+two PcomA; type C, normal P1+hypoplastic P1+two PcomA; type D, two normal P1; type E, two normal P1+one PcomA; type F, normal P1+hypoplastic P1+one PcomA; type G, normal P1+missing P1+one PcomA; type H, normal P1+missing P1+two PcomA; type I, hypoplastic P1+missing P1+two PcomA; type J, two missing P1+two PcomA; type K, two homolateral PCA extended from the internal carotid and basilar arteries

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