Anatomical Variants of the Posterior Part of the Circle of Willis in Patients with Cerebrovascular Diseases

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Abstract

Introduction: The current literature proves that the frequency of anatomical variants of circle of Willis (CoW) has not yet been sufficiently evaluated both in the Romanian population and internationally, and in the North East region of Romania there is no evidence of such research so far. The aim of this study is to identify the frequency and types of anatomical variants of the constituent arteries of the posterior part of the CoW in patients with cerebrovascular diseases diagnosed within the main Neurology hospital in the Northeastern region of Romania, based on macroscopic analysis of arterial specimens obtained at autopsy and the results with data from updated literature.

Material and Methods: A descriptive observational study, conducted retrospectively on 96 patients with cerebrovascular diseases who died over a period of 30 months and underwent an anatomo-clinical autopsy. We analysed the general macroscopic aspects of all anatomical variants of the constituent arteries of the posterior part of the CoW, comparing these to the opposite arteries.

Result: Out of the total of 96 available human brains, 28 cases (29.17%) presented anatomical variants of CoW, among which 11 cases (39.28%) presented at least one anatomical variant of the constituent arteries of its posterior part. The average age of these patients was 59.18 years. 39.36% cases had a single anatomical variant, 64.54% cases had two anatomical variants, and 9.09% associated an anatomical variant of the posterior part of CoW and one of the vertebral arteries. Anatomical variations of the arteries of the posterior part of the CoW were observed in 14 arteries (31.81%) of all the 44 available, and consisted in unilateral or bilateral hypoplasia (20.45%) or absence (15.90%), located either on the right or on the left, and partial fetal posterior cerebral artery (2.27%) located on the left side. We identified seven morphological patterns of the posterior part of CoW in the conditions in which its anterior part does not present any anatomical variants.

Conclusion: The data obtained in the present research allow us to affirm that circle of Willis represents an anatomical structure with a great morphological diversity of its posterior part. This study contributes to the knowledge of this topic in Romania and allows comparisons with data obtained both in the country and abroad.

Keywords: Cerebrovascular disease • Circle of Willis • Anatomical variants • Arterial hypoplasia • Fetal artery

Introduction

The circle of Willis (CoW), also called the arterial circle of Willis or circulus arteriosus cerebri, was originally defined by the English anatomist Thomas Willis (1621–1675), who first described it completely and correctly in 1664 in his book Cerebri Anatomie: cui accessit nervorum descriptio et usus [1], as an arterial anastomotic structure that has a complete symmetry in its shape and configuration [2].

The normal CoW is defined as a closed circuit in which blood can flow from the point of entry to its return to that point through the component vessels, maintaining adequate flow without additional vessels, but the constituent arteries must not be smaller than 1 mm in their outer diameter [3]. Normally, CoW has seven sides, thus being a heptagon-like shape [2]. Can be divided topographically into an anterior part and a posterior part. The anterior part consists of three vascular components, namely: the precommunicating segments (A1) of the two Anterior Cerebral Arteries (ACAs), right and left, which are interconnected through the Anterior Communicating Artery (ACoA); the posterior part consists of four vascular components, namely: the precommunicating segments (P1) of the two Posterior Cerebral Arteries (PCAs), right and left, and the two Posterior Communicating Arteries...
The importance of a symmetrical CoW is twofold. First of all, this arterial structure is essential for maintaining a stable and constant blood flow to the brain as the nerve tissue is very sensitive to the lack of oxygen and of blood nutrients. It can be considered that it has compensatory capacity, depending on the presence of all its arteries and their normal diameter.

The proximal segment (A1) of the Anterior Cerebral Artery (ACA) can provide blood flow to the cerebral hemispheres normally supplied by the contralateral Internal Carotid Artery (ICA) if the Anterior Communicating Artery (AComA) is patent, and the Basilar Artery (BA) can provide collateral flow to the anterior circulation through the proximal segment (P1) of the PCA by reversing blood flow through the PComA [4].

Under conditions of symmetrical CoW, even in patients with stenosis or severe occlusion of the ICA, blood may redistribute to ischemic areas to improve cerebral perfusion, preventing the onset of ischemic events and their progression. On the other hand, any change in the morphology of the constituent arteries can lead to various vascular failure syndromes because the ability of CoW to redistribute blood flow inside the brain depends on the morphology condition of its vessels. Patients who suffer from ICA occlusion, but who have a CoW with efficient collateral circulation have a lower risk of stroke than those who do not have such collaterals [4].

Recent literature various reports variations of CoW from its original definition. Studies conducted so far, be it on autopsy cases or on imaging investigations, showed that a normal CoW occurred in only 18.9% to 42.8% of the population [6-7]. i.e. less half of the cases.

Several studies have also shown that these anatomical variants of CoW have an important role in the development of cerebrovascular disease (ischemic and haemorrhagic stroke), which is one of the most common pathologies, but also of psychiatric disorders [8-10].

As the frequency of anatomical variants of CoW has not yet been sufficiently evaluated in the Romanian population, and in the North-eastern region of the country there is no such research so far, the aim of this study was to identify the frequency and type of anatomical variants of the constituent arteries of the posterior part of the CoW in patients with cerebrovascular disease diagnosed in a regional hospital from the Northeasteren part of Romania Moldova region, based on macroscopic analysis of CoW specimens obtained at autopsy and comparing the results with data from the literature up to date.

Material and method

Study design

Our research is a descriptive observational study, conducted retrospectively on hospitalized cases, by assuming the principles of institutional ethics. The study was performed within the Pathology Department of "Prof. Dr. N. Oblu" Emergency Clinical Hospital, Iași, Romania, mentioning the fact that it is the main neurological and neurosurgical medical unit in the Northeastern region of Romania.

Selected population

The population included in this study consisted of 96 neurological and neurosurgical patients who died of various medical causes in this hospital, in a period of 30 months (01.01.2014-30.06.2018), who underwent an anatomo-clinical autopsy at the request of the attending physician to establish the diagnosis of death. The identification data of each autopsied deceased (gender and age), as well as the macroscopic morphological aspects of the CoW and of its constituent arteries were taken from the Autopsy Register of the Pathology Department within the same hospital.

Selection of samples

We included in the present study only that circles of Willis with anatomical variants of its posterior part, respectively of the proximal segments P1 of the PCAs and of the PComAs.

Macroscopic examination of the Willis polygon

During autopsies, the pathologist performed a detailed morphological and morphometric analysis of each CoW. The constituent arteries of all circles of Willis were observed, as well as the basilar artery (BA) and Vertebral Arteries (VaS), noting any variation in the morphology of each vessel, as well as their point of emergence compared to their pair vessel. Thus, the general macroscopic aspects of the all analysed circles of Willis were recorded, noting and whether an anatomical variant of any of the constituent arteries of the posterior namely: absence, hypoplasia, duplication, fenestration, difference in length and difference in origin and place of discharge, compared to the opposite segments.

The CoW morphology was analyzed related to the following definitions:

A CoW was considered typical if all the component arteries (the pre-communicating segments of the ACAs, both PCAs, AComA and both PComAs were present; when these arteries did not showed any anomaly, when the origin of all vessels contributing to the formation of CoW had the typical origin, and when their outer diameter was no less than 1 mm [11]. The remaining specimens that were different from the above description were considered as “anatomical or abnormal variants” or as “an incomplete CoW” [11-12]. The absence of an artery has been defined either as its absence or as its replacement by a very thin, lumen-free fibres cord [13]. The “hypoplasia” of the P1 segment of the CoW was defined as an outer diameter of the vessel less than 1 mm, but with a patent lumen [13-14]. Because normal PComA has an outer diameter of 1,0-1,5 mm, regardless of its origin, PComA hypoplasia was defined as an outer diameter of less than 0,5 mm, but with a patent lumen[14-18]. We defined the posterior cerebral artery as fetal (PCA) when it originates completely from the ICA, with no connection to the BA or when it retains only a hypoplastic connection with the BA [18], and the diameter of the P1 segment of the PCA is smaller than that of PComA [17], the anomalies of origin describe the situations in which an artery has a different origin from the classical one.

Photographing of available specimens

The photographs of circles of Willis with anatomical variants of their posterior part were taken from the digital archive of the Department of Pathology, where they were stored from the moment they were performed, i.e. during autopsies realized at the request of the clinician to establish, confirm or complete the diagnosis of death. At that time, the pathologist numbered and analysed that circles of Willis and photographed them with a digital camera. The photographs of the circles of Willis we used in the present research were numbered and archived in the archive of our study.

Statistical analysis

The results were collected in a database using Excel and then tabulated. The obtained data were used to calculate the mean, number and percentage, as well as the corresponding graphs. In the end, the obtained data were sorted according to the type of morphological variation of the component arteries of the posterior part of the CoW and were compared with the data from the literature.

Results

Out of the total of 96 available human brains, 68 cases (70.83%) presented the classical form of CoW, i.e., the complete and symmetrical form (Figure 1). The remaining 28 cases (29.17%) were classified as “incomplete” because...
they presented anatomical variants of the constitutive arteries (Figures 1 and 2, and Table 1). Out of these 28 cases with an “incomplete” CoW, 11 cases (representing 11.45% of all 96 CoW we analyzed and 39.28% of all incomplete circles of Willis we included in this study) presented at least one anatomical variant of the arteries of the posterior part of CoW (Figure 2). Of the 11 patients who died with The average age of the whole group was 59.18 years, with a variation between 40 years and 86 years. Female cases ranged in age from 41 to 86 years, with a mean age of 60.8 years, and male cases ranged from 40 to 76 years, with a mean age of 57.83 years. The distribution of analysed cases according to age groups shows a peak in the 5th and 6th decades of life (Figure 4). For female patients there is a peak in the age group of 50-59 years, and for male patients there are two peaks, one in the fifth decade of life and another in the seventh decade of life. In the present study, out of the 11 CoW we have analysed, 4 (36.36%) cases had a single anatomical variant of the posterior part of the CoW, 6 (54.54%) cases had two anatomical variants, and one case (9.09%) associated an When were analysed the distribution of cases according to the affected side and to the type of the anatomical variant, we took into account all 44 arteries from our 11 cases. We identified anatomical variants on the right side in 9 arteries (20.45%) and on the left side in only 8 arteries (18.18%) of all the 44 available arteries (Figure 6). Anatomical variations of the constituent arteries of the posterior part of the CoW were observed in 14 arteries (31.81%) of all the 44 available and consisted of hypoplasia (9/44 arteries; 20.45%) or absence (7/44 arteries; 15.90%), located either on the right or on the left, and partial fetal PComA (1/44 arteries; 2.27%), located on the left side (Figure 7). The hypoplasia of PComA was identified in 7/11 cases of CoW (63.63%), either unilaterally (2/11 cases; 18.18%) (Figures 8 and 9) or bilaterally (2/11 cases; 18.18%) (Figures 8 and 10), or associated with the absence of the contralateral artery (2/11 cases; 18.18%). In 1/11 case (9.09%), PComA hypoplasia was associated with a variant outside of CoW, respectively with hypoplasia of the left VA. The absence of PComA was unilateral in 1/11 cases (9.09%), bilateral in 2/11 cases (18.18%) (Figures 8 and 11), or And associated with hypoplasia of contralateral artery in 2/11 cases (18.18%). Fetal PCA was identified in only one case (9.09%), being located on the left side of the CoW (Figures 8 and 12).

In the present research we identified seven morphological patterns of the posterior part of CoW in the conditions in which its anterior part does not present any anatomical variants (Figure 13).

### Table 1. Patient characteristics and morphological types of the anatomical variants of the posterior part of the CoW.

<table>
<thead>
<tr>
<th>No.</th>
<th>Gender</th>
<th>Age (years)</th>
<th>PCA</th>
<th>PComA +/- other anatomical variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>41</td>
<td></td>
<td>Absence of right PComA</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>40</td>
<td></td>
<td>Absence of left PComA, Absence of right PComA</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>49</td>
<td></td>
<td>Hypoplasia of right PComA</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>50</td>
<td></td>
<td>Absence of right PComA, Hypoplasia of left PComA</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>52</td>
<td></td>
<td>Hypoplasia of left PComA, Hypoplasia of left vertebral artery (AV)</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>54</td>
<td></td>
<td>Absence of right PComA, Absence of left PComA</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>65</td>
<td></td>
<td>Hypoplasia of right PComA, Hypoplasia of the right PComA</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>67</td>
<td></td>
<td>Hypoplasia of the left PComA, Hypoplasia of the right PComA</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>71</td>
<td></td>
<td>Hypoplasia of the left PComA, Hypoplasia of the right PComA</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>78</td>
<td></td>
<td>Hypoplasia of the left PComA, Hypoplasia of the right PComA</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>86</td>
<td>Left partial fetal PCA is anastomosed through a thin arterial branch with the basilar artery (BA)</td>
<td></td>
</tr>
</tbody>
</table>

The present research we identified seven morphological patterns of the posterior part of CoW in the conditions in which its anterior part does not present any anatomical variants (Figure 13).
5. Absence of PComP on one side and hypoplasia of PComA on the opposite side
6. Unilateral fetal PComA
7. Unilateral hypoplastic PComA associated with ipsilateral hypoplastic vertebral artery.

The termination of the PComA was of type I or typical in all 11 cases (100%) because each PComA ended through an anastomosis with PCA that divides it into the P1 segment and the P2 segment. The symmetry of the anastomosis points between PcomA and PCA was identified in 7 cases (63.63%), and in the other 4 cases (36.36%) these points were asymmetric, as they varied between the two parts, right and left. Hartkamp et al. (31) developed a.

Discussion
The anatomical variants we have identified on the posterior part of the CoW result either from the persistence of the vessels which should normally disappeared during embryonic development or from the absence of certain vessels which should have been present at birth [6]. A good knowledge of the anatomical variants of the posterior part of the CoW becomes very important in the surgery of pituitary tumors and aneurysms of the basilar artery because its constituent arteries send a series of perforating arteries in the diencephalon and mesencephalon that can be affected by stretching [19]. The presence
of efficient PComAs is a vital factor for stroke development, as these vessels link the anterior and posterior cerebral circulation, providing a strong source of plasticity in cerebral hemodynamics [20]. Gunnal SA, et al. [21] performed an autopsy study on 170 brains preserved in formalin from people Indian ancestry. These authors identified anatomical variations of PComA in almost half of their cases, these variations being: hypoplasia (25.9%), fetal artery (16.47%), absence (3.52%) and fenestration (0.58%). In contrast to this study, our research identified only hypoplasia, absence and fetal artery as anatomical variants of the posterior part of CoW, but the difference may be correlated to the smaller number of cases we analyzed in our study. The similarity between our study and that of Gunnal SA, et al. [21] consists in the predominance of hypoplasia among the anatomical variants of the posterior part of CoW. However, the absence of PComA ranks secondly, and was followed by the fetal artery, which was only rarely identified. The differences between these two studies consists of the selected population. Our data are not very different from those recently obtained by Kornieieva M, et al. [20], who analyzed the morphological variability of CoW on specimens obtained by anatomical dissection from corpses of Caucasian ancestry and on specimens belonging to living persons, but of Arab ancestry, which they analyzed by angio-MRI. These authors reported that a complete, typical CoW was identified in only 8.3% of autopsied Caucasians and 22.2% of angio-MRI specimens belonging to Arab patients. They also found that the most common variant of the posterior part of the CoW in Caucasian specimens was unilateral fetal PComA, which were recorded in more than a third of cases, followed by unilateral hypoplasia of the posterior communicating artery (PComA). In samples from Arab patients, obtained by angio-MRI, the posterior part of the CoW was incomplete in 26.56% of cases because the PComA was absent or unilaterally hypoplastic in a quarter of all incomplete CoW or bilateral hypoplastic in one-fifth of all incomplete CoW. Unilateral fetal PComA, was registered in 18.7% of incomplete CoW [20]. Our study is similar to this study and to many other reports, because hypoplasia and/or absence of PComA is the most common anatomical variant.
identified only one case of left partial fetal PCA, anastomosed through a thin arterial branch with the basilar artery, that accounted for one tenth of all incomplete CoW from our series, but the number of available cases was very small, thus representing one of the limitations of our study. Variants of the P1 segment of the PCA are very rare and our study did not detect any of them. In 1991, Caruso G, et al. [23], analyzing a series of 100 formalin-fixed human brains, reported only 3% abnormalities at this level, represented by a case of duplication of this segment, a case of fenestration and the third case was a common trunk of the PCA and the superior cerebellar artery, which is also a rare variant. However, in the literature, many articles reported uni- or bilateral hypoplasia as the most common anatomical variant of the posterior cerebral artery (PCA), which has a frequency ranging from 14.5% to 48.3% [20,22,24-26].

Hartkamp MJ, et al. [29] developed a classification of the morphology of the posterior part of CoW on a group of 75 Dutch patients with minimal neurological deficits according to the anatomical variants encountered at this level. They identified 10 morphological patterns, among which bilateral fetal PComA associated with hypoplasia or the absence of both segments P1 was found in 63% of all cases they analyzed by angio-MRI. In second place was unilateral fetal PComA, observed in 27% of all cases. Unilateral hypoplasia or absence of PComA was identified in 41.7% of cases. Finally, on the second place it was the anatomical variant of the posterior part of CoW specimens obtained from autopsy or angio-MRI techniques, in Asia or Europe, have shown that hypoplasia is the most common anatomical variation of the posterior part of CoW [6, 11-12] and this morphological feature was also obtained by us on the first rank (Table 2).

The significance of this finding is that hypoplasia of PComA is considered a predisposing factor for hemispheric infarctions due to slow-flowing blood in ICA occlusions [22-33] It may be asymptomatic unless ipsilateral ICA stenosis occurs [4, 34-35].

Chuang YM, et al. [36] even stated that hypoplastic PComA remains a risk factor for ischemic stroke even without being accompanied by stenosis of ICA. In 2020, Jones JD, et al. [37] performed a meta-analysis of studies that analyzed the anatomical variations of CoW. They found that the presence of at least one anatomical variant was reported in various proportions, ranging from 42.2% to 95.2%, but this percentage varied depended on several factors, especially the analyzed population, respectively whether it represent healthy subjects or patients with cerebrovascular disease, and if the study was performed on corpses or living people using angio-CT or angio-MRI techniques. In addition, the reported prevalence of unilateral hypoplasia and absence of PComA (taken together) ranged from 8% to 28.7% in the literature, and the reported prevalence of bilateral hypoplasia and absence of PComA ranged from 3.7% to 47.5%. It is clear from the literature that anatomical variations of CoW are very common (68.2% ± 14.32).

Clinically, hypoplasia and the absence of PComA are very significant. PComA is essential for connecting the anterior and posterior halves of CoW. A hypoplastic or absent PComA may compromise the ability of CoW to provide collateral circulation. In the present study, bilateral hypoplasia/absence of PComA was shown to be as common as unilateral hypoplasia of the same vessel, which means that the two halves of CoW could be anatomically and functionally isolated from each other without communication between the internal carotid system and the vertebrobasilar system. In the case of a stenosis of ICA, cerebral circulation can be based on the collateral supply of blood from the vertebrobasilar system. Without an efficient functioning of the PComA, the collateral circulation path may be compromised and an ischemic stroke can develop [38]. Chuang YM, et al. [36] point out that a hypoplastic PComA is associated with an increased risk of stroke, especially in the thalamic region. Mukherjee D, et al. [39] suggested that the presence of anatomical variants at the level of CoW may have an impact on the trajectory of microemboli and therefore may lead to infarcts in distal, more unusual areas of PComA.
the brain. Patients with bilateral para-medianthalamic lesions with no lesions other than in the thalamus were more likely to have hypoplastic P1 segments of PCAs or unilateral or bilateral absences of PCoMAs. However, there are large discrepancies of reporting the prevalence of anatomical variants of the posterior part of CoW, probably due to differences in methodology and nomenclature [20,22,26,29,31]. In addition, there are probably population differences in the anatomy of CoW [12,14,20,22,28,40-41] as many studies, conducted on five continents, differences from one ethnic group to another.

**Conclusion**

The data obtained in the present research allow us to affirm that circle of Willis is an anatomical structure with a great morphological diversity of its posterior part. Given that there currently are no data on anatomical variations in the cerebral circulation of the population living in the North-eastern region of Romania, this study contribute to the knowledge of this topic in Romania and allows comparisons with data obtained both in the country and abroad. This study offers the possibility to evaluate the angle architecture of circle of Willis in different groups of patients (with or without cerebrovascular pathology) or healthy subjects, from our country or from other countries as well.

**Ethics Approval and Consent to Participate**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

**Acknowledgment**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Data Availability**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**References**


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