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Anatomical study of circle of Willis on fresh autopsied brains. A study of a Romanian population

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Abstract

Because the circle of Willis (CoW) supplies blood to the brain in case of occlusion of one of the cerebral arteries, identification of any change in its classical shape could be useful in the assessment of cerebrovascular morbidity. The purpose of our research was to study the anatomical variants of CoW identified on fresh brains obtained at the clinical autopsies of adult deceased patients belonging to a specific population (Northeastern region of Romania), as no data are available for Romania population up to date. The study group included consecutive patients who died in Prof. Dr. Nicolae Oblu Emergency Clinical Hospital, Iaşi, Romania, due to medical causes between January 1, 2014 and June 30, 2016, to whom a clinical autopsy was performed. From a total of 96 circles of Willis, 29.17% presented an atypical morphology. We identified eight types of anatomical variants, which affected simultaneously both the posterior and the anterior parts of CoW in 46.42% of cases. The most frequent anatomical variants were hypoplasia (20.91%), followed by the absence of an artery (3.06%), and partially fetal type artery (2.04%). 67.86% of atypical CoW exhibited more than one anatomical variant of an artery in one circle. We identified nine of the 23 morphological patterns that were published to date, and also nine new types. Our research proved that in the population living in the Northeastern part of Romania the anatomical variations of circles of Willis are very polymorphic, with particular morphological aspects.

***Keywords*:** circle of Willis, anatomical variant, hypoplasia, partially fetal artery, fenestration.

Introduction

Even though many attempts were made along the time to understand the morphology and function of the arterial structure lying at the base of the brain, only Thomas Willis (1621–1675) was the first anatomist who correctly described it in 1664 [1]. In his book, "*Cerebri Anatome: cui accessit nervorum descriptio et usus*", the author presented it as an arterial symmetrical anastomotic anatomical structure and since then, in honor of him and his discovery, the *circulus arteriosus cerebri* has been called the circle of Willis (CoW) [2].

In the last two decades, many authors analyzed and reported not only various anatomical variants of the component arteries of this arterial intracranial anastomosis, but they also identified the fact that more than half of all circles of Willis they have studied presented significant anatomical changes compared to the classical version, from which it departs more or less [3–5].

CoW is located on the inferior surface of the brain and surrounds the optic chiasm and other anatomical structures of the interpeduncular fossa [6]. In English literature, this anatomical structure is known as the "arterial circle" because the constituent arteries join altogether in a circular shape, thus connecting the carotid system with the vertebral-basilar system [6, 7]. However, some authors did not consider this arterial structure as being a true circle but rather an arterial polygon with a variable number of sides. This arterial structure is most often considered to be heptagon-shaped that is made as follows: anterior communicating artery (AComA); antero-lateral: two anterior cerebral arteries (ACAs), left and right; posterolateral: two posterior communicating arteries (PComA), left and right; posterior: two posterior cerebral arteries (PCAs), left and right [8], and this shape we will use in the present research.

In our days, stroke represents one of the greatest challenges of the public health systems as major morphological changes, such as disturbances of the blood–brain barrier, appears in the brain of the affected patients [9].

Because the CoW supplies blood to the brain, in case of occlusion of one of the cerebral arteries, identification of anatomical variants that could be present at this level could be useful in the assessment of stroke (ischemic or hemorrhagic) [10–12], especially in the Romanian population, as Romania it situated among the first 10 countries in the world in terms of this morbidity [13].

Moreover, knowing the prevalence, incidence, and types of anatomical anomalies that could affect the component arteries of the CoW could be useful for the understanding of some psychiatric conditions [14].

Also, knowing which the most frequent anatomical variants of CoW are, neurosurgeons could better plan their surgical interventions in case of ruptured intracranial aneurysms [8] because they need to know the hemodynamics of cerebral circulation for a given patient.

Aim

The purpose of our research was to identify the anatomical variants of circles of Willis identified on fresh brains obtained at clinical autopsies of adult deceased patients with neurological and neurosurgical conditions belonging to a specific population (Northeastern region of Romania), as such studies have not been realized in Romania up to date.

Patients, Materials and Methods

Study design

The present study was carried out within the Department of Pathology, Prof. Dr. Nicolae Oblu Emergency Clinical Hospital, Iaşi, Romania, and it is an intra-hospital descriptive observational study that follows the principles of ethical research.

Selected population

The study group included consecutive patients who died in Prof. Dr. Nicolae Oblu Emergency Clinical Hospital, between January 1, 2014 and June 30, 2016, due to medical causes and to whom a clinical autopsy was performed in order to establish or complete the medical causes of death. The gender and age of the deceased patients, as well as the gross morphology and the outer diameters of the component arteries of CoW (measured using a calibrated grid) were recorded from the Necropsy Registry of the Department of Pathology within the same Hospital. We also retrieved from the Digital Archive of the same Laboratory the photographs of CoW that were taken during clinical autopsies with a Sony digital camera, and re-analyzed them in order to establish the presence of any asymmetry in the configuration of the CoW, such as: hypoplasia of an artery, as well as any arterial absence, duplication, or fenestration, but also any difference in length, origin or place of discharge of any of its component arteries, by comparison with the opposite one.

Definitions of anatomical variants identified in the component arteries of the CoW

Based on previous studies on brains obtained at autopsy, we made the following considerations:

(*i*) A typical CoW was defined as an anatomical arterial structure with the presence of all its seven component vessels: two pre-communicating segments A1 of ACAs, two pre-communicating segments P1 of PCAs, one AComA and two PComAs, with the origin of its vessels presenting their typical origin, with their external diameter being not less than 1 mm, and with the absence of any anatomical variants, such as duplication, triplication, fenestration, etc. [15]. The rest of the circles of Willis that differed from the description mentioned above were considered to be "atypical" [16].

(*ii*) The absence of a component artery of CoW was considered when it cannot be identified, or it was replaced by a very thin fibrous cord without a lumen.

(*iii*) A component artery of a CoW was considered to be hypoplastic when its outer diameter was less than 1 mm, except for communicating arteries (AComA and PComAs), which were considered hypoplastic when its outer diameter was less than 0.5 mm [17].

(*iv*) PCA was defined as "fetal" (fPCA) when it originates entirely from the internal carotid artery (ICA) and having no connection to the basilar artery (BA). PCA was considered to be "partially fetal" (pfPCA) when it originates from the ICA and retains a small atresic connection with the BA [18].

Statistical analysis

The data we obtained from our research were introduced into a database using Excel program, tabulated, and later used to calculate the mean, number, and percentage of items we were followed, as well as to make the corresponding graphs. Finally, the circles of Willis were sorted according to their gross morphology and the results were compared with the literature data.

Results

From the total of 96 fresh available circles of Willis obtained at clinical autopsy, 68 (70.82%) cases presented the classical shape of the CoW and only 28 (29.18%) cases were categorized as "atypical" or "with anatomical variants" (Figure 1).

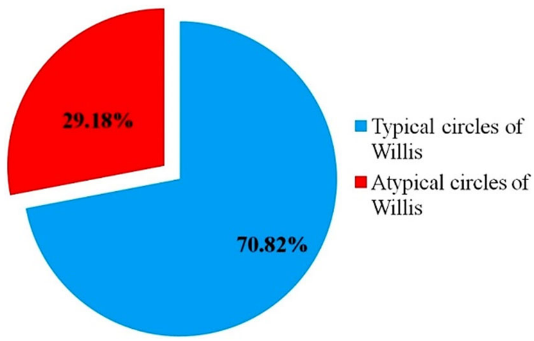

Figure 1 – *Distribution of cases according to the morphological appearance of their circle of Willis (typical vs atypical).*

Of all the 28 deceased patients with atypical CoW, 53.57% were male and 46.42% were female, with a M:F ratio of 1.15. The average age of this group was 61.78 years, the youngest patients being 39 years old, and the oldest being 83 years old. The mean age of female deceased patients was 60.15 years, but the mean age of male deceased patients was 65.6 years. In our series, patients deceased mostly in their 6th decade of life (14.28% of all female patients) and in the 7th decade of life (21.42% of all male patients). Taken together, 32.14% of all patients with atypical CoW died in their seventh decade of life (Figure 2).

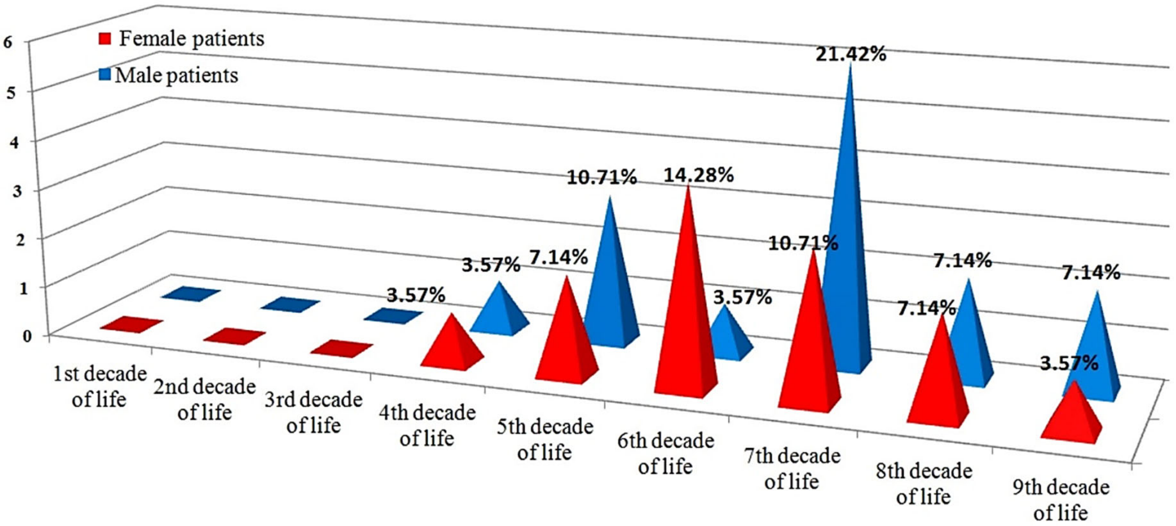

Figure 2 – ***Distribution of atypical circles of Willis according to cadavers' age decades and gender.***

The anterior part of the atypical circles of Willis presented anatomical variants in 10.71% of cases, the posterior part in 42.85% of cases, but in 46.42% of all cases the anatomical variants were identified on arteries belonging to both parts (Figure 3).

On the left side of the atypical circles of Willis, we identified anatomical variants in 21.42% of cases, on the right side in 35.71% of cases, and bilateral anatomical variants were identified in 42.85% of cases (Figure 4).

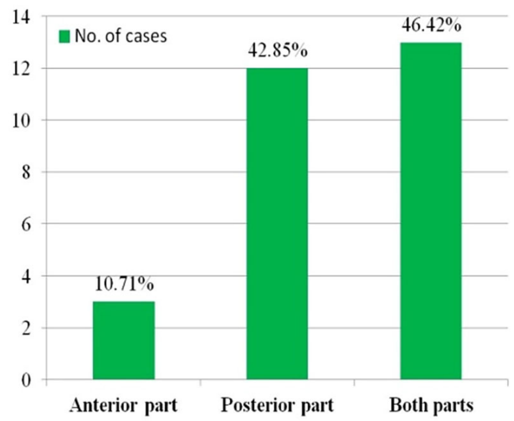

Figure 3 – ***Distribution of atypical circles of Willis according to the affected side (anterior vs posterior).***

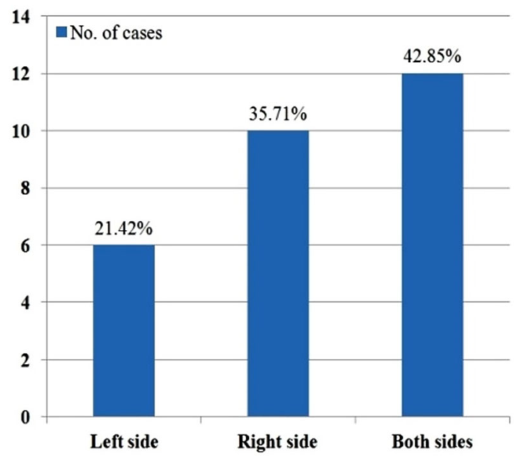

Figure 4 – ***Distribution of atypical circles of Willis according to the affected side (left vs right).***

Considering all 196 arteries that make up the 28 atypical circles of Willis we have analyzed, we found out that 69.38% had a normal appearance, but 30.61% of them presented various anatomical variants (Figure 5). 32.14% of all 28 cases with atypical CoW presented a single anatomical variant of the component arteries of the circles of Willis, and 67.86% of them exhibited multiple anatomical variants in the form of two (32.14%) associated anatomical variants, three (25%) associated variants, four (7.14%) associated variants and even five (3.57%) associated variants within the same CoW (Figure 6).

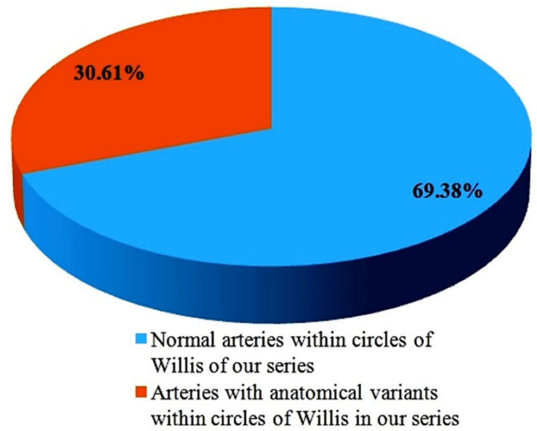

Figure 5 – ***Distribution of anatomical variants of the arteries within the analyzed atypical circles of Willis.***

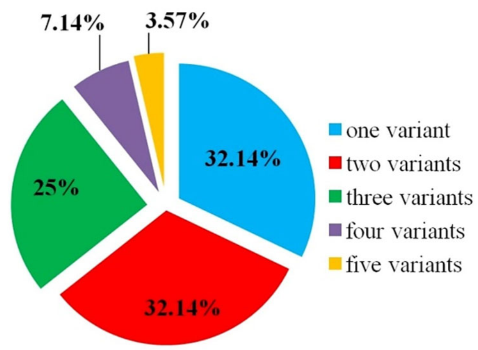

Figure 6 – ***Distribution of cases according to the number of vessels affected by anatomical variants within the same circle of Willis.***

Eight types of anatomical variants and the normal one were identified at the level of the component arteries of the CoW from our series (Figure 7). The first in rank was normal anatomy (69.38%), followed by uni- or bilateral hypoplasia (Figures 8–11), identified in 20.91% of all 196 analyzed arteries, then the absence of an artery (3.06%), partially fetal type artery (2.04%) (Figures 12–15). Some anatomical variants were quite rare: longer length of an artery with twisting path (1.53%), duplication (1.53%) (Figures 10 and 13), fenestration (0.51%), common trunk of two arteries (0.51%), and azygos artery (0.51%).

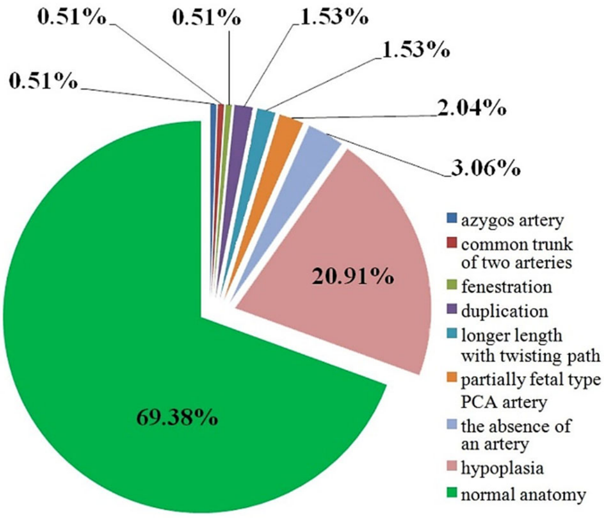

Figure 7 – ***Morphological type and percentage of anatomical variants of the component arteries of circles of Willis identified in the present series. PCA: Posterior cerebral artery.***

PComAs and ACAs presented hypoplasia as their most frequent anatomical variant (39.28% of all PComAs and 16.07% of all ACAs respectively), followed by the absence of the AComA (21.42% of all these arteries), pfPCA (7.14% of all these arteries), duplication of an artery, represented by 7.14% of all AComAs and 1.78% of all ACAs, but also artery with a longer length than the one on the opposite side, which also takes a tortuous path that affected 3.57% of all ACAs and 1.78% of all PComAs. Rare anatomical variants were arteries with abnormal origin from a common trunk with another vessel that normally has its origin outside the CoW (1.78% of all PCAs), fenestration of a vessel and formation of the azygos artery (1.78% of all ACAs for each type) (Figures 16–19).

If we consider all 96 analyzed CoW, we identified nine of the 23 morphological patterns that were published to date (Table 1, Figure 20). The most common pattern was type 1 (classical, symmetrical), which represented 70.83%), followed by type 4 (5.20%), type 6 (4.16%), type 8 (3.12%), and types 5 (Figure 8), 7, 9, 14, 18 (Figure 9), each of them representing only 0.51% of all cases.

Table 1 – ***Classification of morphological configurations of CoW in our series of 96 cases – after Lazorthes et al. (1979) [19], Eftekhar et al. (2006) [20] and De Silva et al. (2009) [5]***

Morphological configuration type	No. of cases	Percentage [%]
Type 1 (classical CoW)	68	70.83
Type 4 (unilateral hypoplastic PComA)	5	5.2
Type 5 (hypoplastic PComA and AComA)	1	0.51
Type 6 (bilaterally hypoplastic PComAs)	4	4.16
Type 7 (bilateral hypoplastic PComAs and hypoplastic AComA)	1	0.51
Type 8 (Unilateral hypoplastic ACA-A1 segment)	3	3.12
Type 9 (Unilateral hypoplastic PCA-P1 segment)	1	0.51
Type 14 (hypoplastic ACA-A1 and hypoplastic contralateral PComA)	1	0.51
Type 18 (bilaterally hypoplastic PComAs and ACAs-A1 segment)	1	0.51

ACA: Anterior communicating artery; AComA: Anterior communicating artery; CoW: Circle of Willis; PCA: Posterior cerebral artery; PComA: Posterior communicating artery.

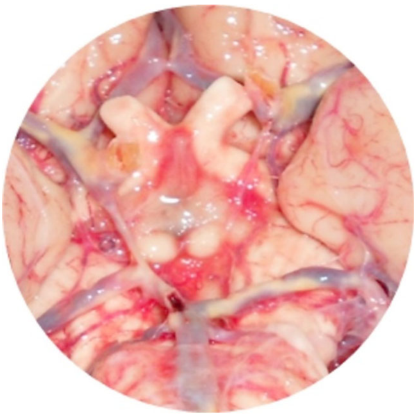

Figure 8 – ***Type 5 morphological configuration of CoW: hypoplastic left PComA and hypoplastic AComA (Authors' anatomical collection). AComA: Anterior communicating artery; CoW: Circle of Willis; PComA: Posterior communicating artery.***

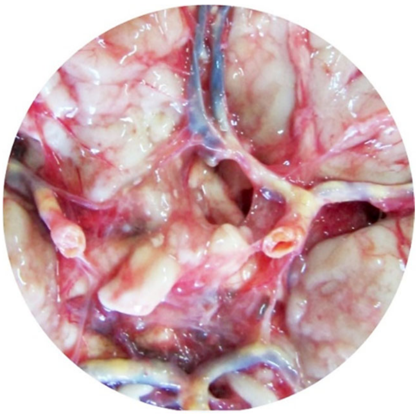

Figure 9 – ***Type 18 morphological configuration of CoW: hypoplastic right ACA, hypoplastic right PComA, and hypoplastic left PComA (Authors' anatomical collection). ACA: Anterior communicating artery; CoW: Circle of Willis; PComA: Posterior communicating artery.***

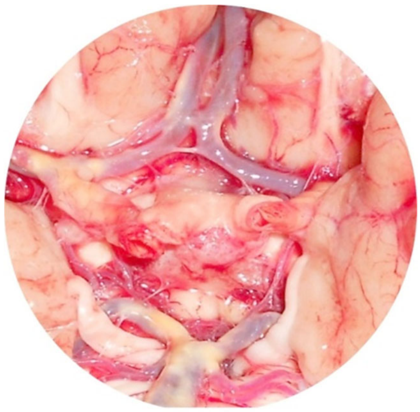

Figure 10 – ***A new type of configuration of CoW: duplication of AComA, duplication of right ACA in A1 segment, hypoplasia of left PComA, and hypoplasia of right PComA (Authors' anatomical collection). ACA: Anterior communicating artery; AComA: Anterior communicating artery; CoW: Circle of Willis; PComA: Posterior communicating artery.***

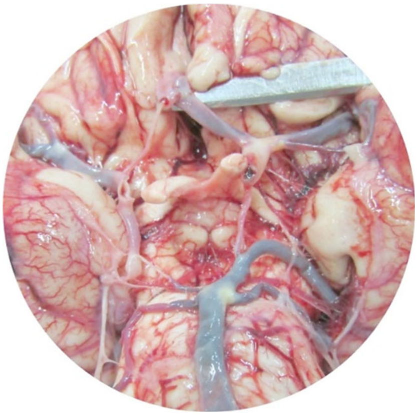

Figure 11 – ***A new type of configuration of CoW: hypoplasia of right ACA, hypoplasia of left PCA, and partially fetal right PCA (Authors' anatomical collection). ACA: Anterior communicating artery; CoW: Circle of Willis; PComA: Posterior cerebral artery.***

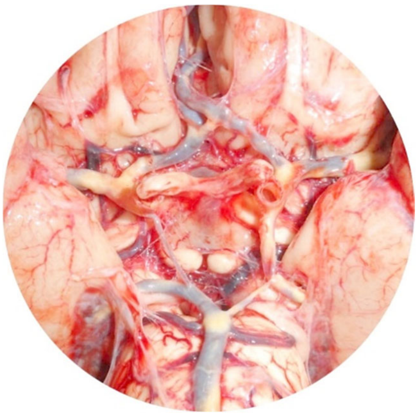

Figure 12 – ***A new type of configuration of fresh autopsied CoW: partially fetal left PCA (Authors' anatomical collection). CoW: Circle of Willis; PCA: Posterior cerebral artery.***

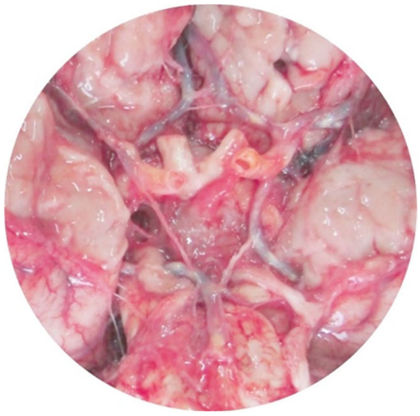

Figure 13 – ***A new type of configuration of fresh autopsied CoW: duplication of AComA and partially fetal left PCA (3.57%) (Authors' anatomical collection). AComA: Anterior communicating artery; CoW: Circle of Willis; PCA: Posterior cerebral artery.***

Figure 14 – ***A new type of configuration of fresh autopsied CoW: hypoplasia of the right PComA and partially fetal left PCA (Authors' anatomical collection). CoW: Circle of Willis; PCA: Posterior cerebral artery; PComA: Posterior communicating artery.***

Figure 15 – ***A new type of configuration of fresh autopsied CoW: hypoplasia of AComA, partially fetal right PCA and hypoplasia of left PComA (Authors' anatomical collection). AComA: Anterior communicating artery; CoW: Circle of Willis; PCA: Posterior cerebral artery; PComA: Posterior communicating artery.***

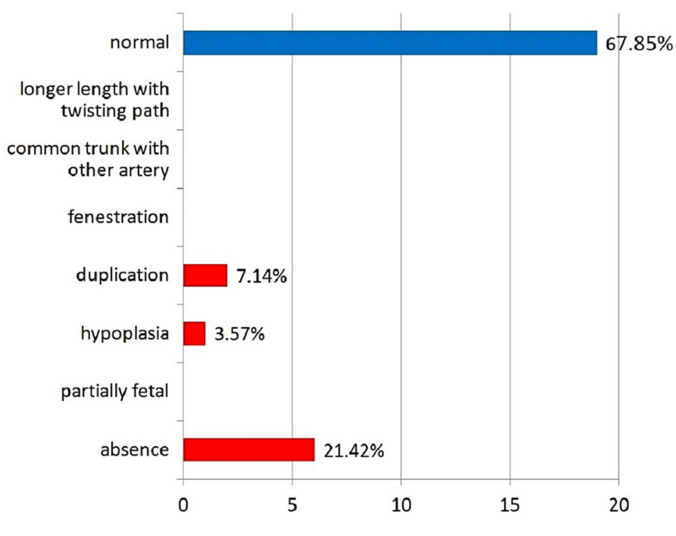

Figure 16 – ***Anatomical variants of anterior communicating artery (AComA).***

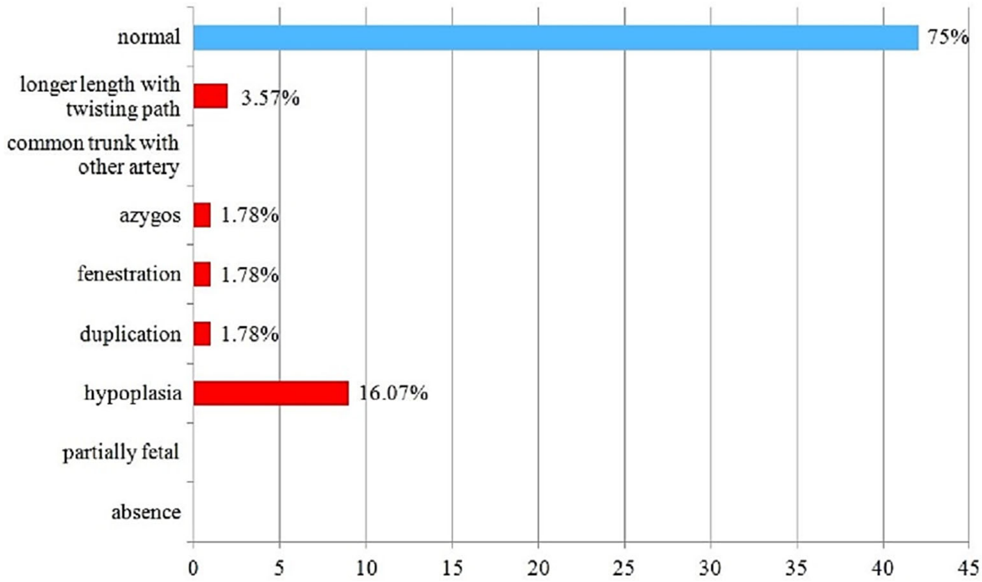

Figure 17 – *Anatomical variants of anterior cerebral artery (ACA).*

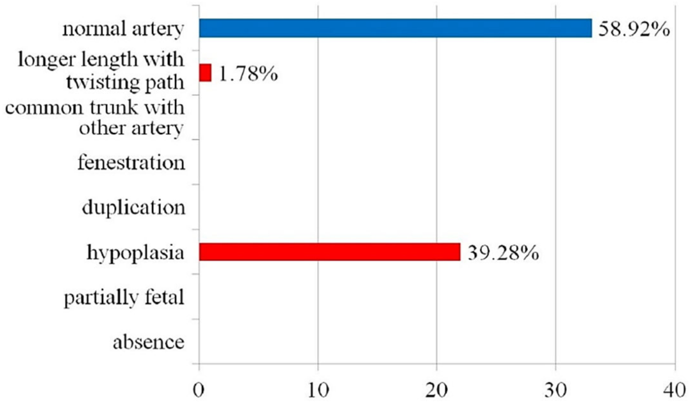

Figure 18 – *Anatomical variants of posterior communicating artery (PComA).*

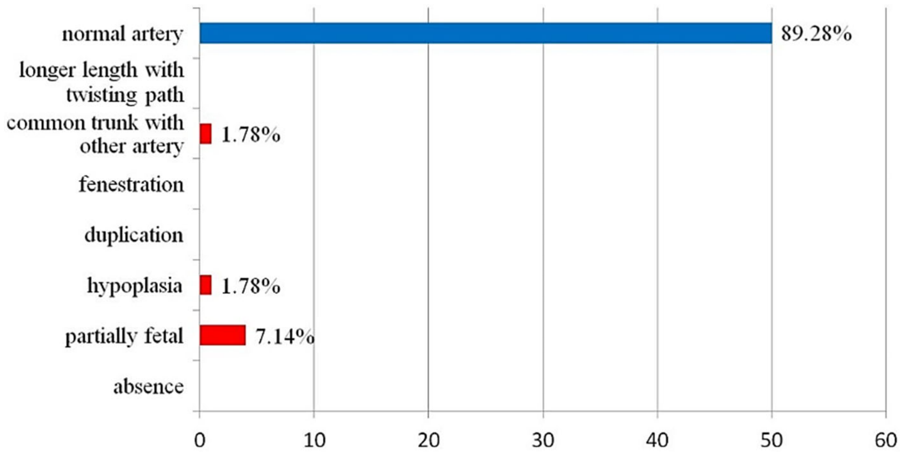

Figure 19 – *Anatomical variants of posterior cerebral artery (PCA).*

Of the 28 circles of Willis with anatomical variants in our series, in 35.71% we identified new associations (Figures 10–15). These are the following: (*i*) incomplete CoW with absence of AComA, hypoplasia of left ACA, and hypoplasia of right PComA (7.14%); (*ii*) incomplete CoW with absence of AComA, fenestration of right ACA and hypoplasia of right PComA (3.57%); (*iii*) complete CoW with AComA duplication, right ACA duplication, and bilateral PComA hypoplasia (3.57%) (Figure 10); (*iv*) complete CoW with duplication of AComA, and common origin of PCA and superior cerebellar artery in the same arterial trunk (3.57%); (*v*) complete CoW with hypoplasia of right ACA, partially fetal right PCA, and hypoplasia of left PComA (3.57%) (Figure 11); (*vi*) complete CoW with partially fetal left PCA (3.57%) (Figure 12); (*vii*) complete CoW with duplication of AComA and partially fetal left PCA (3.57%) (Figure 13); (*viii*) complete CoW with hypoplasia of the right PComA and partially fetal left PCA (3.57%) (Figure 14); (*ix*) complete CoW with hypoplasia of AComA, partially fetal right PCA, hypoplasia of left PComA (3.57%) (Figure 15).

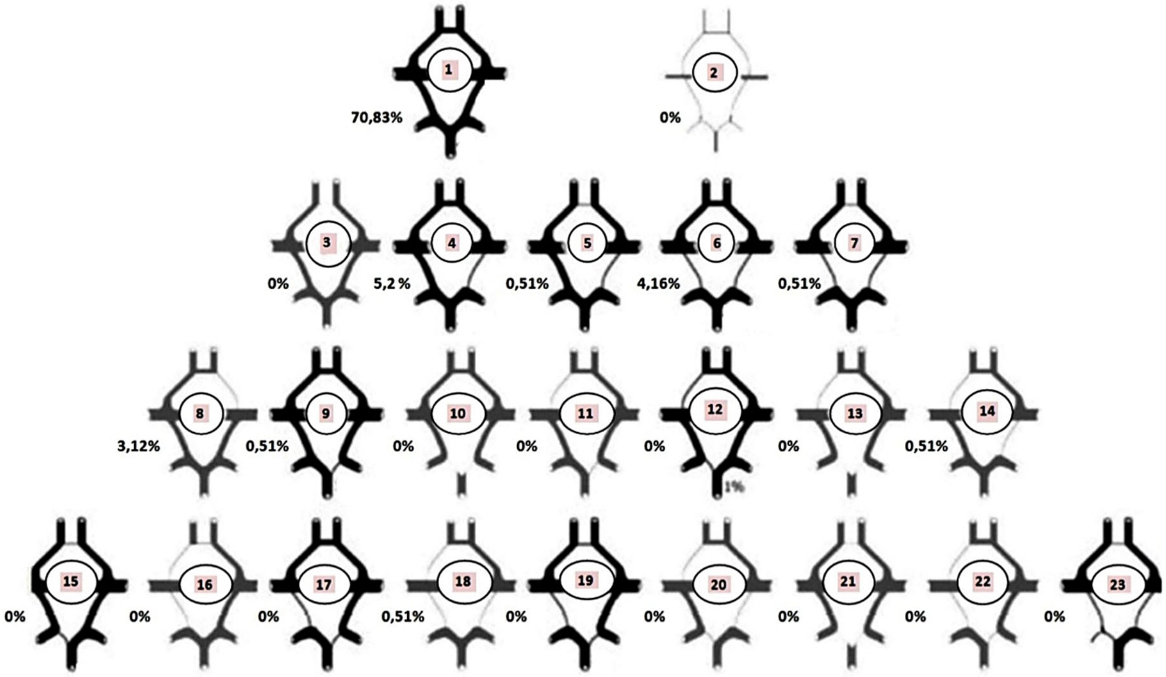

Figure 20 – *Percentages of morphological types of CoW in our series of 96 cases: Type 1 – All arterial segments (AComA, A1 segments of ACAs, PComAs, P1 segments of PCAs) are normal; Type 2 – All arterial segments (AComA, A1 segments of ACAs, PComAs, P1 segments of PCAs) are hypoplastic; Type 3 – Hypoplastic AComA; Type 4 – Unilateral hypoplastic PComA; Type 5 – Unilateral hypoplastic PComA and hypoplastic AComA; Type 6 – Bilateral hypoplastic PComAs; Type 7 – Bilateral hypoplastic PComAs and hypoplastic AComA; Type 8 – Unilateral hypoplastic A1 segment of ACA; Type 9 – Unilateral hypoplastic P1 segment of PCA; Type 10 – Bilateral hypoplastic P1 segments of PCAs; Type 11 – Hypoplastic P1 segment of PCA and hypoplastic contralateral segment A1 of ACA; Type 12 – Hypoplastic P1 segment of PCA and hypoplastic ipsilateral segment A1 of ACA; Type 13 – Bilateral hypoplastic segments P1 of PCAs and unilateral hypoplastic A1 segment of ACA; Type 14 – Hypoplastic A1 segment of ACA and hypoplastic contralateral PComA; Type 15 – Hypoplastic AComA and hypoplastic ipsilateral P1 segment of PCA; Type 16 – Hypoplastic PComA, hypoplastic ipsilateral A1 segment of ACA and hypoplastic AComA; Type 17 – Hypoplastic PComA and hypoplastic contralateral P1 segment of PCA; Type 18 – Bilateral hypoplastic PComAs and bilateral hypoplastic A1 segments of ACAs; Type 19 – Hypoplastic AComA, hypoplastic PComA, and hypoplastic contralateral P1 segment of PCA; Type 20 – Hypoplastic P1 segment of PCA, hypoplastic contralateral PComA, and hypoplastic ipsilateral A1 segment of ACA; Type 21 – Bilateral hypoplastic P1 segments of PCAs and hypoplastic AComA; Type 22 – Hypoplastic PComA, hypoplastic ipsilateral A1 segment of ACA, and hypoplastic contralateral P1 segment of PCA; Type 23 – Bilateral hypoplastic PComAs and hypoplastic P1 and P2 segments of PCAs (schematic representation of types was realized after Eftekhar et al. (2006) [20]). ACA: Anterior communicating artery; AComA: Anterior communicating artery; CoW: Circle of Willis; PCA: Posterior cerebral artery; PComA: Posterior communicating artery.*

Discussions

Anatomical variants of CoW have been identified since the 16th century by famous anatomist Andreas Vesalius (1514–1564). He was the first one who described the anatomical variants of the arterial circle from the base of the human brain and even illustrated the morphological aspects of two variants: the absence of AComA and duplication of the ICA [2]. Three centuries later, as brain research gained momentum, the Irish physician Richard Quain (1816–1898), analyzing 1040 autopsied brains, published, in 1844, a case showing PCA originating in the ICA [21], due to failure to take its normal post-fetal origin from the BA, a variant called fPCA, which is a common variant of the cerebral circulation, being seen in 20% of cases.

Fawcett & Blachford, two doctors from Bristol, published, in 1905, the results of their study on 700 autopsy specimens and demonstrated, based on illustrations, that circles of Willis can present many anatomical variants, namely double, triple, or absent AComA [22]. Then, in 1916, an English anatomist and physician from Manchester, J.S.B. Stopford [23], published images of several types of anatomical variants found in his autopsy series demonstrating that AComA may be unique, absent by fusion of the two ACAs, full dual or partial dual, triple, quadruple or networked.

In the last decade, studies that have analyzed circles of Willis obtained at autopsy (Table 2), either clinical or forensic, present a variable number of anatomical variants, but the percentages depended on the patients, if they were alive or deceased, on the method they used, and the clinical pathology they have had. Poudel & Bhattarai (2010), from Manipal College of Medical Sciences (Nepal), analyzed 35 formalin-fixed circles of Willis, obtained by clinical autopsy. They identified various anatomical variants of the component arteries in only 8.6% of the cases [24]. On the contrary, De Silva *et al.* (2009), in Sri Lanka, reported the presence of a classical arterial structure only in 14.2% of their 225 analyzed circles of Willis, but their cases were from forensic autopsies [5]. Our study, carried out on 96 fresh circles of Willis obtained at clinical autopsy from patients admitted in neurological and neurosurgical clinics, revealed atypical circles in almost one-third of cases, thus representing intermediate values between those reported by other studies working also on specimens obtained at clinical and forensic autopsies. Compared to other reports, even though the patients from the present study were previously admitted within neurological and neurosurgical clinics, our research proved that the prevalence of anatomical variants in this selected population was quite low because not all of our cases presented a cerebrovascular pathology, and the circles of Willis were obtained at consecutive routine clinical autopsies.

Table 2 – ***Types of CoW in clinical versus forensic autopsy series, according to author, country, type of case series and method of investigation***

Authors	Country	Case series	Method of investigation	CoW classical	CoW abnormal
Poudel & Bhattarai (2010) [24]	Nepal	35 formalin-fixed brains	Clinical autopsy	91.4%	8.6%
Kapoor *et al.* (2008) [25]	India	1000 formalin-fixed brains	Forensic autopsy	45.2%	54.8%
Iqbal (2013) [17]	India	50 fresh brains	Clinical autopsy	48%	52%
Raghavendra *et al.* (2014) [26]	India	50 fresh brains	Clinical autopsy	56%	44%
Siddiqi *et al.* (2013) [3]	Lahore	51 formalin-fixed brains	Forensic autopsy	23.6%	76.4%
De Silva *et al.* (2009) [5]	Sri Lanka	225 formalin-fixed brains	Forensic autopsy	14.2%	85.8%
Nordon & Rodrigues Júnior (2012) [27]	Brazil	50 fresh brains	Clinical autopsy	46%	54%
Pascalau & Padurean (2014) [28]	Romania, Cluj	10 formalin-fixed brains	Clinical autopsy	–	100%
Our series (2022)	Romania, Iaşi	96 fresh brains	Clinical autopsy	70.83%	29.17%

CoW: Circle of Willis.

Some autopsy studies showed a higher prevalence of anatomical variants of CoW in the male patients [29, 30] and we also identified this male predominance in our series.

Also, in an autopsy study, conducted by Hashemi *et al.* (2013), in Iran, a much higher predominance of male patients (84.5%) was found among the deceased patients. But the mentioned authors did not find any significant difference between the anatomical variants and the gender of patients [31].

Jin *et al.* (2016) analyzed the morphological features of circles of Willis in 281 Chinese patients with a family history of stroke using computed tomography (CT) angiography. The average age of their patients was 50.9±10.5 years, these values being lower than those identified in our study. Among the respective patients, male patients were also more numerous [32].

In the angiographic studies performed to determine anatomical variations of CoW, the age of the patients is usually around 50 years old. Harizi (Shemsi) *et al.* (2015), in Albania, using angio-CT, found out that more than half of their patients were aged >55 years [33].

Alawad *et al.* (2009), in Sudan, had a sample of 143 patients investigated with magnetic resonance angiography (MRA) and identified a median age of 53 years (variations between 40–65 years) [34] (Table 3).

Table 3 – ***Age of the cases with CoW exhibiting anatomical variants according to different authors, countries, case study groups, and methods of investigation***

Authors	Country	Case study group (No. of patients)	Method of investigation	Age [years]	
Harizi (Shemsi) *et al.* (2015) [33]	Albania	60 patients with cerebrovascular disease	Angio-CT	45% (<55 years)	55% (>55 years)
		60 control persons		85% (<55 years)	15% (>55 years)
Alawad *et al.* (2009) [34]	Sudan	143 patients	Angio-MRI	Average age: 53 years (variations between 40–65 years)	
Hoksbergen *et al.* (2000) [11]	The Netherlands	12 cadavers	Clinical autopsy	Average age: 75 years (variations between 51–91 years)	
Nordon & Rodrigues Júnior (2012) [27]	Brazil	50 cadavers	Clinical autopsy	Average age: 60.39 years	
Our series (2022)	Romania	96 fresh brains	Clinical autopsy	Average age: 61.78 years	

CoW: Circle of Willis; CT: Computed tomography; MRI: Magnetic resonance imaging.

In contrast, patients in whom CoW was studied after their death were much older. In the study by Hoksbergen *et al.* (2000), in the Netherlands, the average age of those autopsied and included in the study was 75 years (variations between 51–91 years) [11].

In Brazil, Nordon & Rodrigues Júnior analyzed the anatomical variations of CoW on a number of 50 cadavers with an average age of 60.39 years [27] (Table 3). Therefore, in autopsy studies, the average age of the deceased in which anatomical variations of CoW are analyzed is usually around 60 years, but in living patients in which imaging aspects of CoW are analyzed, the age is less than 55 years. In our study carried out on fresh brains obtained at the clinical autopsy, we obtained values that are in line with literature.

Also, in our study, the posterior part of the CoW showed four times more anatomical variants compared to the anterior part, but almost half of the cases showed anatomical variants in both the anterior and posterior parts. Same findings were reported recently by Zaki *et al.* (2019) [35], and Nordon &

Rodrigues Júnior (2012) identified 8-fold more anatomical variants in the posterior part of the CoW compared to the anterior part [27].

Anatomical variants can affect both left- and right-sided arteries of the CoW. Macchi *et al.* (1996), in Italy, found that anatomical variants occurred more frequently on the left side than on the right side of CoW [36]. Raghavendra *et al.* (2014), in India, found more anatomical variants of CoW on the right side than on the left side [26]. In our study, we identified more anatomical variants on the right side than on the left, but in almost half of the cases both sides had at least one anatomical variant.

Numerous autopsy studies report the predominance of CoW with unique anatomical variants. Kapoor *et al.* (2008) found in over 90% of their cases only unique anatomical variants [25] and Pradhan *et al.* (2009) [37] and Raghavendra *et al.* (2014) [26] reported only unique anatomical variants in their series. Macchi *et al.* (1996) [36] reported 84% of CoW as having unique anatomical variants, but Pascalau & Padurean (2014) [28], in Romania, found a higher number of circles of Willis with multiple anatomical variants in their series of 10 formalin-fixed brains. In contrast to all the mentioned reports, our research also identified many more cases with multiple anatomical variants than with single anatomical variants on CoW specimens obtained at clinical autopsy.

Similar to Nordon & Rodrigues Júnior (2012), in Brazil [27], we also identified two, three, four or even five anatomical variant associations within the same CoW. Within the multiple anatomical variants, two vessels were the most frequently involved, but the involvement of five vessels of a CoW was also identified, even though it was a rare event.

In our study, one-third of all analyzed CoW component arteries (196 vessels) presented various anatomical variants, both in the anterior and posterior segments of the CoW. The most common anatomical variant was hypoplasia of an artery, mostly of the PComAs, but all arteries could be affected by this anatomical variant. Duplication was the second in rank, followed by greater length of an artery, which also takes a tortuous course. Arterial fenestrations as well as azygos artery were rare events. In his study, Iqbal (2013) also identified hypoplasia of a component artery of the CoW as the most common anatomical variant (24%), followed by duplication of a vessel (10%), fetal PCA (10%) and the absence of an artery (6% of all cases) [17]. Even on CT cerebral angiography or 3T time-of-flight MRA images, the most common anatomical variants are also hypoplastic PComA [38, 39].

When we analyzed the anatomical variants of each of the constituent arteries of the CoW, we found out five different types of such anomalies at the ACA level, among which hypoplasia was the most common, as other authors also reported [40].

Regarding AComA, in our study, its absence was the most encountered variant along with duplication and hypoplasia, but Kardile *et al.* identified duplication as the most common variation (10%) of this artery [41]. In an MRA study, it was found that hypoplasia and aplasia of ACA are the most frequent anatomical variants, but duplication could also be identified, even if in a small number of cases. The same anatomical types of variants were encountered at ACA level [42]. The smallest number of variants was identified at PComAs level, as only hypoplasia and longer length with twisting path were noted. Many other authors also reported hypoplasia as being the most common for this artery, be it in angiographic as well as in autopsy studies [43].

PCAs presented three types of anatomical variants, the most numerous being the partially fetal type. Krishnamurthy *et al.* (2008) made also an autopsy study on 89 formalin-fixed circles of Willis taken from an Indian population and found out that PCAs exhibited only a single anatomic variant, *i.e.*, anomalous origin and only in very small number of cases (2.2%) [44]. On the other hand, a Macedonian study realized on CT-angiographies of the CoW identified fetal configuration in more than one fifth of their cases (22.64%), but also the transitional configuration in 7.54% of the patients they have studied [45].

There are reports of many more other types of anatomical variants at the CoW level: plexiform artery, triplication, accessory artery, fusion, hyperplasia, aplasia, as Singh *et al.* (2017) found out in their cadaveric study realized in India [46].

Few articles showing multiple anatomical variants of CoW were published up to date. Using circles of Willis obtained during forensic autopsies, Kapoor *et al.* (2008) reported only 7.4% of all samples they have studied as having multiple anatomical variants [25].

A group of Italian researchers analyzed 100 circles of Willis of healthy individuals they have investigated by angio-MRI and found out that only 16% of cases presented multiple anatomical anomalies [36].

Iqbal (2013), in India, found that 24% of 50 circles of Willis they have analyzed presented a single anatomical variant of the component arteries. Multiple anomalies were more numerous (28% of cases), among which 20% had two anatomical variants and 8% had more than two anatomical variants [17]. These authors recorded the association of hypoplastic PComA with contralateral fetal-type PCA, which was found by us in one case, with or without an association with hypoplasia of AComA, or the association of hypoplastic PComA with duplicated AComA, also found by us, but our case also associated right ACA duplication, and bilateral PComA hypoplasia.

In our study, when taking CoW as a whole, one-third of atypical circles showed single anatomical variants, and two-thirds multiple anatomical variants, with involvement of two to five arteries of the same CoW. Some other studies reported higher percentages of multiple variants. Realizing a similar study with ours, but on 225 Sri Lankan adult circles of Willis, De Silva *et al.* (2009) found out that more than half of them had multiple anatomical abnormalities [5].

Of the 23 configurations of CoW, already described by Lazorthes *et al.* (1979) [19] and completed by De Silva *et al.* (2009) [5] and el Khamlichi *et al.* (1985) [47], in the present study we identified only nine types, just like the Polish authors Klimek-Piotrowska *et al.* (2016) also found in an autopsy study conducted in Poland [48].

As in many other studies [46–49], types 4, 6, and 8 were also present in our study in the highest percentages. But, in contrast to these, in which the most common type of CoW was type 6, in our series the most common anatomical configuration was type 4 (unilateral hypoplastic PComA), followed by type 6 (bilateral hypoplastic PComAs), which was, however, in a smaller percentage compared to those reported by the above authors.

Type 14 (hypoplastic A1 segment of ACA and hypoplastic contralateral PComA) was within the same values reported by the above authors, but type 18 (bilateral hypoplastic PComAs and bilateral hypoplastic A1 segments of ACAs) was identified in much lower percentage than in the other published series (Table 4). Also, in our series, we identified a much higher percentage of other new configurations which can be the results of some changing in the microenvironment during the embryogenesis [50], may be due to some particular living conditions of the population in this region of our country.

Table 4 – *Comparisons between the types of CoW obtained in our study and those reported by various studies, according to authors, country, and publishing year*

Type	Author (year)	Riggs & Rupp (1963) [49]	el Khamlichi *et al.* (1985) [47]	Lazorthes *et al.* (1979) [19]	Eftekhar *et al.* (2006) [20]	De Silva *et al.* (2009) [5]	The present study
	Country	USA	Morocco	France	Iran	Sri Lanka	Romania
	No. of examined brains	994	100	200	102	225	96
Type	**Configuration**						
1	Typical CoW – all arterial segments are normal	19%	18%	14.5%	28%	14%	70.83%
2	All arterial segments are hypoplastic	5%	0%	5%	0%	0%	0%
3	Hypoplastic AComA	9%	11%	4.5%	0%	14%	0%
4	Unilateral hypoplastic PComA	9%	14%	14%	20%	11.5%	5.20%
5	Unilateral hypoplastic PComA and hypoplastic AComA	4%	6%	5%	4%	7%	0.51%
6	Bilateral hypoplastic PComAs	13%	24%	22%	27%	23%	4.16%
7	Bilateral hypoplastic PComAs and hypoplastic AComA	7%	10%	17%	4%	16%	0.51%
8	Hypoplastic ACA-A1	5%	2%	1.5%	0%	3%	3.12%
9	Hypoplastic PCA-P1	5%	3%	2.5%	0.9%	0.8%	0.51%
10	Bilateral hypoplastic PCA-P1	3%	1%	3%	0%	0.4%	0%
11	Hypoplastic PCA-P1 and hypoplastic contralateral ACA-A1	0.2%	0%	0%	0%	0%	0%
12	Hypoplastic PCA-P1 and hypoplastic ipsilateral ACA-A1	2%	1%	1.5%	0.9%	2%	0%
13	Bilateral hypoplastic PCA-P1 and ACA-A1	0.5%	0%	0.5%	0%	0.4%	0%
14	Hypoplastic ACA-A1 and hypoplastic contralateral PComA	0.7%	0%	0.5%	0%	0%	0.51%
15	Hypoplastic AComA and hypoplastic ipsilateral PCA-P1	3.5%	4%	2%	0.9%	3%	0%
16	Hypoplastic PComA, hypoplastic ipsilateral ACA-A1, and hypoplastic AComA	2%	3%	1%	0%	0%	0%
17	Hypoplastic PComA and hypoplastic contralateral PCA-P1	3%	0%	1.5%	2%	0.4%	0%
18	Bilateral hypoplastic PComAs and bilateral hypoplastic ACA-A1	6%	0%	3%	0%	2%	0.51%
19	Hypoplastic PComA, hypoplastic AComA, and hypoplastic contralateral PCA-P1	2%	1%	0.5%	0.9%	0%	0%
20	Hypoplastic PCA-P1, hypoplastic contralateral PComA, and hypoplastic ipsilateral ACA-A1	1%	1%	0%	0%	0%	0%
21	Bilateral hypoplastic PCAs-P1 and hypoplastic AComA	1%	0%	0.5%	0%	0.4%	0%
22	Hypoplastic PComA, hypoplastic ipsilateral ACA-A1, and hypoplastic contralateral PCA-P1	0.3%	0%	0%	0%	0%	0%
23	Bilateral hypoplastic PComAs and hypoplastic PCA-P1 and PCA-P2	0.5%	1%	0%	0.9%	2%	0%
24	Other	0.5%	1%	0%	0.9%	2%	11.48%

ACA: Anterior communicating artery; AComA: Anterior communicating artery; CoW: Circle of Willis; PCA: Posterior cerebral artery; PComA: Posterior communicating artery.

Conclusions

Our research on circles of Willis obtained at clinical autopsies that were performed on deceased adult patients with cerebrovascular diseases found data similar to those in the specialized literature, but also some results had a particular aspect, different from the data published so far. Hypoplasia of an artery was the most common anatomical variant in these circles of Willis, but, unlike all other studies with which we compared our results, we identified the presence of multiple anatomical variants in two-thirds of cases, and there were simultaneously affected two up to five component arteries of the CoW. Of the 23 configurations of the circles of Willis that were published so far, in the present study we identified only nine types, and in contrast to literature data, in our series we identified another nine new types. Therefore, the data obtained in our study demonstrate the fact that in the population living in the Moldova region or the Northeastern part of Romania, the anatomical variations of circles of Willis are very polymorphic, with particular aspects compared to other studies published so far.

Conflict of interests

The authors declare that they have no conflict of interests.

References

[1] Willis T. *Cerebri Anatome: cui accessit nervorum descriptio et usus*. Typis Tho. Roycroft, Londini, UK, 1664, 20. https://anatomia.library.utoronto.ca/islandora/object/anatomia%3ARBAI015

[2] Dumitrescu AM, Costea CF, Cucu AI, Dumitrescu GF, Turliuc MD, Scripcariu DV, Ciocoiu M, Tănase DM, Turliuc S, Bogdănici CM, Nicoară SD, Cărăuleanu A, Schmitzer S, Sava A. The discovery of the circle of Willis as a result of using the scientific method in anatomical dissection. Rom J Morphol Embryol, 2020, 61(3):959–965. https://doi.org/10.47162/RJME.61.3.38 PMID: 33817741 PMCID: PMC8112754

[3] Siddiqi H, Ansar T, Fasih S. Variations in cerebral arterial circle of Willis in patients with hemorrhagic stroke: a computed tomography angiographic study. J Rawalpindi Med Coll, 2013, 17(2):215–218. https://www.journalrmc.com/volumes/1395217935.pdf

[4] Klimek-Piotrowska W, Kopeć M, Kochana M, Krzyżewski RM, Tomaszewski KA, Brzegowy P, Walocha J. Configurations of the circle of Willis: a computed tomography angiography based study on a Polish population. Folia Morphol (Warsz), 2013, 72(4):293–299. https://doi.org/10.5603/fm.2013.0049 PMID: 24402749

[5] De Silva KRD, Silva R, Gunasekera WSL, Jayesekera RW. Prevalence of typical circle of Willis and the variation in the anterior communicating artery: a study of a Sri Lankan population. Ann Indian Acad Neurol, 2009, 12(3):157–161. https://doi.org/10.4103/0972-2327.56314 PMID: 20174495 PMCID: PMC2824931

[6] Jinkins JR. Atlas of neuroradiologic embryology, anatomy, and variants. Lippincott Williams & Wilkins, Philadelphia, USA, 2000, 358–359. https://www.abebooks.com/9780781716529/Atlas-Neuroradiologic-Embryology-Anatomy-Variants-0781716527/plp

[7] Osborn AG. Diagnostic cerebral angiography. 2nd edition, Lippincott Williams & Wilkins, Philadelphia, PA, USA, 1999, 105. https://www.worldcat.org/title/939394590

[8] Kayembe KN, Sasahara M, Hazama F. Cerebral aneurysms and variations in the circle of Willis. Stroke, 1984, 15(5):846–850. https://doi.org/10.1161/01.str.15.5.846 PMID: 6474536

[9] Dahnovici RM, Pintea IL, Mălăescu DG, Busuioc CJ, Predescu A, Mogoantă L. Microscopic aspects of macrophage system cells in hemorrhagic stroke in humans. Rom J Morphol Embryol, 2011, 52(4):1249–1253. PMID: 22203930

[10] De Caro J, Ciacciarelli A, Tessitore A, Buonomo O, Calzoni A, Francalanza I, Dell'Aera C, Cosenza D, Currò CT, Granata F, Vinci SL, Trimarchi G, Toscano A, Musolino RF, La Spina P. Variants of the circle of Willis in ischemic stroke patients. J Neurol, 2021, 268(10):3799–3807. https://doi.org/10.1007/s00415-021-10454-4 PMID: 33786665

[11] Hoksbergen AWJ, Fülesdi B, Legemate DA, Csiba L. Collateral configuration of the circle of Willis: transcranial color-coded duplex ultrasonography and comparison with postmortem anatomy. Stroke, 2000, 31(6):1346–1351. https://doi.org/10.1161/01.str.31.6.1346 PMID: 10835455

[12] Roman-Filip CC, Stîngaciu AR, Catană MG, Dan AA, Bălaşa AF, Juravle C, Grosu F. Atypical posterior circulation strokes: a case-based review of rare anatomical variations involved. Rom J Morphol Embryol, 2021, 62(1):289–293. https://doi.org/10.47162/RJME.62.1.31 PMID: 34609434 PMCID: PMC8597371

[13] Pavaloiu R, Mogoanta L. Clinical, epidemiological and etiopathogenic study of ischemic stroke. Curr Health Sci J, 2017, 43(3):258–262. https://doi.org/10.12865/CHSJ.43.03.13 PMID: 30595886 PMCID: PMC6284836

[14] Blackburn IW. Anomalies of the encephalic arteries among the insane. A study of the arteries at the base of the encephalon in two hundred and twenty consecutive cases of mental disease, with special reference to anomalies of the circle of Willis. J Comp Neurol Psychol, 1907, 17(6):493–517. https://doi.org/10.1002/cne.920170604 https://onlinelibrary.wiley.com/doi/10.1002/cne.920170604

[15] Siddiqi H, Tahir M, Lone KP. Variations in cerebral arterial circle of Willis in adult Pakistani population. J Coll Physicians Surg Pak, 2013, 23(9):615–619. PMID: 24034183

[16] Sinha I, Ghosal AK, Basu R, Dutta I. Variation in the pattern of circle of Willis in human brain – a morphological study and review. Al Ameen J Med Sci, 2014, 7(1):13–19. http://ajms.alameenmedical.org/articlepdfs/ajms%20v.7.n1.2014%20p%2013-19.pdf

[17] Iqbal S. A comprehensive study of the anatomical variations of the circle of Willis in adult human brains. J Clin Diagn Res, 2013, 7(11):2423–2427. https://doi.org/10.7860/JCDR/2013/6580.3563 PMID: 24392362 PMCID: PMC3879841

[18] Shaban A, Albright KC, Boehme AK, Martin-Schild S. Circle of Willis variants: fetal PCA. Stroke Res Treat, 2013, 2013:105937. https://doi.org/10.1155/2013/105937 PMID: 23577277 PMCID: PMC3618940

[19] Lazorthes G, Gouazé A, Santini JJ, Salamon G. Le cercle artériel du cerveau (circulus arteriosus cerebri) [The arterial circle of the brain (*circulus arteriosus cerebri*)]. Anat Clin, 1979, 1(3):241–257. https://doi.org/10.1007/BF01654581 https://link.springer.com/article/10.1007/BF01654581

[20] 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. https://doi.org/10.1186/1471-2377-6-22 PMID: 16796761 PMCID: PMC1543654

[21] Quain R. The anatomy of the arteries of the human body, with its applications to pathology and operative surgery: in lithographic drawings with practical commentaries. Taylor and Walton, London, UK, 1844, 510. https://collections.nlm.nih.gov/catalog/nlm:nlmuid-8712312-bk

[22] Fawcett E, Blachford JV. The circle of Willis: an examination of 700 specimens. J Anat Physiol, 1905, 40(Pt 1):63.2–70. PMID: 17232664 PMCID: PMC1287340

[23] Stopford JSB. The arteries of the *pons* and *medulla oblongata*. J Anat Physiol, 1916, 50(Pt 2):131–164. PMID: 17233055 PMCID: PMC1289065

[24] Poudel PP, Bhattarai C. Anomalous formation of the *circulus arteriosus* and its clinico-anatomical significance. Nepal Med Coll J, 2010, 12(2):72–75. PMID: 21222400

[25] Kapoor K, Singh B, Dewan LIJ. Variations in the configuration of the circle of Willis. Anat Sci Int, 2008, 83(2):96–106. https://doi.org/10.1111/j.1447-073X.2007.00216.x PMID: 18507619

[26] Raghavendra, Shirol VS, Daksha D, Anil KRY, Desai SP. Circle of Willis and its variations; morphometric study in adult human cadavers. Int J Med Res Health Sci, 2014, 3(2):394–400. https://doi.org/10.5958/j.2319-5886.3.2.081 https://www.ijmrhs.com/abstract/circle-of-willis-and-its-variations-morphometric-study-in-adult-human-cadavers-1492.html

[27] Nordon DG, Rodrigues Júnior OF. Variations in the brain circulation – the circle of Willis. J Morphol Sci, 2012, 29(4):243–247. http://www.jms.periodikos.com.br/article/587cb4b77f8c9d0d058b481e

[28] Pascalau R, Padurean VA. Circle of Willis: anatomical variations important in cerebral vascular pathology. Abstracts of the 15th International Congress for Medical Students and Young Health Professionals, Romania, Medicalis 2014. Int J Med Stud, 2014, 2(Suppl 1):S40 (Abstract No. 25). https://ijms.pitt.edu/IJMS/article/view/53/26

[29] Bahaddur A, Chandan G. Anatomical variants of circle of Willis in south Indian population: a study by using magnetic resonance angiography. Int J Sci Res, 2015, 4(5):1077–1080. https://www.ijsr.net/get_abstract.php?paper_id=SUB153633

[30] Zulu H, Buumba PN, Silitongo M, Erzingastian K, Mudenda B. Anatomical variations of the circle of Willis as seen at the University Teaching Hospital, Lusaka, Zambia. J Prev Rehabil Med, 2016, 1(2):61–66. https://doi.org/10.21617/jprm.2016.0102.12 https://www.researchgate.net/publication/311651167_

Anatomical_Variations_of_the_Circle_of_Willis_as_seen_at_the_University_Teaching_Hospital_Lusaka_Zambia
[31] Hashemi SMR, Mahmoodi R, Amirjamshidi A. Variations in the anatomy of the Willis' circle: a 3-year cross-sectional study from Iran (2006–2009). Are the distributions of variations of circle of Willis different in different populations? Result of an anatomical study and review of literature. Surg Neurol Int, 2013, 4:65. https://doi.org/10.4103/2152-7806.112185 PMID: 23772335 PMCID: PMC3680999
[32] Jin ZN, Dong WT, Cai XW, Zhang Z, Zhang LT, Gao F, Kang XK, Li J, Wang HN, Gao NN, Ning XJ, Tu J, Li FT, Zhang J, Jiang YJ, Li NX, Yang SY, Zhang JN, Wang JH, Yang XY. CTA characteristics of the circle of Willis and intracranial aneurysm in a Chinese crowd with family history of stroke. BioMed Res Int, 2016, 2016:1743794. https://doi.org/10.1155/2016/1743794 PMID: 26881211 PMCID: PMC4736327
[33] Harizi (Shemsi) E, Rroji A, Cekaj E, Gabrani S. Anatomical variations of the circle of Willis and cerebrovascular accidents in transitional Albania. South Eastern Eur J Public Health, 2015, 3(1). https://doi.org/10.4119/seejph-1800 https://www.seejph.com/index.php/seejph/article/view/1800
[34] Alawad AHM, Hussein MA, Hassan MA. Morphology and normal variations of the cerebral arterial circle "of Willis" in Khartoum Diagnostic Centre. Khartoum Med J, 2009, 2(2): 215–219. https://eeese.uofk.edu/index.php/kmj/article/view/406
[35] Zaki SM, Shaaban MH, Abd Al Galeel WA, El Husseiny AAW. Configuration of the circle of Willis and its two parts among Egyptian: a magnetic resonance angiographic study. Folia Morphol (Warsz), 2019, 78(4):703–709. https://doi.org/10.5603/FM.a2019.0015 PMID: 30761512
[36] Macchi C, Catini C, Federico C, Gulisano M, Pacini P, Cecchi F, Corcos L, Brizzi E. Magnetic resonance angiographic evaluation of *circulus arteriosus cerebri* (circle of Willis): a morphologic study in 100 human healthy subjects. Ital J Anat Embryol, 1996, 101(2):115–123. PMID: 8997907
[37] Pradhan P, Baral K, Dan U, Prasad R. Morphological study of circle of Willis – a short review. J Anat Soc India, 2009, 58(1): 35–39. https://www.researchgate.net/publication/286701182_Morphological_Study_Of_Circle_Of_Willis_-_A_Short_Review
[38] Dhakal P, Kayastha P, Paudel S, Suwal S, Sharma MR, Ghimire RK. Anatomical variations in circle of Willis in patients undergoing CT cerebral angiography in a tertiary hospital in Nepal: a descriptive cross-sectional study. JNMA J Nepal Med Assoc, 2020, 58(232):1065–1068. https://doi.org/10.31729/jnma.5893 PMID: 34506369 PMCID: PMC8028512
[39] Hindenes LB, Håberg AK, Johnsen LH, Mathiesen EB, Robben D, Vangberg TR. Variations in the circle of Willis in a large population sample using 3D TOF angiography: the Tromsø Study. PLoS One, 2020, 15(11):e0241373. https://doi.org/10.1371/journal.pone.0241373 PMID: 33141840 PMCID: PMC7608873
[40] Han YK, Kim S, Yoon CS, Lee YM, Kang HC, Lee JS, Kim HD. A1 segment hypoplasia/aplasia detected by magnetic resonance angiography in neuropediatric patients. Ann Child Neurol, 2011, 19(3):231–239. https://www.annchildneurol.org/journal/view.php?number=568
[41] Kardile PB, Ughade JM, Pandit SV, Ughade MN. Anatomical variations of anterior communicating artery. J Clin Diagn Res, 2013, 7(12):2661–2664. https://doi.org/10.7860/JCDR/2013/6664.3725 PMID: 24551604 PMCID: PMC3919289
[42] Yokuş A, Toprak N, Gündüz AM, Akdeniz H, Akdemir Z, Dündar İ, Arslan H. Anterior cerebral artery and anterior communicating artery variations: assessment with magnetic resonance angiography. World Neurosurg, 2021, 155:e203–e209. https://doi.org/10.1016/j.wneu.2021.08.027 PMID: 34400324
[43] Gunnal SA, Farooqui MS, Wabale RN. Anatomical variability of the posterior communicating artery. Asian J Neurosurg, 2018, 13(2):363–369. https://doi.org/10.4103/ajns.AJNS_152_16 PMID: 29682035 PMCID: PMC5898106
[44] Krishnamurthy A, Nayak SR, Ganesh Kumar C, Jetti R, Prabhu LV, Ranade AV, Rai R. Morphometry of posterior cerebral artery: embryological and clinical significance. Rom J Morphol Embryol, 2008, 49(1):43–45. PMID: 18273501
[45] Dodevski A, Tosovska Lazarova D, Mitreska N, Aliji V, Stojovska Jovanovska E. Posterior cerebral artery – variation in the origin and clinical significance. Pril (Makedon Akad Nauk Umet Odd Med Nauki), 2014, 35(1):163–168. PMID: 24798602
[46] Singh R, Kannabathula AB, Sunam H, Deka D. Anatomical variations of circle of Willis – a cadaveric study. Int Surg J, 2017, 4(4):1249–1258. https://doi.org/10.18203/2349-2902.isj20171016 https://www.ijsurgery.com/index.php/isj/article/view/1180
[47] el Khamlichi A, Azouzi M, Bellakhdar F, Ouhcein A, Lahlaidi A. [Anatomic configuration of the circle of Willis in the adult studied by injection technics. Apropos of 100 brains]. Neurochirurgie, 1985, 31(4):287–293. PMID: 4088399
[48] Klimek-Piotrowska W, Rybicka M, Wojnarska A, Wójtowicz A, Koziej M, Hołda MK. A multitude of variations in the configuration of the circle of Willis: an autopsy study. Anat Sci Int, 2016, 91(4):325–333. https://doi.org/10.1007/s12565-015-0301-2 PMID: 26439730
[49] Riggs HE, Rupp C. Variation in form of circle of Willis. The relation of the variations to collateral circulation: anatomic analysis. Arch Neurol, 1963, 8:8–14. https://doi.org/10.1001/archneur.1963.00460010024002 PMID: 13973856
[50] Dumitrescu AM, Costea CF, Furnică C, Turliuc MD, Cucu AI, Bogdănici CM, Turliuc Ş, Dumitrescu GF, Sava A. Morphological aspects of the vasculogenesis and angiogenesis during prenatal edification of the circle of Willis: a review. Rom J Morphol Embryol, 2021, 62(3):679–687. https://doi.org/10.47162/RJME.62.3.04 PMID: 35263395 PMCID: PMC9019668

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