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Circle of Willis Variants and Intracranial Aneurysm Risk: Evidence from an Autopsy-Based Study

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Abstract: *This study investigates the correlation between anatomical variants of the Circle of Willis (CoW) and the presence of intracranial aneurysms (IcAs), a relationship insufficiently addressed in current literature. We conducted a 12-year retrospective observational study on 221 adult autopsied patients admitted to the "Prof. Dr. N. Oblu" Emergency Clinical Hospital in Iași, Romania. Demographic data, aneurysm morphology (location, diameter), and CoW anatomical variants were analyzed. IcAs were found in 29 cases (13.12%), most frequently located at the Anterior Communicating Artery (55.2%), with a majority measuring under 10 mm in diameter. A strong association was observed between IcAs and atypical CoW configurations (96.55%), particularly when three or four anatomical variants coexisted. No gender predisposition was identified. The mean age of patients increased with aneurysm size, yet larger aneurysms were less often associated with progression to death. Our findings suggest that the presence of multiple CoW variants significantly increases the likelihood of developing IcAs. These results may enhance prognosis and support clinical decision-making frameworks for managing cerebral aneurysms.*

Keywords: *intracranial aneurysms; autopsy; atypical Circle of Willis; anatomical variants.*

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1. Introduction

The cerebral arteries display a distinct histoarchitectural organization of the wall, i.e. lacking the external elastic lamina and having a thinner adventitial layer (Tulamo et al., 2010). Near the bifurcations of the cerebral arteries, the vascular muscular middle layer begins to gradually reduce, so that at the level of the bifurcation itself it is replaced by the adventitia (Idowu et al., 2008). This particular vascular anatomy creates a point of minimal resistance, which is exposed to elevated haemodynamic stressors from the blood flow reaching this level, especially in patients with arterial hypertension, and for this reason, intracranial aneurysms (IcAs) are formed, usually having a sac-like shape (Diagbouga et al., 2018). Once formed, the natural evolution of an unruptured IcA can either lead to rupture, or an increase in its diameter, with subsequent rupture, or it may remain stable over time (Morel, Bijlenga, & Kwak, 2022). It seems that there is a shear force on the arterial wall that can cause the rupture of the IcA, but collagen turnover in the vascular wall has also been implicated (Hackenberg et al., 2020).

There are a significant number of articles in the literature demonstrating the presence of great variability in the morphology of the circle of Willis (CoW), both in healthy populations and in patients with various neurological diseases (Dumitrescu et al., 2022; Dumitrescu et al., 2020a) or psychiatric conditions (Dumitrescu et al., 2024).

In the population from the North-Eastern region of Romania, from which the subjects of this study originate, multiple arterial anatomical variants have been identified, such as the aberrant subclavian artery, which can be associated with ectopic origins of the vertebral arteries or common carotid arteries (Nedelcu et al., 2024a), the aberrant right gastric vein (Arhire et al., 2024), but especially at the level of the arteries in the cephalic region, such as supernumerary fronto-orbital arteries that originate from the contralateral anterior cerebral artery (ACA), and are associated with a partially duplicated anterior communicating artery (ACoA) (Nedelcu et al., 2016).

Just as neuroinflammations or brain tumors cause certain neurological and/or psychiatric symptoms depending on their location, the location of IcAs, especially those of significant calibre, is associated with symptoms caused by the compression of adjacent nervous structures (Tawk et al., 2021). For this reason, it is important to accumulate new knowledge about the demographic aspects of the patients with IcAs, as well as regarding the aneurysmal diameter of IcAs. Moreover, information related to the association of these aneurysms with the anatomical variants of CoW are important in the management of these patients as it can aid in preventing severe neurological sequelae or perioperative mortality, after surgical or endoscopic treatment of these IcAs.

The purpose of this paper was to identify the demographic characteristics of patients with IcAs, the morphology of these aneurysms, and the morphology of CoW, at which level this vascular pathology develops, in order to identify a possible correlation between the presence of anatomical variants of CoW and the development of IcAs, as there is only limited data on this subject in the literature.

2. Materials and Methods

2.1. The selected population

This research is a descriptive observational study conducted retrospectively on 221 adult patients (aged ≥ 18 years), who were admitted to the "Prof. dr. N. Oblu" Emergency Clinical Hospital, Iași, Romania, over a period of 12 years (January 1, 2011 - December 31, 2022), for neurological or neurosurgical symptoms and signs, who died during hospitalization and on whom an autopsy was performed to determine the cause of death at the request of the attending physician.

For each case, a database was created, including information extracted from the patients' electronic medical records and from the autopsy protocol of the Laboratory of Pathology within the same hospital, namely: the demographic data of each patient (gender and age), the presence/absence

of IcAs, the macroscopic aspects of possible aneurysms (location and diameter), and possible associated anatomical variants of CoW.

In this research, the anatomical variants of the component arteries of the circle of Willis (CoW) were used as follows:

- Hypoplasia of the CoW arteries, except for the Posterior Cerebral Artery (PCA), was defined as an external diameter of the vessel less than 1 mm (Iqbal, 2013; Edith, Mwaka, & Sam, 2017; Kamath, 1981; Hegedus & Molnar, 1987).
- Hypoplasia of the Posterior Communicating Artery (PCoA) was defined as the artery with an external diameter of less than 0.5 mm (Iqbal, 2013; Edith, Mwaka, & Sam, 2017; Kamath, 1981; Hegedus & Molnar, 1987).
- The fetal-type PCoA represents the artery that completely originates from the Internal Carotid Artery (ICA), with no connection to the Basilar Artery (BA) or maintains only a hypoplastic connection with BA (Hegedus & Molnar, 1987), and the diameter of the P1 segment of the PCA is smaller than that of PCoA (Kamath, 1981).

In addition, it was considered that CoW can be divided into an anterior part, which is derived from ICA and comprises the two paired Anterior Cerebral Arteries (ACAs) and the ACoA, a posterior part, made of two paired PCAs, originating in the vertebrobasilar system, and the two paired PCoAs, having their origin in the Internal Carotid system (Dumitrescu et al., 2021a).

The inclusion criteria for this study were as follows: (1) adult patients aged ≥ 18 years; (2) clinical autopsy performed; (3) identification of an IcA; (4) availability of the relevant medical record for data extraction. The exclusion criteria were as follows: (1) patients aged < 18 years; (2) the cause of death was traumatic and a forensic autopsy was performed; (3) absence of IcA; (4) incomplete medical data; (5) patients who died in the hospital with a known cause of death and were released at the request of the family without autopsy.

2.2. Ethical considerations

All patients or their legal representatives provided written informed consent for the use of biological material in medical research at the time of admission. Informed consent for the performance of the autopsy was also obtained from the representatives of all patients included in this study.

This research was approved by the Ethics Committee of the "Prof. Dr. N. Oblu" Emergency Clinical Hospital in Iași and by the Research Ethics Committee of the "Grigore T. Popa" University of Medicine and Pharmacy in Iași.

Statistical analysis

The statistical analysis was performed using SPSS 29.0. Descriptive statistics were conducted to summarise the dataset's central tendency and dispersion. Qualitative variables were characterised by calculating absolute and percentage frequencies, while quantitative variables were characterised by calculating the mean, standard deviation (SD), and median (in cases where the normal distribution law was not met). The analytical study was conducted using the Chi-square test to investigate associations between qualitative variables. p-values < 0.05 were considered statistically significant, and p-values < 0.01 were considered highly statistically significant.

3. Results

Out of the total of 221 cases in the initial study group, only 29 patients (13.12% of all cases) had at least one IcA, identified during the autopsy examination. In the group of patients with IcAs, the male-to-female ratio was 1:1.

We conducted a comparative study based on the external diameter of the aneurysm, examining the basic characteristics of the patient cohort. The correlations between the mean ± SD age of the subjects studied and the diameter of the intracranial aneurysms (IcAs) demonstrated that subjects without aneurysms had a mean±SD age of 63.90 ± 14.80. On the other hand, subjects with

an aneurysm having a diameter <10 mm had a mean±SD age of 59.31 ± 15.07 years, subjects with an aneurysm having a diameter between 10 mm and 20 mm had a mean±SD age of 54.12 ± 10.85 years, while those with an aneurysm with a diameter >20 mm were the oldest subjects (66.50 ± 6.85 years). The subject with multiple IcAs, with diameters between 10 mm and 20 mm, was the youngest (42 years). The differences between the age values associated with the diameter values of IcAs, although identifiable, did not reach statistical significance (p= 0.144). The patient with multiple IcAs having diameters between 10 mm and 20 mm was identified as male. The majority (75.0%) of those with IcAs having diameters between 10 mm and 20 mm were also male; 75.0% of the subjects with aneurysms having diameters >20 mm were female, while subjects with aneurysms <10 mm were relatively evenly distributed by gender (Table 1).

Table 1. Comparative study of the demographic data of patients based on the external diameter of their intracranial aneurysms

	External diameter of the intracranial aneurysm										GLOBAL (n = 221): p-value (Kruskal-Wallis / Chi-squared test)	ANEURYSM GROUP (n = 29): p-value (Kruskal-Wallis / Chi-squared test)
	Absence of aneurysm		Single aneurysm (diameter <10 mm)		Single aneurysm between 10mm and 20 mm		Single aneurysm (>20 mm)		Multiple aneurysms (diameters between 10 mm and 20 mm			
	(n = 192)		(n = 16)		(n = 8)		(n = 4)		(n = 1)			
Age (mean ± SD)/ Median age	63.90± 14.80/ 65,50		59.312± 15.076/ 56,00		54.12± 10.85/ 55.50		66.50± 6.85 / 65.50		42,00 /		H = 5.419 p = 0.144	H = 4.413 p = 0.220
Gender	n	%	n	%	n	%	n	%	n	%	Chi2 = 5.154 p = 0.272	Chi2 = 4.221 p = 0.239
Male	116	60.4	7	43.8	6	75.0	1	25.0	1	100.0		
Female	76	39.6	9	56.3	2	25.0	3	75.0				

Patients without IcAs, as well as those with aneurysms with diameter >20mm, had a median age of 65.50 years. In contrast, patients with aneurysms with a diameter <20mm were much younger, with a median age of 55.50 years. Patients with multiple aneurysms were the youngest (42 years).

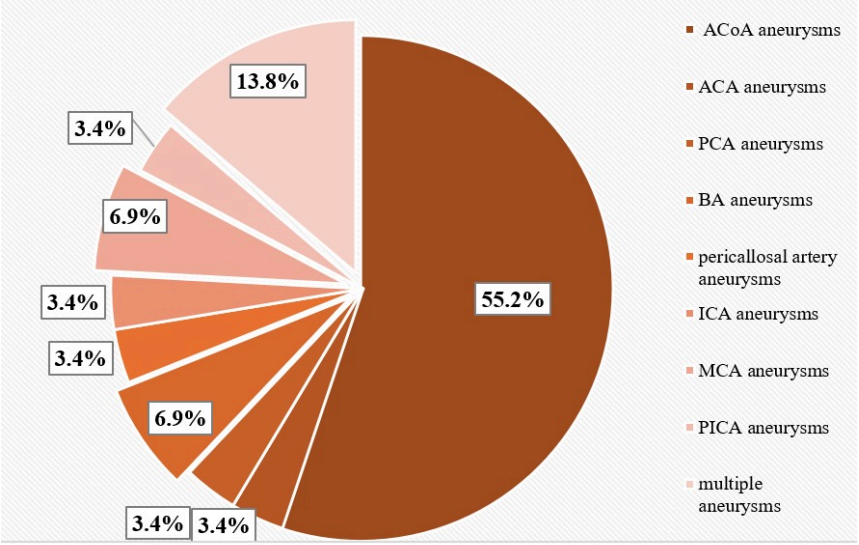

Figure 1. Structure of the cohort based on the location of the intracranial aneurysms

The most common were ACoA aneurysms (55.2% of all cases), followed equally by MCA aneurysms (6.9%), and BA aneurysms (6.9%). Additionally, multiple aneurysms were observed in 13.8% of the total patients (Figure 1).

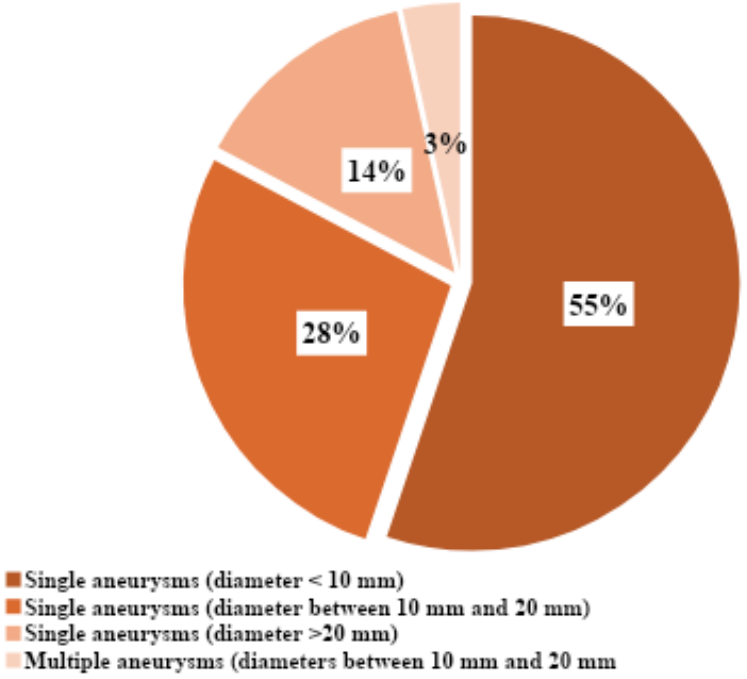

Figure 2. Structure of the cohort based on the external diameter of the intracranial aneurysms.

In the study group, the most common IcAs comprised those measuring <10 mm in diameter (55.2%). In the second place (27.6%) were aneurysms with a diameter between 10 mm and 20mm, and in the third place (13.8%) were those with a diameter >20mm. The least frequently encountered IcAs in this series were cases with multiple aneurysms (3.4%), with an external diameter between 10 mm and 20mm (Figure 2).

The overall analysis of all 221 subjects highlighted the fact that 2.5% of subjects with a typical configuration of CoW, presented a Posterior Inferior Cerebellar (PICA) aneurysm, while 15.5% of patients with an atypical CoW, presented one or more IcAs, of which 8.8% were located at ACoA level. These data did not have statistical significance in the overall analysis ($p_{GLOBAL} = 0.253$), but had statistical significance in the analysis of the aneurysm cohort only ($p_{ANEURYSM\ GROUP} = 0.001$) (Table 2).

3.44% of all IcAs were associated with a typical CoW, while the remaining 96.56% were associated with an atypical CoW (Figure 3).

By location, the majority of IcAs were found at the level of ACoA (55.17%), BA (6.9%), and MCA (6.9%). IcAs also developed at the level of: PCA (3.44%), pericallosal artery (3.44%), ICA (3.44%), and PICA (3.44%). Multiple aneurysms developed only within an atypical CoW and accounted for 13.8% of all IcAs (Figure 3).

Table 2. Structure of the cohort based on the location of the intracranial aneurysms and the configuration of the Circle of Willis

Aneurysm location	Configuration of the Circle of Willis Polygon				Pearson Chi-squared test
	typical		atypical		
	n	%	n	%	
Absence of aneurysm	39	97.5	153	84.5	GLOBAL: Chi2 = 11.347 p = 0.253 ANEURYSM GROUP: Chi2 = 29.000 p< 0.001**
ACoA aneurysm			16	8.8	
ACA aneurysm			1	0.6	
PCA aneurysm			1	0.6	
BA aneurysm			2	1.1	
pericallosal artery aneurysm			1	0.6	
ICA aneurysm			1	0.6	
MCA aneurysm			2	1.1	
PICA aneurysm	1	2.5			
multiple aneurysms			4	2.2	
Total	40	100.0	181	100.0	

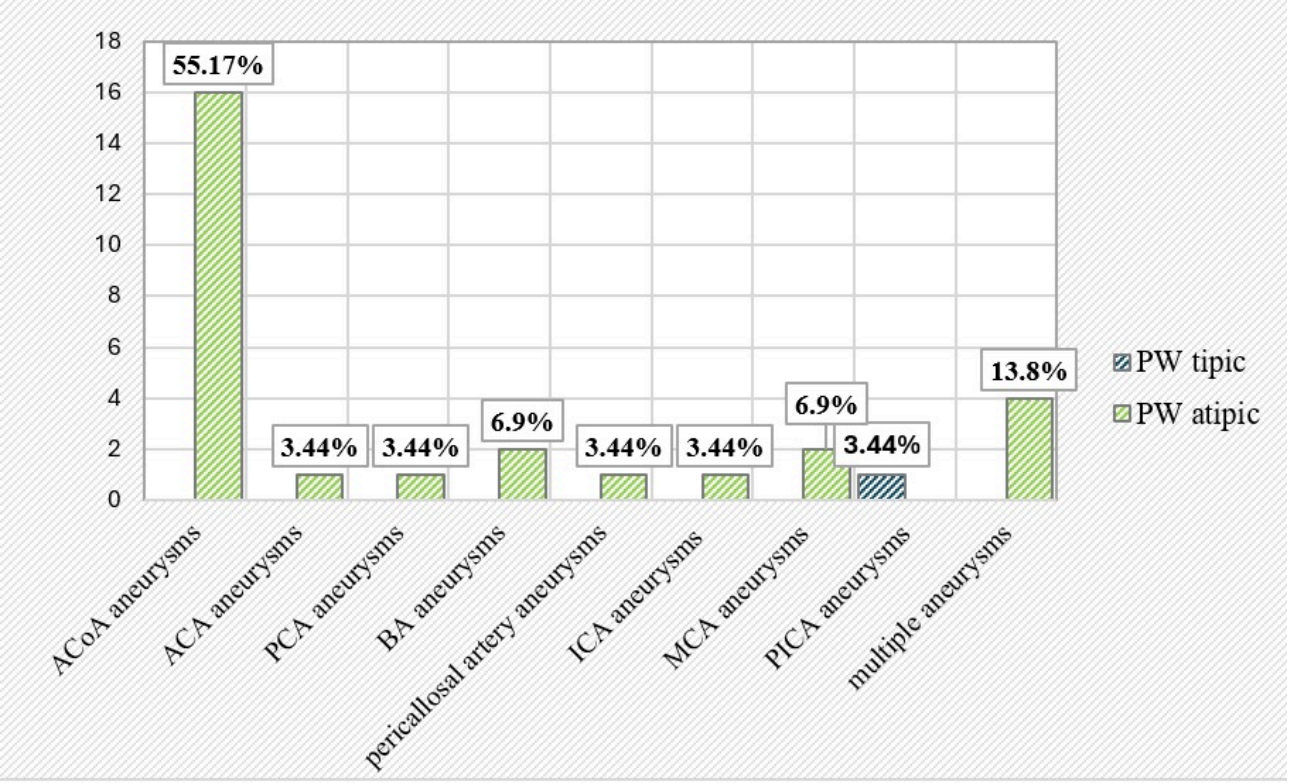

Figure 3. Structure of the cohort based on the location of the aneurysms and the configuration of the Circle of Willis

The most IcAs were located in the anterior part of the circle of Willis (ACA, ACoA) (58.62%), while the fewest (3.44%) were found in the posterior part of the CoW, at the level of PCA. 37.93% of all IcAs were located outside the CoW, specifically at the level of MCA, in the pericallosal artery, ICA, and PICA (Fig. 4).

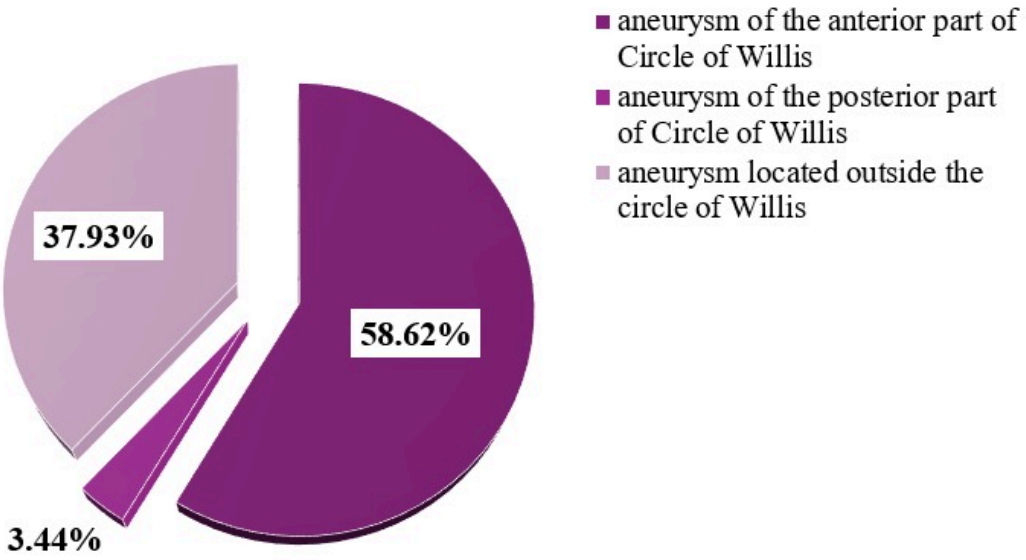

Figure 4. Structure of the analyzed group based on the location of the intracranial aneurysm (at the level of the Circle of Willis or outside of it)

Among the 40 subjects with a typical CoW configuration, only 2.5% (the patient with a PICA aneurysm) had an aneurysm with a diameter >20 mm. Among the 181 subjects with an atypical CoW, 8.8% presented with an aneurysm having a diameter <10 mm, 4.4% had aneurysms with diameters between 10 mm and 20 mm, and only 1.7% of these subjects had an aneurysm with a diameter >20 mm. These data did not show statistical significance in the overall analysis ($p_{GLOBAL} = 0.179$), nor in the analysis of the aneurysm group alone ($p_{ANEURYSM\ GROUP} = 0.091$) (Table 3).

Table 3. Structure of the group based on the size of the aneurysms and the configuration of the Willis polygon

	Configuration of the Circle of Willis				**Pearson Chi-squared test**
	typical		**atypical**		
Aneurysm size	**n**	**%**	**n**	**%**	
Absence of aneurysm	39	97.5	153	84.5	GLOBAL: Chi2 = 6.288 p = 0.179 ANEURYSM GROUP: Chi2 = 6.473 p = 0.091
Single aneurysm (diameter < 10 mm)			16	8.8	
Single aneurysm (diameter between 10 mm and 20 mm)			8	4.4	
Single aneurysm (diameter >20 mm)	1	2.5	3	1.7	
Multiple aneurysms (diameters between 10mm and 20 mm)			1	0.6	
Total	40	100.0	181	100.0	

Aneurysms having a diameter <10 mm and multiple aneurysms with diameters between 10 mm and 20 mm, were only associated with an atypical CoW, while aneurysms with a diameter >20 mm were associated with both typical and atypical CoW (Figure 5).

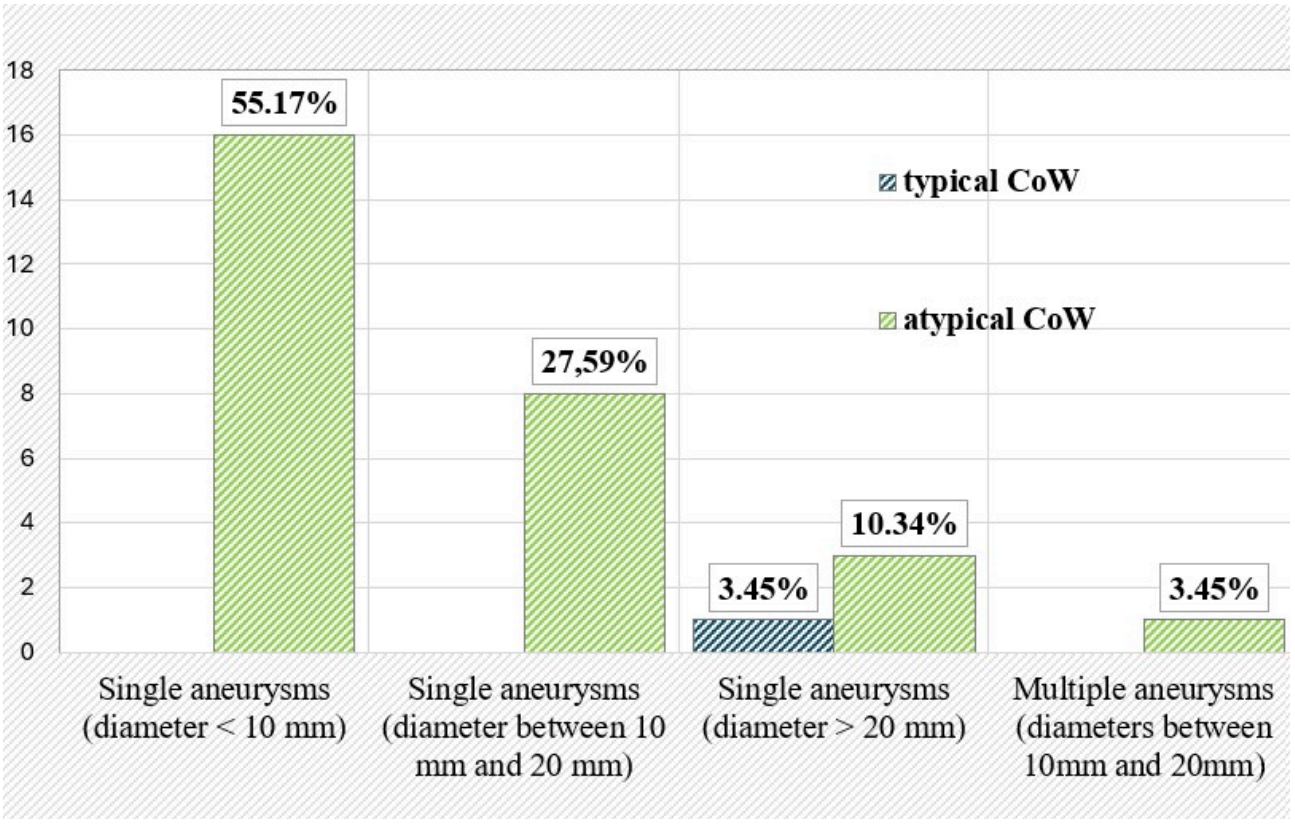

Figure 5. Structure of the aneurysms group based on their external diameter and the configuration of the Circle of Willis

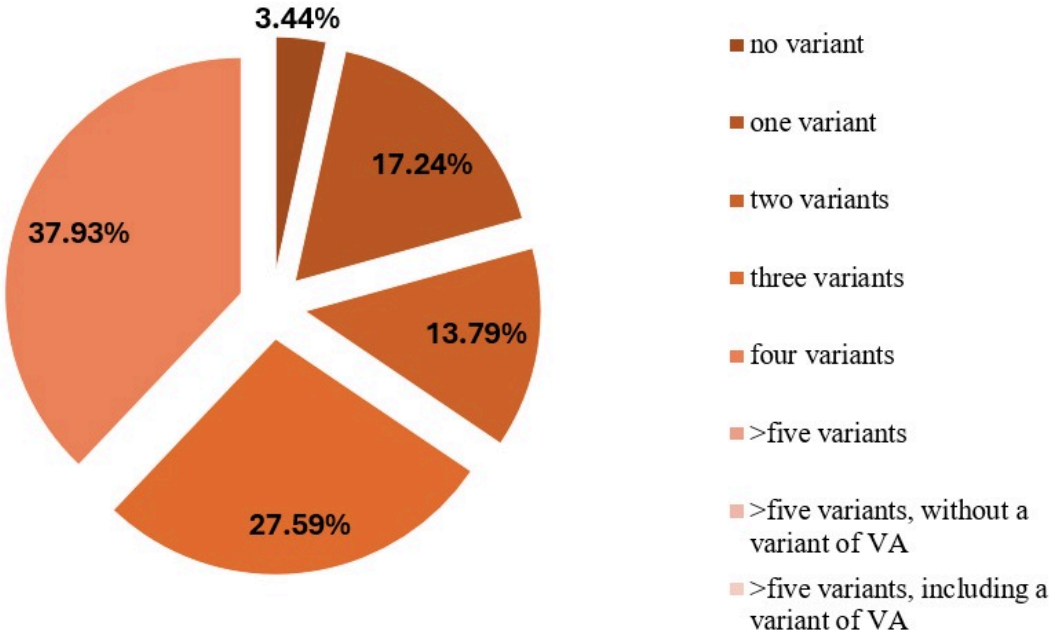

Figure 6. Structure of the aneurysms group based on the number of the anatomical variants within the same circle of Willis

Among the 29 cases with IcAs, regardless of their diameters, 37.93% were associated with four anatomical variants of CoW, while 27.59% were associated with the presence of three anatomical variants. Additionally, 17.24% were associated with the presence of one anatomical variant, and 13.79% of subjects exhibited two anatomical variants of CoW. 3.44% of subjects with intracranial aneurysms were not associated with anatomical variants of the CoW (Fig. 6).

The analysis of associations between the number of anatomical variants of CoW and the external diameter of the associated IcA shows the following: 2.5% of patients with CoW without anatomical variants presented an IcA with a diameter >20mm; 25% of patients with one anatomical variant of CoW presented aneurysms with diameters <10mm or >20 mm; 8.7% of patients with two anatomical variants and 24.4% of patients with four variants presented aneurysms with variable diameters (either <10mm, between 10mm and 20mm, and >20mm); 14.8% of those with three variants presented single aneurysms with a diameter <20 mm, or multiple aneurysms.

Table 4. Structure of the aneurysms group based on the external diameter of the aneurysms and the number of anatomical variants within the same Circle of Willis

Number of anatomical variants of CoW	**Aneurysms number and external diameters**										Pearson Chi-squared test
	absence of aneurysm		Single aneurysm (<10 mm)		Single aneurysm (10mm - 20 mm)		Single aneurysm (>20 mm)		multiple aneurysm (10mm – 20 mm)		
	n	%	n	%	n	%	n	%	n	%	
absence of any variant	39	97.5					1	2.5			GLOBAL: Chi2 = 26.033 p = 0.571 ANEURYSMS GROUP: Chi2 = 13.223 p = 0.353
one variant	15	75.0	4	20.0			1	5.0			
two variants	42	91.3	2	4.3	1	2.2	1	2.2			
three variants	46	85.2	4	7.4	3	5.6			1	1.9	
four variants	34	75.6	6	13.3	4	8.9	1	2.2			
five variants	10	100.0									
more than five variants, excluding the variant of VA	2	100.0									
more than five variants, including the variant of VA	4	100.0									
Total	192	86.9	16	7.2	8	3.6%	4	1.8%	1	0.5	

None of the patients with five or more anatomical variants of CoW presented intracranial aneurysms. However, these data did not show statistical significance ($P_{GLOBAL} = 0.571$; $P_{ANEURYSMS\ GROUP} = 0.353$) (Table 4, Figures 7-11).

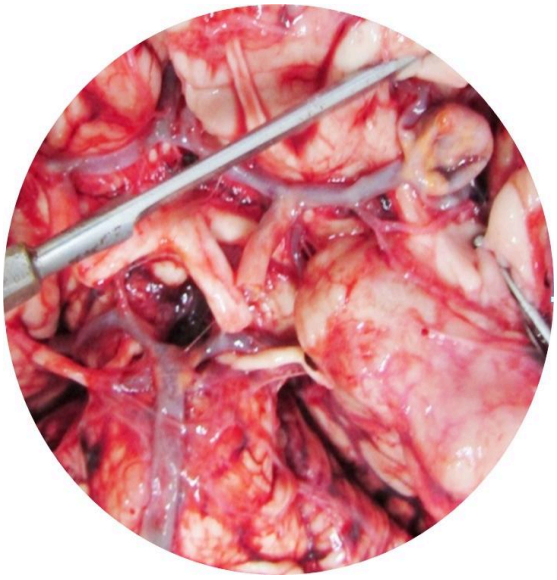

Figure 7. Autopsy image. M, 62 years old. Atypical CoW (hypoplasia of ACoA and hypoplasia of left PCoA) associated with a ruptured left MCA aneurysm (diameter=30 mm), with subarachnoid hemorrhage

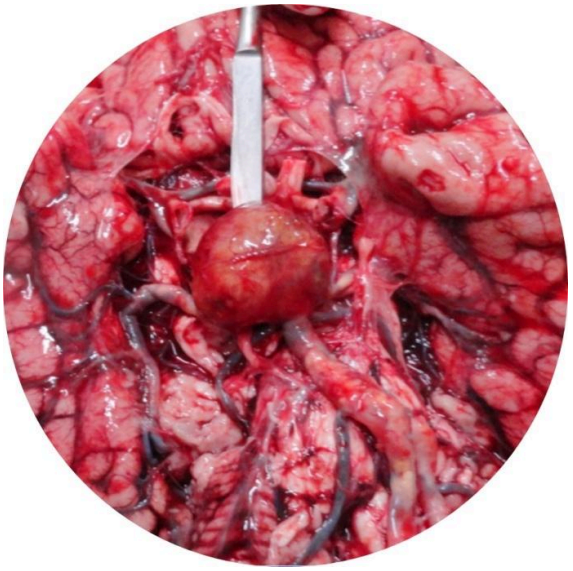

Figure 8. Autopsy image. M, 60 years old, atypical CoW (bilateral hypoplasia of left and right PCoA) associated with a giant, partially thrombosed, unruptured aneurysm (diameter=55 mm), located at the bifurcation of BA

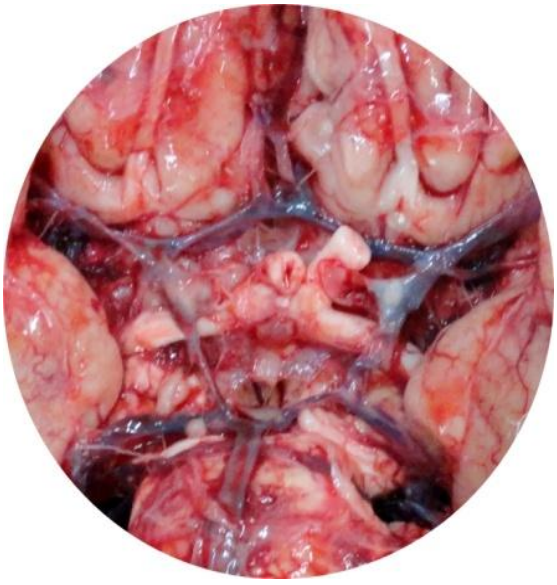

Figure 9. Autopsy image. M, 50 years old. Atypical CoW (bilateral hypoplasia of the left and right PCoA) associated with a small unruptured ACoA aneurysm (diameter=4mm)

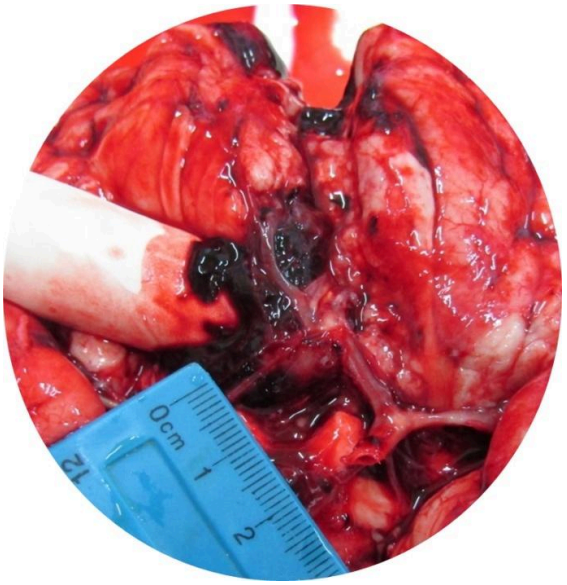

Figure 10. Autopsy image. M, 58 years old, atypical CoW (hypoplasia of the right PCoA, hypoplasia of the left PCoA, and hypoplasia of the right ACA) associated with a ruptured ACoA aneurysm (diameter=12mm), with subarachnoid hemorrhage

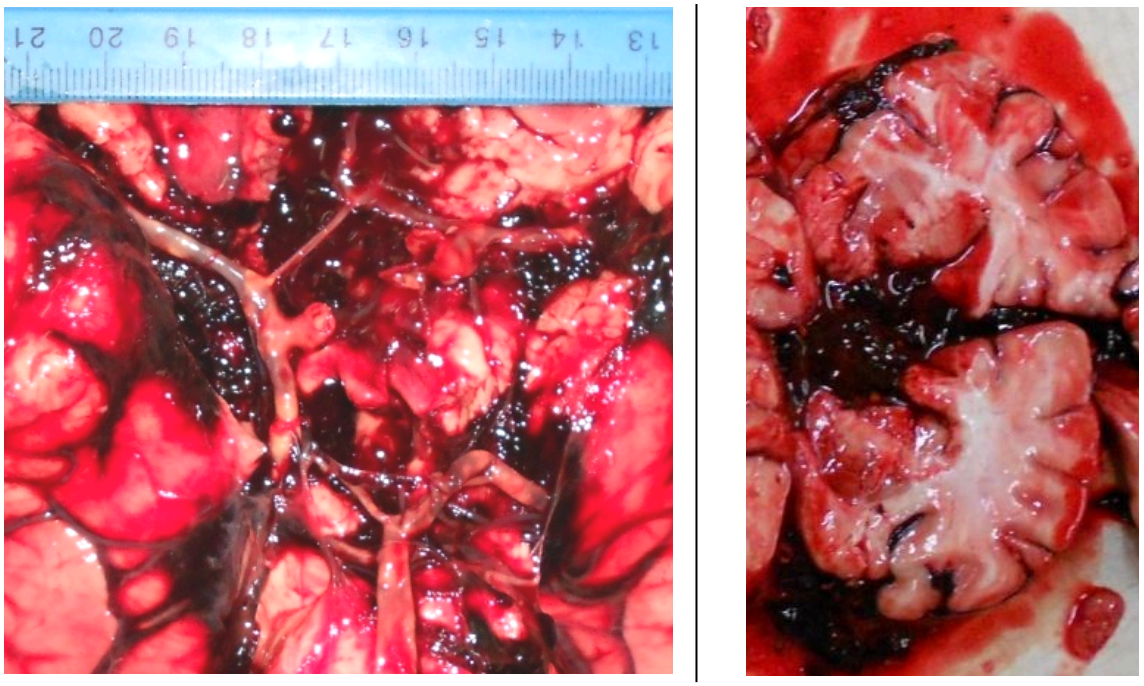

Figure 11. Autopsy image. F, 60 years old. A). Atypical CoW (hypoplastic right ACA, fetal-type right PCoA anastomosed through a very thin arterial branch with the superior cerebellar artery (SCA), and hypoplasia of left PCoA) associated with a ruptured AcoA aneurysm and subarachnoid hemorrhage. B): The appearance of the brain after frontal section highlighted massive interhemispheric subarachnoid hemorrhage and ventricular flooding

4. Discussions

Literature states that unruptured IcAs occur in 3%-5% of the general population (Hurford et al., 2021), but this percentage varies depending on the studied population, with prevalence rates as high as 10.3% in a region of China, among subjects with a history of subarachnoid hemorrhage (Liu et al., 2022).

Published research so far has shown that the rupture of IcAs is determined by various risk factors: female gender, age, aneurysm location, arterial hypertension, current cigarette smoking, smoking intensity and duration, and history of subarachnoid hemorrhage (Kim et al., 2021; Zuurbier et al., 2022; Zheng, Sun, & Zhang, 2020; Can et al., 2017; Oberman et al., 2021; Henry et al., 2023).

Patients with IcAs have an average age that varies from study to study depending on ethnicity, geographical region, sample size, methodology, and aneurysm location. A study from Canada published an angiographic series of 507 patients with IcAs, whose median age was 46 years, while those with ruptured aneurysms had a median age of 47 years (Weir, Disney, & Karrison, 2002). In another angiographic study conducted in the USA (Lazzaro, Ouyang, & Chen, 2012), the median age of patients with ruptured and unruptured ACoA and PCoA aneurysms was 57.5 years, most of them being female. On the other hand, another angiographic study conducted in Argentina (Oberman et al., 2021) on patients with AcoA and PCoA aneurysms reported a median age of 62 years (mean age ± SD: 60.63 ± 1.36 years). Additionally, a group of 264 Chinese patients with ruptured IcAs studied via Computed Tomography-angiography (CTA) had an average age of 50 years, most of them being female. The majority of ruptured aneurysms were identified in the age group of 40-49 years (34.5%) (Liu et al., 2015).

In the present study, a variation in median age was found based on the diameter of the IcAs. Aneurysms with diameters <20 mm were associated with a younger median age (under 56 years), while aneurysms with diameters >20 mm were identified in older patients (over 65 years). In contrast, patients with multiple aneurysms died at very young ages (42 years). This may be

attributed to the fact that participants in this study were selected from a series of deceased individuals from a tertiary, highly specialized hospital, where autopsies were performed.

Compared to other imaging studies (Rinaldo et al., 2020; Hindenes et al., 2023; Lazzaro, Ouyang, & Chen, 2012), which reported that IcAs are more frequent in female subjects, in this autopsy study, we did not identify a predominant association of one of the genders with ruptured or unruptured IcAs. This finding may represent a peculiarity of our geographical region, as other researchers have identified anatomical variations of various intracranial structures in the same area (the Northeastern region of Romania), such as a particular prevalence of the *ponticulus posticus* (arcuate foramen), identified mostly in its incomplete form and in young adults (21-40 years), which led authors to consider a genetic cause (Nedelcu et al., 2023). Furthermore, the same authors analyzed 100 brains from adults with non-neurological pathology residing in the same geographical area and showed that there is a triangular fossa of the third cerebral ventricle, for which they determined morphometric dimensions (Nedelcu et al., 2024b).

Angiographic data from the literature have reported that 84%-97% of all cases of IcAs can develop mainly in the anterior part of the CoW and that 79%-97% of intracranial aneurysms are unique, with only a small percentage being multiple (Dharia et al., 2020; Rinaldo et al., 2020; Liu et al., 2015). Our autopsy study confirmed these data as it identified the predominant location of IcAs in the anterior part of CoW and found multiple aneurysms in only about one-tenth of cases.

In terms of frequency of their location, IcAs are mostly located at the level of AcoA (24.8% - 40% of cases) (Rinaldo et al., 2020), followed by PCoA aneurysms, with percentages ranging from 13% to 33.1% (Zheng, Sun, & Zhang, 2020). MCA aneurysms rank third, with percentages ranging from 12.6% (Zheng, Sun, & Zhang, 2020) to 19.3% of cases (Rinaldo et al., 2020).

In our series, we also identified AcoA aneurysms as being the most common and even at a much higher percentage than in the literature (about 55%), probably because these aneurysms rupture most frequently and lead to the emergency presentation of the patient to the hospital. However, the second place was occupied by MCA and BA aneurysms, at equal percentages (about 7%).

The external diameter and location of IcAs are often considered predictive factors for a possible rupture of the intracranial aneurysm. There is an annual risk of 0.05% for rupture of the IcAs in asymptomatic patients when the maximum diameter of the aneurysm is <10 mm (International Study of Unruptured Intracranial Aneurysms Investigators, 1998). A rupture risk of 0.52% has been demonstrated for aneurysms with diameters between 7 mm and 12 mm, which are located in the anterior circulation, and 2.9% for aneurysms of the same diameters, but located in the posterior circulation (Wiebers et al., 2003). Another study highlighted the fact that an aneurysm size ≥5 mm, associated with the anterior direction of the dome of the aneurysm, flow angle, and parent-daughter angle, predisposes the intracranial aneurysm to rupture (Pahwa, Goyal, & Chaurasia, 2022). There are numerous other studies, angiographic or neurosurgical, reporting that ruptured IcAs have diameters <10 mm (Medetov et al., 2022; Liu et al., 2015). In our autopsy study, IcAs with external diameters <10 mm, especially located at the ACoA level, were more frequently associated with fatal outcomes.

The relationship between IcAs and anatomical variations within the same CoW, has been primarily studied angiographically, but reports on this topic are quite rare. One such study found a prevalence of 81% of anatomical variants of the CoW in patients with IcAs. 34% of the anatomical variants were located in the anterior part of the CoW, 66% in the posterior part, and 16% were located in both the anterior and posterior parts (Aburto-Murrieta et al., 2025).

Our series identified similar data, as of the 29 analyzed aneurysms, only one case with a PICA aneurysm presented a typical configuration of the CoW, probably because this artery has no connection with CoW. The remaining cases (97.5%) of IcAs were associated with various types of anatomical variants of CoW, which varied from one to four variants. As such, we consider like some other authors (Li et al., 2025), that there is an association between IcAs and variants of CoW,

because such arterial variations cause changes in the distribution of arterial blood flow, especially in the case of arterial atherosclerosis, which narrows the vascular lumen.

In order to obtain information about the hemodynamic factors contributing to the occurrence of aneurysms, it is important and necessary to analyze the relationship between these anatomical variants and the location of the aneurysms. There are very few reports addressing this issue. An angiographic study (Hassanin et al., 2023), conducted on 210 patients with ruptured and unruptured ACoA aneurysms, found that hypoplasia of the A1 segment of either ACA was significantly higher in the ACoA aneurysm group than in the control group. The authors concluded that there is a definite correlation between the formation of AcoA aneurysms and hypoplasia of the A1 segment of the ACA, as a result of blood flow disturbances at this level. Some other authors (Dumitrescu et al., 2021b) also concluded that in cases of ACA asymmetry, the ACoA aneurysm appears to be caused by increased hemodynamic stress, due to a compensatory shunt of blood through the ACoA.

Additionally, PCoAs asymmetry is significantly correlated with aneurysms at the bifurcation between PCoA and ICA. A CTA study (Oberman et al., 2021) analysed the significance of anatomical variants of the CoW in the formation and rupture of ACoA and PCoA aneurysms. The authors reported that 61.5% of the analysed aneurysm cases also presented anatomical variants, particularly in the anterior part of CoW.

Especially an incomplete CoW, due to the absence of some of the constituent arteries, is most susceptible to developing IcAs (Negatie et al., 2025), because these variations can lead to significant hemodynamic changes at the level of ICAs or BA, with increased stress on the vessel wall (Ophelders et al., 2024; Soylu, Ozturk, & Akan, 2019).

Patients with the absence of all three communicating arteries, i.e. AcoA, and right and left PCoAs, in the same CoW, have 4.2 times higher chances of having an IcA, and adults whose CoW lacks the P1 segment of the PCA, have 3.6 times higher chances of having an IcA (Hindenes et al., 2023). Other authors have reported that IcAs were more likely to occur in an incomplete CoW, although this association was not statistically significant, as identified in the present research.

On the other hand, an autopsy study of a series of 73 deceased individuals, aged between 51 and 89 years (mean age = 67.7±9.96), found that 93% of the analysed circles of Willis presented at least one anatomical variant, and that 15.06% of cases had IcAs. Additionally, IcAs developed within a CoW with various anatomical variants, such as fetal/embryonic configuration of CoW, H-shaped AcoA, X-shaped ACA, early duplication of MCA, hypoplasia of PCoA, proximal ACA asymmetry, distal ACA duplication, and absence of ACA (Wijesinghe et al., 2020). These data are almost similar to those identified in the present research.

A recent meta-analysis (Feng et al., 2023) examined nearly 5000 studies investigating AcoA and PCoA aneurysms. The results showed that the presence of a hypoplastic/aplastic A1 segment was significantly correlated with the formation and rupture of ACoA aneurysms, while the fetal-type variant of the P1 segment of PCA was implicated in the pathogenesis and rupture of PCoA aneurysms.

Comparing the data reported by various studies, we find that autopsy investigations identified more cases of aneurysms associated with atypical CoW than angiographic studies. One reason may be that autopsy, providing a direct research method, can much better highlight the presence of all anatomical variants of CoW. Conversely, performing an autopsy already implies that the patient's evolution with an aneurysm was towards exitus, thus concretely highlighting that the presence of anatomical variants within the CoW represents a risk factor for aneurysm rupture and poor prognosis of the disease.

AcoA aneurysms are the most common, especially in the presence of unilateral hypoplasia of the A1 segment of ACA, which is also the main risk factor for the rupture of this aneurysm, as it increases blood flow in the contralateral A1 segment of ACA and, therefore, leads to an increase in intramural pressure at the ACA-AcoA junction (Zamora-Chavarría et al., 2023).

Analysing hemodynamic filling patterns in angiographic investigation, a group of Turkish authors (Kaya, Tahtabasi, & Yıldırım, 2023) reported that a typical CoW is predominantly

associated with unruptured aneurysms, but an atypical CoW, especially one characterised by agenesia/hypoplasia of the A1 segment of ACA and fetal-type PCoA, is associated with a substantially increased incidence of ruptured aneurysms. Therefore, the more anatomical variants of CoW, both of its anterior and posterior parts, the greater the risk of aneurysm rupture, at least for AcoA aneurysms. Our study, being an autopsy study, demonstrates that the presence of three or four variants at the level of the same CoW, was associated with the evolution towards the death of the respective patient. There are also some other studies demonstrating that ACoA aneurysm associated with four anatomical variants of CoW leads to a patient's death (Dumitrescu et al., 2020b).

Currently, due to the accelerated evolution of technology, it has become clear that AI can be used for real-time individualised therapeutic planning and continuous monitoring of a patient's evolution. In the future, with the development of deep learning, the integration of AI algorithms within CTA scans, as well as within autopsy findings, will make it possible to obtain much more insights into the relationship between the development and rupture of intracranial aneurysms and the presence of anatomical variants of CoW.

5. Conclusions

The present study found a directly proportional relationship between the median age of the patient with an intracranial aneurysm and the diameter of that aneurysm, but an inversely proportional correlation between the diameter of the aneurysm and the evolution towards death.

In contrast, no predominant association of either gender with the development of intracranial aneurysms was identified, although the female gender was mainly associated with intracranial aneurysms, having a diameter of less than 10mm or greater than 20mm, while the male gender was predominantly associated with aneurysms with diameters between 10mm and 20mm, both single and multiple, which may represent a peculiarity of the population in the North-Eastern region of Romania.

Depending on their location, the most common intracranial aneurysms were those developed at the level of the Anterior Communicating Artery (AcoA), as well as at the level of the Middle Cerebral Artery (MCA) and the Basilar Artery (BA), which also suggests a particular pattern of development of intracranial aneurysms in the studied population.

Depending on their diameter, the most common aneurysms were those with diameters smaller than 10mm, which can rupture in the presence of other risk factors. For this reason, once such an aneurysm is discovered, even if small, the patient should consult a neurosurgeon and opt for endovascular treatment or aneurysm clipping.

This research has demonstrated that there is a statistically significant correlation between the presence of intracranial aneurysms and the atypical configurations of the circle of Willis, particularly those with three or four anatomical variants, located in both the anterior and posterior parts. Therefore, we can conclude that a significant risk factor for the development of intracranial aneurysms is the presence of an atypical circle of Willis.

These data are important from a prognostic point of view, and for the development of decision trees for the treatment of patients with intracranial aneurysms, as well as serve as a reference for comparative analyses in future studies.

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