REVIEW

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Cross-sectional angiographic imaging of anatomical variations in the circle of Willis: A literature review

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SUMMARY

The circle of Willis supplies blood to the brain and other pivotal structures, and has considerable importance in clinical teaching and practice. Studies have described angiographic anatomical variations in the circle of Willis in populations diverse in age, gender, race, and geographical region using different research methodologies, including study designs and diagnostic modalities. This comprehensive review compares and contrasts the findings of these studies in terms of prevalence, comorbidities, and clinical applications of anatomical variations across these different studies. Moreover, an embryological and physiological basis of these variations has been discussed in this review.

PubMed, Medline, and Google Scholar were searched for full-text scientific papers in English published from 1980 to 2018 about anatomical variations in the circle of Willis on CT and MRI angiograms. Most articles concluded that there was a relationship between some anatomical variations and age, gender, race, and comorbidities. Some anatomical variations in the circle of Willis are related to age, gender, race, and comorbidities. Future studies focusing on the detectability of small blood vessels using magnetic resonance imaging and computed tomography are warranted.

Key words: Circle of Willis – Angiography – Anatomical variations – Magnetic resonance imaging – Computed tomography

INTRODUCTION

The circle of Willis (COW), named after Thomas Willis who first described it in 1664, is a polygonal, intracranial collateral circulation formed between the carotid and vertebrobasilar arterial systems. It supplies blood to the brain and other pivotal adjacent structures, assuming considerable importance in clinical teaching and practice. Therefore, a thorough understanding of its anatomical variations, their prevalence, and associated factors is warranted. Even as numerous review articles have collated information on various anatomical variations in the COW reported in the literature, they do not focus on angiographic evidence nor do they examine the putative relationship of these variations with factors such as age, gender, race, and comorbidities, as suggested by numerous authors (Bhattacharya et al., 2004; Dimmick and Faulder, 2009; Glagov et al., 1987; Krabbe-Hartkamp et al., 1998; Lesley and Dalsania, 2004; Maaly and Ismail, 2011; Osborn, 1999; Qiu et al., 2015).

Therefore, the aim of this review is to compare and contrast the findings of published articles on angiographic anatomical variations in the COW, their prevalence, associated comorbidities, clinical applications, as well as their relationship with age, gender, and ethnicity.

METHODOLOGY

Information Sources

PubMed, Medline, and Google Scholar were

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searched for full-text scientific papers in English published from February 1980 to February 2018.

Study Selection

Articles were selected based on reporting findings based on the angiography, and those reporting findings based on the dissection of human cadavers were excluded. The accepted articles to be part of this review had to be written in English language only.

Data Collection Process

The data were collected, then the results of the collected articles were compared, mentioning each article's sample size, participants' gender, participants' ethnicity, used imaging modality, and findings.

Supplementary Material

The used keywords in the search engine are the following: "circle of Willis," "cerebral circle," "anterior cerebral artery," "posterior cerebral artery," "anterior circle," "posterior circle," "ICA," "vertebrobasilar system," "anterior communicating artery," "posterior communicating artery," "vascular anatomy of the head," "anatomical variations," "congenital anomalies," "hypoplasia," "aplasia," "agenesis," "symmetry," "asymmetry," "CT," "MRA," and "angiography".

REVIEW OF LITERATURE

The COW is composed of the basilar artery (BA), the anterior communicating artery (ACoA), and a pair each of anterior cerebral arteries (ACAs), posterior cerebral arteries (PCAs), internal carotid arteries (ICAs), and posterior communicating arteries (PCoAs). The complete COW (with none of the component arteries being absent or hypoplastic) is observed only in 20–25% of humans (Karatas et al., 2015). Although Kondori et al. (2017) reported finding the compete COW in 20.9% of healthy Iranian adults, they found no relationship between gender and the presence of anatomical variations.

Qiu et al. (2015) observed the complete COW in 12.24% of normal Chinese male individuals,

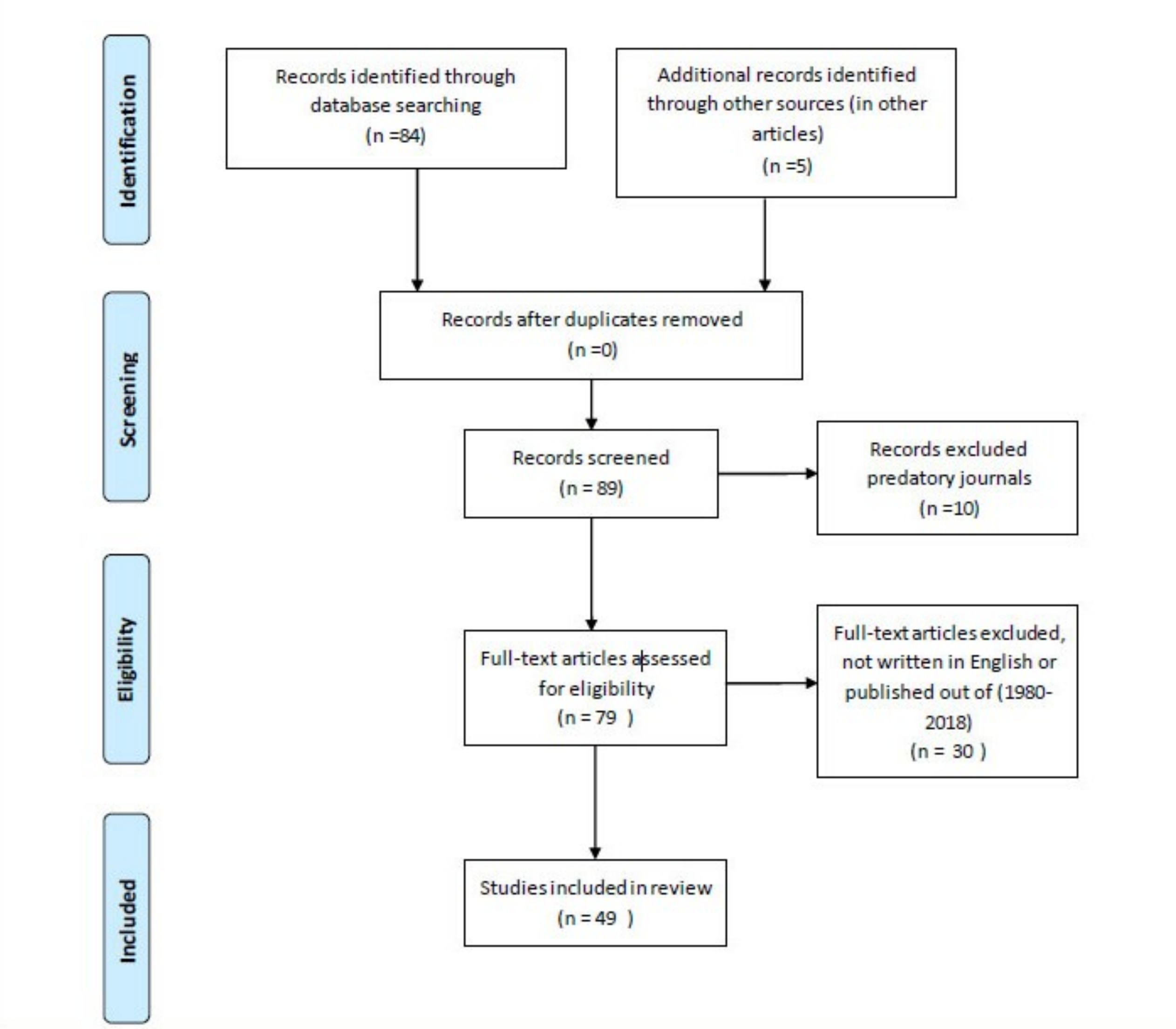

Fig 1. A PRISMA diagram to show the process of collecting the articles.

among whom 4.67% had developmental variations, including hypoplasia of either posterior or anterior circulation, even as 7.75% had normal complete development of the COW. A partially complete COW was seen in 70.17% of study subjects, with 66.29% having a complete anterior part. The remaining 17.59% did not have the A1 segment of the ACA on one side and showed bilateral absence of the PCoA. Hypoplasia, unilateral or bilateral, was found in 70.26% of the subjects.

Maaly and Ismail (2011) conducted a study in the Egyptian population and found the complete COW in 46.7% of the subjects, most of whom were female (52.8%); these findings were similar to those of Afifi et al. (2011) and Hartkamp et al. (1999). Shaikh and Sohail (2018) conducted a similar study in Pakistan and observed an incomplete anterior circle in 20% and an incomplete posterior circle in 77% of the study participants.

A complete COW was more likely to be observed in younger and female participants (Krabbe-Hartkamp et al., 1998). Among patients with carotid stenosis, complete anterior and posterior circles were seen in 60% and 70% of the participants, respectively, which is higher than the prevalence in normal subjects (Osborn, 1999). In a similar study involving patients with ICA stenosis, Hartkamp et al. (1999) observed the complete COW in 55%, complete anterior circle in 88%, and complete posterior circle in 63% of the patients.

Anterior Circulation

The ICA has two parts: cranial and caudal. The cranial part forms primitive olfactory arteries that give rise to the ACA, the middle cerebral artery (MCA), and the anterior choroidal artery. The ACoA originates from the plexiform vascular network.

Kondori et al. (2017) reported that the anterior part of the COW was complete in 80.95% of the subjects. The most common type of anatomical variation in this part involved the origin of the MCA (71.42%).

Qiu et al. (2015) studied magnetic resonance angiography (MRA) images of 2246 healthy Chinese male individuals, and found that among those with complete anterior circulation, the most common anatomical variation was the presence of the window pattern of ACoA (55.77%). Asymmetrical and unilateral hypoplasia of the ACA was more common in subjects with complete anterior circulation (29.92%) than in those with incomplete circulation (21.42%), even as anatomical variations in the A1 segment of the ACA were more frequent in the right side than in the left ($Z = 9.944$, $p < 0.001$).

Furthermore, they observed four distinct ACoA morphologies: absent, single, double, and multi-branch. In contrast, the ACA showed six possible patterns: normal, double tubular, Y-shaped, ampulla, circle, and window. Though the ACoA was absent in 11 (17.05%) participants, a single tubular root was found in 72.61% of them, even as the ACoA was obscured in 29 participants due to closeness to the bilateral A2 segment of the ACA. In addition, the authors found that patency of the ACoA is related to the development of the A1 segment of the ACA in 28.22% of the individuals (Qiu et al. 2015). Maaly and Ismail (2011) found that the anterior part of the COW was complete in 68.3% of the subjects; this finding was similar to the findings of Chen et al. (2004), and Krabbe-Hartkamp et al. (1998).

Arterial fenestration involves duplication of the segmental artery or separation of the arterial lumen into separate lumina by the endothelium that may or may not share the same adventitia. There is a relationship between fenestration and aneurysm, which is caused by weakening of the tunica media that subsequently involves all three layers of the vessel wall. It is caused by trebling the tunica media. Arterial fenestration is more common in the vertebrobasilar system than in the carotid system (Lath and Taneja, 2008). The embryological basis for fenestration of ACA, MCA, and PCA is still unclear (Osborn, 1999).

Posterior Circulation

In the embryo, the posterior circulation of the caudal division of the ICA develops to form the PCoA. The caudal division of the ICA communicates with the PCA, even as the paired dorsal longitudinal arteries fuse to form the basilar artery (BA). The PCA joins the vertebrobasilar system once its development is complete.

In the COW, the most common anatomical variations are absence, hypoplasia, “infundibulum” PCoA, and fetal type posterior communicated artery (FTP) with the hypoplastic P1 segment (Kondori et al., 2017; Maaly and Ismail, 2011; Krabbe-Hartkamp et al., 1998). Anomalies of the posterior circulation were more common than the anterior, with PCoA hypoplasia being the most frequent (38%). Posterior circulation was complete in 20.95% of the subjects (Kondori et al., 2017). Occipital lobe development controls anatomical characteristics of the posterior part of the COW (Tomsick et al., 1979).

Akgun et al. (2013) found no significant association between gender and anatomical variations in posterior circulation. Moreover, Maaly and Ismail (2011) found that the posterior part of the COW was complete in 38.3% of individuals; these results are similar to those of Chen et al. (2004), and Krabbe-Hartkamp et al. (1998) (25-52%) respectively. The posterior part of the COW was observed to be complete in 40% of younger and 37.5% of older participants (Maaly and Ismail, 2011).

Developmental Configurations

Based on development, there are three types of

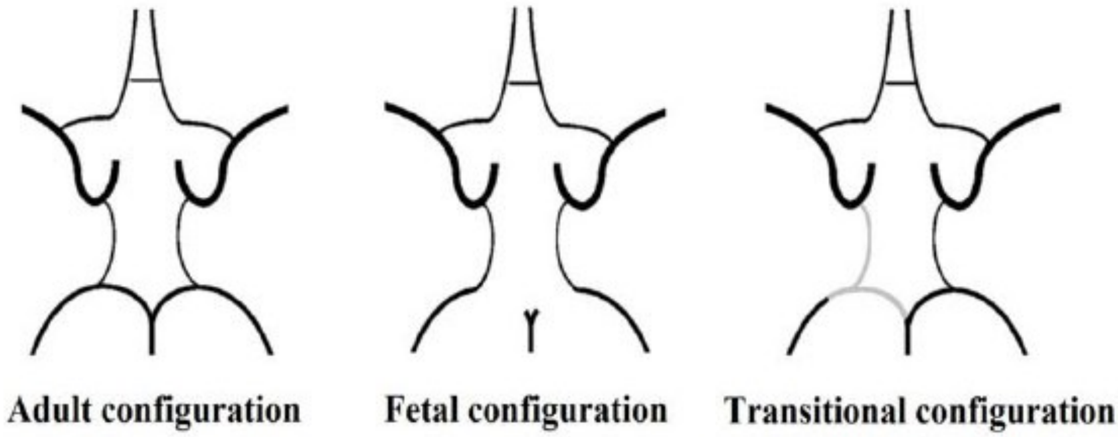

Fig 2. Types of configuration based on development.

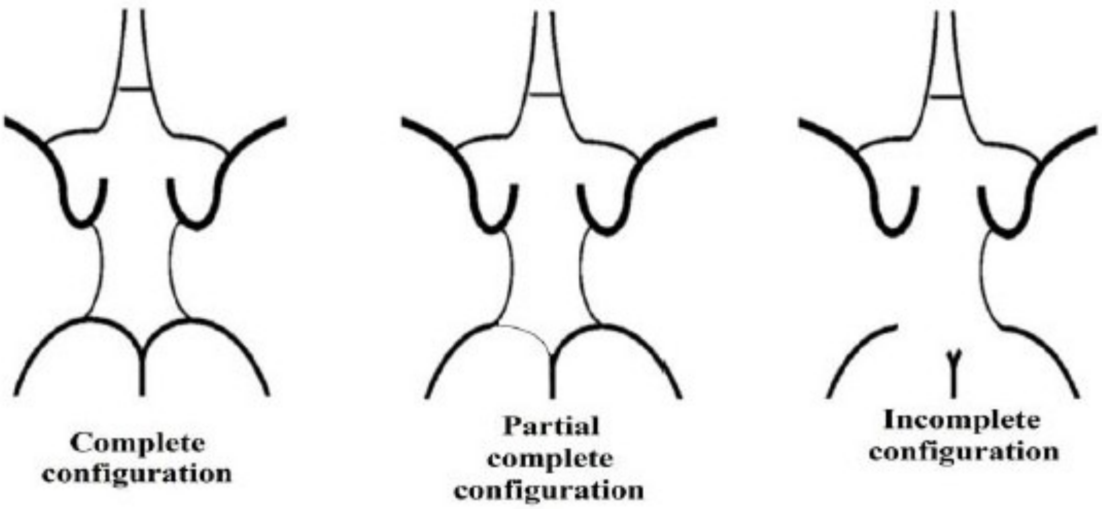

Fig 3. Types of configuration based on the morphology.

configuration: adult, fetal and transitional (see Fig. 2). Karatas et al. (2015) evaluated the COW morphology in computed tomography (CT) scans of 100 Turkish patients, and found that the full circle was present in 71%, adult configuration in 82%, fetal configuration in 17%, and transitional configuration in 1%. Furthermore, a study by Dodevski et al. (2014) reported the presence of the adult configuration in 70%, fetal configuration in 23%, and transitional configuration in 7% of subjects, whereas the corresponding values in another study were 76.25%, 11.87%, and 2.5% respectively (Lesley and Dalsania, 2004). For the prevalence of various configurations of the circle of Willis based on development, see Table 1.

Morphological Configurations

Based on morphology, there are three types of configuration: complete, partially complete, and incomplete configuration (see Fig. 3). A study conducted in China reported the presence of the complete COW in 12.24%, partially complete circle in 70.17%, and incomplete configuration in 17.59% of individuals (Qiu et al., 2015), whereas the corresponding values were 45%, 38.3%, and 16.7% in another study involving Egyptian adults (Afifi et al., 2011). For the prevalence of various morphological configurations of the circle of Willis, see Table 2.

Table 1. Prevalence of various developmental configurations of the circle of Willis

Author (year)	Population	Method	Sample size	Adult configuration %	Fetal configuration %	Transitional configuration %
Li at el. (2011)	Chinese	CTA	163	85.63	11.87	2.5
Dodevski (2014)	Macedonian	CTA	53	70	23	7
Karatas et al. (2015)	Turkish	CTA	100	82	17	1
Yeniçeri et al. (2017)	Turkish	3D TOF MRI	384	85	13	2

3D TOF MRI, three-dimensional time-of-flight magnetic resonance imaging; CTA, computed tomography angiography.

Table 2. Prevalence of various morphological configurations of the circle of Willis

Author (year)	Country	Sample size	Method	Entire complete circle %	Complete anterior circle %	Complete posterior circle %
Krabbe-Hartkamp et al. (1998)	The Netherlands	150	3D TOF MRI	42	74	52
Chen et al. (2004)	China	507	3D TOF MRI	21	78	25
Li et al. (2010)	China	107	Multidetector CTA	27	79	31
Maaly & Ismail (2011)	Egypt	250	3D TOF MRI	46.7	68.3	38.3
Qiu et al. (2015)	China	2246	3D TOF MRI	12.24	55.77	16.07
Kondori et al. (2017)	Iran	525	3D TOF MRI	20.9	80.95	20.95
Shaikh & Sohail (2018)	Pakistan	135	3D TOF MRI	22	80.8	22

3D TOF MRI, three-dimensional time-of-flight magnetic resonance imaging; CTA, computed tomography angiography.

Anterior Cerebral Artery

The A1 segment of the ACA was hypoplastic or absent in 10-15% of individuals (Karatas et al., 2015). Hypoplasia of the A1 segment of the ACA on performing MRA has been reported in 3% of individuals, and that of the A2 segment in 2% (Taşar et al., 2004). An azygous ACA was present in the A2 segment above the ACoA with a prevalence of 0.3-2% (Auguste et al., 2004), while the prevalence of fenestration was 10% (Bożek et al., 2012).

Patrux et al. (1994) have described the existence of the A4 and A5 segments of the ACA that extend above the corpus callosum and separate at the level of the choroidal fissure. Three types of ACA anomalies have been reported: single ACA, bi-hemispheric ACA, and single branch combined with the second segment of the hypoplastic ACA. Bi-hemispheric ACA, which is found in 2–7% of individuals, was present on one side of the A1 segment and divided into branches that supplied both hemispheres, whereas the A1 segment on the opposite side was hypoplastic. A bi-hemispheric ACA was difficult to differentiate from a true azygous ACA, unless a hypoplastic A2 segment was present on the contralateral side (Osborn, 1999). A saccular azygous ACA was common (13-71%) (Karatas et al., 2015). An accessory ACA arose from the ACoA, and was present in 3% of subjects (Tomsick et al., 1979), whereas ACA hypoplasia was reported in 10% of subjects (Bożek et al., 2012), more commonly on the right side, although a case report records its coexistence bilaterally with the normal A1 segment of the ACA (Given and Morris, 2002).

An infra-optic ACA has been reported as a rare variant, arising from the ICA near the origin of the ophthalmic artery, whereby it follows an infra-optical course. Its typical course involves passing vertically below the ophthalmic nerve and above the ACoA, anterior to the optic chiasma between the two optic nerves, before finally ascending in the interhemispheric fissure (Given and Morris, 2002).

A study reported the presence of the recurrent artery of Heubner, a perforating branch arising from the A1 (14.3%) or A2 (23.3%) segment of the ACA near the area of the ACoA. It was 0.8 mm in diameter and supplied the head of the caudate nucleus, the anterior horn of the internal capsule, and the anterior part of the lentiform nucleus (Loukas et al., 2006).

Fenestration of the A1 segment of the ACA was present in 0.058% of individuals (Saikia et al., 2014), whereas only a single case of a fenestrated A2 segment on performing angiography has been reported in the literature to date (Taşar et al., 2004). Trifurcation of the A2 segment of the ACA due to persistence of the median callosal artery was seen in 2-13% of individuals (Osborn, 1999), whereas that of the A1 segment of the ACA was found in 1-2% (Patrux et al., 1994).

Another rare variant is the persistent primitive olfactory artery, which either arises as a branch of the ACA or replaces its proximal part, after which it joins the ACA distally. It takes a 180-degree “hairpin turn,” then it passes anteriorly and then inferomedially along the olfactory tract on the same side, and forms the “hairpin” by turning posterosuperiorly to the ACA in the absence of the ACoA (Qiu et al., 2015). The persistent primitive olfactory artery is prone to a saccular aneurysm (Taşar et al., 2004). Qiu et al. (2015) have classified the morphology of ACA based on its origin and the existence of the ACoA.

Anterior Communicating Artery

Although one study reported the prevalence of absent or fenestrated ACoA to range between 10% and 15%, with a mean of 12.5% (Karatas et al., 2015), another study found ACoA fenestration to be rather common (40%) (De Gast et al., 2008). The A1 segment and ACoA were the most common sites for anatomical variations in anterior circulation. Hypoplasia of the A1 segment was present in 10% of individuals, whereas the A1 segment was absent in 1-2% of individuals. While a study found that the ACoA was unilateral in 60%, plexiform in 10-33%, double in 18%, and fenestrated in 12-21% of individuals (De Gast et al., 2008), another study reported ACoA absence in 5%, duplication in 18%, and fenestration in 12-21% (Patrux et al., 1994). A complex ACoA was seen to have a higher prevalence in male subjects (52.31%) than in female subjects (46.05%), whereas the converse was true for aplastic (23.26% female subjects, 15.88% male subjects) and trifurcated (1.86% female subjects, none in male subjects) ACoAs (Lath and Taneja, 2008). The most common anatomical variations in younger participants were single as well as multiple ACoAs, whereas single and hypoplastic ACoAs were common in subjects in older age groups (Maaly and Ismail, 2011).

Internal Carotid Artery

The human vascular anatomy can vary in origin, course, size, and diameter, and in most cases, these variations are a consequence of embryological development rather than of a pathological nature (Karatas et al., 2015). An aberrant ICA is a rare anatomical variation as a result of agenesis of the first cervical ICA segment and serves as a collateral pathway. This vessel develops from fusion of the caroticotympanic branch with the inferior tympanic branch of the ascending pharyngeal artery (Saikia et al., 2014). An aberrant ICA is identified as a vessel of small diameter, posterior to the ICA, on top of the jugular bulb. Furthermore, it is visible in the hypotympanum as an enhancing mass. In addition, the bony plate separating the tympanic cavity from the ICA and the vertical segment of the carotid canal are both absent. (Caldemeyer, 1998) noted that an aberrant ICA was more common on the right side (90%) in women, whereas another study demonstrated 30% concomitance with the stapedial artery (Mokin et al., 2012).

Often associated with an abnormal ICA was the persistent stapedial artery connecting the ICA with the facial artery. It was present in 0.48% of individuals and was often accompanied by the absence of normal origin of the middle meningeal artery.

Rarely, the ICA has been seen to arise from the aorta. Furthermore, it may be fenestrated – only six cases have yet been reported globally (Mokin et al., 2012); duplicated –two separate arteries with different origin and no distal congregation (Mokin et al., 2012); or with lateral branches including the superior thyroid artery, ascending pharyngeal artery, and persistent stapedial artery (Mokin et al. 2012). Anastomosis between the carotid and vertebrobasilar arteries has been noted in 15% of the cases (Mokin et al. 2012).

The presence of the dorsal ophthalmic artery is a rare anatomical variation arising from the cavernous segment of the ICA and entering the orbit through the superior orbital fissure (Taşar et al., 2004). During development, the anterior ophthalmic artery normally persists and the dorsal ophthalmic artery regresses. However, rarely, the situation switches between the two, resulting in a persisting dorsal ophthalmic artery that arises from the cavernous segment of the ICA and enters the orbit through the superior orbital fissure (Taşar et al., 2004).

Of the seven segments of the ICA, four (cavernous, clinoid, ophthalmic, and communicating segments) are intracranial. Normal variations in the ICA, including a paramedian “kissing” ICA, usually occur in the cavernous segment, which passes inside the sella turcica, as well as clinoid segment where the ICA becomes tortuous (Osborn, 1999).

The clinoid segment is also known as the carotid siphon. The ophthalmic segment is the usual site where the ophthalmic artery arises in the intradural position in 90% of individuals (Osborn, 1999). Sometimes, the MCA arises from the thalamic segment of the ICA (0.5%), and the ophthalmic artery arises from the MCA (0.5%) (Osborn, 1999). Lateral cerebral angiograms afford the best visualization of the ophthalmic segment of an intradural ICA (Osborn, 1999). Any aneurysm in this segment can cause subarachnoid hemorrhage on rupture (Osborn, 1999). Furthermore, the ophthalmic artery may arise from the cavernous segment of the ICA in 8% of cases or may be of ectopic origin in 4% (Osborn, 1999). An isolated ICA is a combination of two anatomical variations: fetal PCA and absent A1 segment of the ACA on the same side.

ICA dysgenesis is classified into aplasia, agenesis, and hypoplasia. When an organ fails to develop despite the presence of a precursor, the condition is termed as aplasia. Agenesis implies complete failure of organ development, while hypoplasia indicates incomplete development. All three types imply absence of the ICA, but to a varying degree. Cases of aplasia and agenesis entail complete absence of the ICA, whereas hypoplasia results in narrowing of the entire length of the ICA.

Agenesis of the ICA occurs in less than 0.01% of cases and is unilateral in most cases (Luh et al., 1999). Moreover, bilateral agenesis of the ICA constitutes less than 10% of all cases of vascular agenesis, whereas prevalence of ICA hypoplasia is 0.079% and that of aplasia and hypoplasia combined is 0.13% (Shaikh and Sohail, 2018).

There are more than 25 cases of ICA agenesis reported in the literature (Oliveira et al., 2014). The carotid canal usually appears during early gestation, and its absence indicates ICA congenital anomaly (Rumboldt et al., 2003). The ICA may be missing either completely or partially. A small fibrous strand, which is a remnant of ICA aplasia, may sometimes be present; however, angiography alone cannot differentiate between aplasia and agenesis. A study reported that 24 out of 60 cases of hypoplasia were bilateral (Mokin et al., 2012).

Agenesis and hypoplasia can be differentiated by performing CT scans at the level of the skull base based on the presence (or absence) of the small bone covering the carotid canal (Rumboldt et al., 2003). Evaluation of vessel diameter also helps in the diagnosis of an asymmetrical ICA and hypoplasia. Many articles do not mention the methods used to calculate the symmetry, asymmetry, or hypoplasia and do not address issues when the ICA is enlarged on one side (Żurada and Gielecki, 2007). Instead, they describe ICA diameter as equal (i.e., no appreciable difference) or slight or marked asymmetry (Rumboldt et al., 2003). Furthermore, it is pivotal that ICA aplasia or hypoplasia should not be confused with acquired diseases such as atherosclerosis, dissection, or fibromuscular dysplasia (Rumboldt et al., 2003).

The ophthalmic artery is the direct continuation of the ICA in cases of ICA hypoplasia (Kolbinger et al., 1993). In cases of ICA agenesis or unilateral hypoplasia, cerebral perfusion is compensated by either the ICA on the other side or by bilateral vertebrobasilar vessels. In addition, it has been noted that when one ICA is absent, it is associated with the presence of intrasellar intracarotid communicating arteries and an increased risk of an aneurysm (Karatas et al., 2015).

Carotid-basilar anastomoses are transient segments during development that connect primordial carotid and hind brain circulation. These segments are named after the most proximal cranial nerve (from superior to inferior): persistent trigeminal artery, otic artery, hypoglossal artery, and proatlantal intersegmental artery. All of them disappear when the PCA develops, but when one fails to obliterate, it is termed as persistent carotid-basilar anastomosis. These anatomical variations can affect collateral circulation in case of vascular occlusive disease; for example, an isolated ICA will supply MCA ipsilaterally and PCA bilaterally when there is no flow from ICA of the other side or from the vertebrobasilar system.

The persistent trigeminal artery (PTA) connects carotid arteries of the fetus to the dorsal longitudinal neural arteries, which are precursors of the vertebrobasilar system (Osborn, 1999). Though Qiu et al. (2015) reported observing the PTA in only 3 of the 2246 individuals they examined, another study found the PTA prevalence to be 0.2-0.6% (Oelerich and Schuierer, 1997). Saltzman types are anatomical variants of the PTA. Saltzman type 1 PTA supplies the vertebrobasilar system and is associated with hypoplastic BA and absent PCoA, whereas Saltzman type 2 PTA supplies the superior cerebellar artery where the patent PCoA supplies the PCA and is prevalent equally in both types (Oelerich and Schuierer, 1997).

There are eight published cases in humans of the persistent otic artery describing its origin from the petrosal part of the ICA in the carotid canal, followed by a lateral course via internal carotid canal anastomosis with the BA (Luh et al., 1999; Yeniçeri et al., 2017). According to Tomsick et al. (1979), they were the first to demonstrate the persistent otic artery on performing angiography. However, Bhattacharya et al. (2004) wrote a letter to the editor of the American Journal of Neuroradiology expressing dissent, claiming that it was not the presentient otic artery, but a low-lying trigeminal artery or a remnant of the stapedial artery. Furthermore, they pointed out that instead of low-quality, single-view angiographic images that could not substantiate the claim made by Tomsick et al. (1979), three-dimensional images should be used to prove the existence of the persistent otic artery by delineating its origin, course, and termination (Bhattacharya et al., 2004).

The persistent hypoglossal artery is the second common artery after the PTA, with a prevalence of 0.02-0.10% (Oelerich and Schuierer, 1997). It connects the carotid and vertebrobasilar systems at the C1-C3 level and courses through the hypoglossal canal. The accurate diagnosis of an arterial anomaly depends on the size of the hypoglossal canal (Oelerich and Schuierer, 1997). One study reported the prevalence of the persistent hypoglossal artery at 0.06%, that of Saltzman type I combined with proatlantal intersegmental artery at 0.12%, and that of Saltzman type II combined with persistent trigeminal artery at 0.06% (Zampakis et al., 2015).

Forty cases of proatlantal intersegmental artery have been reported in the literature (Luh et al., 1999). This artery was found to originate from carotid arteries at the C2-C4 level and join the vertebral artery in the suboccipital region (Luh et al., 1999). Of the two types of intersegmental arteries, the type arising from the external carotid artery is more common (50%) than that arising from the posterior aspect of the ICA (38%) (Kolbinger et al., 1993). The proatlantal intersegmental artery has been found to be associated with a 10% increase in the risk of an aneurysm (Kolbinger et al., 1993).

Posterior Communicating Artery

The most common site of anatomical variations in the COW is the PCoA. The prevalence of hypoplasia of single or paired PCoA ranges from 25 to 34% with a mean of 30% (Karatas et al., 2015). An embryological study showed that PCoAs originate from the ICA and that the vertebrobasilar system is supplied by the trigeminal artery, which is a branch of the ICA until the formation of PCoAs, connecting the carotid and vertebrobasilar systems. Furthermore, the author claims that hemodynamic changes during development, particularly in the first month of intrauterine life, may considerably impact the development of the COW, resulting in anatomical variations (Padget, 1948).

Akgun et al. (2013) found that 65.2% of the 135 subjects they studied had at least one anatomical variation in the vertebrobasilar system, with the right PCoA being absent in 40.7% of subjects and the left PCoA absent in 41.4%. In cases of PCoA hypoplasia, one or both PCoAs were found to be small or absent in one-fourth of all magnetic resonance imaging (MRI) angiograms (Akgun et al., 2013).

PCoA infundibulum is seen in 6-17% individuals, with a mean prevalence of 10%. It is a funnel-shaped dilatation of the PCoA at its origin from the ICA, and appears on the angiogram as a symmetrical dilation with a diameter of approximately 2 mm. Care must be taken to differentiate it from a PCoA-ICA aneurysm (Jiménez-Sosa et al., 2017). According to Dimmick and Faulder (2009), no case of PCoA duplication on an angiogram has yet been reported. Zampakis et al. (2015) observed the presence of fetal PCoA in 25% of the population.

Fetal PCoA, which is seen in 17 to 25% individuals with a mean of 20%, originates from the ICA with an absent or hypoplastic P1 segment (Jiménez-Sosa et al. 2017). PCoA fenestration is rare (a single case has been reported in the literature (Tripathi et al., 2003)), and its developmental mechanism is unclear (De Gast et al., 2008)

Posterior Cerebral Artery

Some authors suggest that the calcarine artery, which is a terminal branch of the PCA in the calcarine fissure, is the P4 segment of the PCA (Oelerich and Schuierer, 1997). Hypoplastic PCA is seen in 15-22% of the subjects (Qiu et al., 2015).

A fetal (origin of the) PCA occurs when the fetal PCA fails to regress, and was seen in 20-30% of cases, with 10% on the right side, 10% on the left, and 8% bilaterally in the general population (Caldemeyer, 1998; Tomsick et al., 1979). It was found to be unilateral in 37.8% of cases and bilateral in 31.7% (Luh et al., 1999).

A fetal PCA is diagnosed when the diameter of the PCoA is the same or larger than the P1 segment of the ipsilateral PCA, thereby implying that the ICA constitutes the major source of blood supply to the occipital lobe instead of the vertebrobasilar system. An uncommon variation is the absence of the P1 segment of the fetal PCA (Qiu et al., 2015).

Qiu et al. (2015) classified PCA variations into four types based on the existence and development of the P1 segment of the PCA and PCoA: 1) well-developed P1 segment with a diameter lesser than the ACoA; 2) P1 segment diameter lesser by half of the ipsilateral ACoA; 3) P1 segment is absent and formed by extension of the PCoA; 4-PCA extends from the BA and ICA.

They found that complete posterior circulation was seen only in 16.07% of individuals, whereas it was incomplete in 83.93%, mostly due to unilateral or bilateral absence of PCoA or fetal-type posterior cerebral artery (FTP) (Qiu et al., 2015). The PCoA was present in 29.92% of individuals. It was seen in the right side in 16.07%, in the left side in 13.85%, and bilaterally in 21.86% of individuals. Bilateral absence of the PCoA was noted in 48.22% and total FTPs in 19.50% of individuals. The FTPs were observed to be bilateral in 4.09% of cases and unilateral with two terminal branches arising from one side in 1.24%, with 13.27% on the right side and 10.28% on the left (Qiu et al., 2015). Some researchers claim that the FTP prevents communication between the anterior and posterior circles (Van Raamt et al., 2006).

A maldeveloped or absent P1 segment of the PCA was observed in 17.54% of subjects, unilateral P1 segment of the PCA in 6.99%, absent unilateral P1 of PCA in 7.16%, bilateral hypoplasia in 0.44%, and bilateral absence of P1 segment of the PCA in 1.24% (Qiu et al., 2015). Normal development of the P1 segment of the left PCA was noted in 92.28%, and that of the right PCA in 90.16% of subjects. Hypoplasia of the P1 segment of the PCA was present in the left side in 3.16%, and on the right in 4.72% of subjects. Absence of the P1 segment of the PCA was found in the left side in 4.54%, and on the right in 5.12% of subjects (Qiu et al., 2015). Qiu et al. (2015) found that there were more variations in the PCA in the right side ($Z = 2.576$, $p = 0.01$), and there was a significant relationship between the developmental type of the A1 segment of ACA and distribution of PCA ($\chi 2 = 9.188$, $p = 0.002$).

Basilar Artery

BA fenestration is commonly seen near the vertebrobasilar junction (Lath and Taneja, 2008) and occurs either as a result of failure of regression of temporary bridging arteries that connect the longitudinal neural arteries or failure of fusion of bilateral neural arteries in the fifth fetal week (Goldstein et al., 1999). An angiographic study revealed the prevalence of BA fenestration to be 0.6% (Yeniçeri et al., 2017), of which 7% resulted in aneurysms (Saikia et al., 2014). Completely separated or duplicated BAs may occur as a result of non-fusion of neural longitudinal arches (Goldstein et al., 1999).

Arterial Diameters

Globally, advanced techniques in MRI have enabled the detection of blood vessels with diameters ranging from 6 to 8 mm (Kominami et al., 1999; Krabbe-Hartkamp et al., 1998; Qiu et al., 2015). Though Kominami et al. (1999) found that it was possible to visualize vessels of diameters over 7 mm using three-dimensional time-of-flight MRI, another study suggested that maximum intensity projection and volume rendering MRA can show vessels with diameters of 6 mm (Kominami et al., 1999).

This is important as blood vessels of 1 mm diameter can provide blood supply and function as nutrient arteries, as opposed to hypoplastic blood

Table 3. Diameters of the blood vessels of the circle of Willis

Author (year)	Country	ACA diameter mm	PCA diameter mm	ICA diameter mm	ACoA diameter mm	PCoA diameter mm	BA diameter mm
Krabbe-Hartkamp et al. (1998)	Netherlands	1.90	1.90	3.700	1.40	1.200	3.20
Chen et al. (2004)	China	1.98	1.80	3.175	-	-	2.85
Hafez et al. (2007)	Egypt	1.80	1.80	3.850	1.15	1.150	-
El-Barhoun et al. (2009)	Australia	2.00	2.00	4.450	-	-	3.20
Maaly & Ismail (2011)	Egypt	1.96	1.84	3.680	1.15	1.200	3.01
Tekale & Ambiye (2016)	India	1.31	1.32	2.690	0.98	0.965	-
Yeniçeri et al. (2017)	Turkey	1.59	1.80	4.280	-	1.120	2.85

ACA, anterior cerebral artery; ACoA, anterior communicating artery; BA, basilar artery; ICA, internal carotid artery; PCA, posterior cerebral artery; PCoA, posterior communicating artery.

vessels, which do not contribute to perfusion, as their lumen is obliterated and as such cannot be catheterized according to (Kaplan, 1956). Kaplan (1956) claimed that if the P1 segment of the PCA, A1 segment of the ACA, PCoA, or ACoA were less than 1 mm, then, the concomitant presence of vaso-occlusive disease would hamper collateral circulation.

Qiu et al. (2015) explained that when MRI did not help visualize blood vessels of diameters less than 5 mm, they were regarded to be absent on the scan, whereas the study by Chen et al did not take into account blood vessels with diameters below 0.8 mm, which made their result an unrealistic reflection of the existent anatomical variations (Chen et al., 2004).

Akgun et al. (2013) found the mean PCA diameter to be 2.52 ± 0.36 mm, with the diameter of the right PCA being 2.56 ± 0.43 mm and that of the left being 2.43 ± 0.34 mm. They also reported that diameter of the normal ACA-A1 segment was 1.5 mm with ± 0.5 standard deviation between vessels of the right and left side, with mild variation ranging from 0.5 mm to 1.0 mm (Akgun et al., 2013). In hypoplasia, the vessel diameter was noted to be half of that of the normal side.

Qiu et al. (2015) found that FTPs were related to the developmental situation of the A1 segment of the ACA. They explained that because the carotid system develops prior to the vertebrobasilar system, the PCoA takes form earlier to the PCA. If the ACoA is maldeveloped, the ipsilateral PCoA will receive more blood flow and consequently have a diameter larger than the PCA, which is known as pure FTP.

According to Maaly and Ismail (2011), there was a significant difference between genders in terms of the mean diameters of four vessels of the COW: ICA, A1 segment of ACA, ACoA, and BA. In relation to age, the centripetal vessels and proximal vessels supplying the COW, which include the ICAs and BA, were larger in older participants, whereas the distal part of the arteries, which supply the brain centrifugally, were smaller (Maaly and Ismail, 2011). The comparison of average of blood vessels' diameter of the circle of Willis in multiple studies is expressed in the Table 3.

Symmetry and Asymmetry

Żurada and Gielecki (2007) have proposed the vascular asymmetry coefficient (VAC) that measures the symmetry, asymmetry, and hypoplasia of blood vessels. It determines differences in the mean diameter of two selected blood vessel segments, which can be used with paired vessels of large diameter in the brain and is expressed as a percentage:

$$VAC = \left(1 - \frac{dICAn}{dICAw}\right) \times 100,$$

where dICAn is the average diameter of the narrow segment and dICAw is the average diameter of the wider area.

Mujagić et al. (2016) studied MRA images of 1000 subjects and reported that the mean inner diameter of the ICA was 4.24 ± 0.44 mm, with the diameter being significantly larger in men (4.40 ± 0.45 mm) than in women (4.14 ± 0.39 mm) ($p < 0.0001$). They found the ICA to be symmetrical on both sides in 93.9% of subjects, noting only a single case of ICA hypoplasia (0.1%). No relationship was detected between the prevalence of anatomical variations and gender, as well as between asymmetry or hypoplasia and the side of ICA. In 23 (38.3%) subjects with ICA asymmetry, they noted aplasia or hypoplasia of the A1 segment of the ACA on the side of the ICA of reduced diameter. Aplasia and hypoplasia of the A1 segment of the ACA was found in 10% of cases.

Classification of Variations

The classification system for COW anatomical variations was proposed by (Lippert and Pabst, 1985). Krabbe-Hartkamp et al. (1998) minimally modified this system: completed, partial completed, and non-completed. The circle is integral when all parts are visualized and all blood vessels have diameters larger than 8 mm (Krabbe-Hartkamp et al., 1998). It is partially complete when anterior and posterior circulation are complete. However, this classification ignores physiological and pathological changes in hemodynamics, which can lead to variation. Unilateral as well as bilateral fetal-type PCAs are classified as complete (Krabbe-Hartkamp et al., 1998).

According to Li et al. (2011), anatomical variations in the COW may be classified into four types from the evolutionary point of view: archetype, combined type, modern type, and transition type. However, this classification system did not account for morphological integrity, making it inapplicable in clinical practice.

Qiu et al. (2015) proposed a new classification system based on four elements: situation of development of blood vessels, difference between diameters of vessels on both sides, presence of ACoA and PCoA, and relationship between the P1 segment of the PCA and PCoA. They found that the diameter of A1 segment of the ACA was between 5 mm and 10 mm and that if the difference between the diameters of vessels on the right and left was more than 0.5 mm, it led to a change in hemodynamics and consequent differences between the right and left sides of the ACA (Qiu et al., 2015). The theory of Devinsky et al. (1993) suggested that variations in the A1 segment of the ACA reveal dominant left-sided development, which is similar to the relationship between right-handedness and dominance of the left cerebral hemisphere.

CT and MRI Detectability

Qiu et al. (2015) reported the inability of MRI to visualize blood vessels smaller than 6 mm. Differentiation between the PCoA and anterior choroidal artery was an issue, which was resolved by tracking the course of the blood vessel to identify it (Krabbe-Hartkamp et al., 1998). Sensitivity and specificity of computed tomography angiography (CTA) in detecting normal arteries of the COW were both of 90%, whereas with regard to hypoplastic arteries, its sensitivity dropped to 52.6% and specificity rose to 98.2% (Afifi et al., 2011). Patrux et al. (1994) claimed that MRI had 100% sensitivity for the ACA, MCA, and PCA but lower sensitivity for the ACoA (89.2%) and PCoA (81.3%). Even as CT showed good specificity for hypoplastic segments, its sensitivity was low (Afifi et al., 2011), whereas MRI had low sensitivity for motion and was unsafe in case of clipped aneurysms.

DISCUSSION

In 1997, Barboriak and Provenzale reviewed all published case reports of anatomical variations in the COW reported by dissection studies, because there were no angiographic studies published at that time (Barboriak and Provenzale, 1997). Their review reported that ACoA duplication and aneurysm formation were unrelated; however, a later study has provided evidence to the contrary (Nam et al., 2015). Barboriak and Provenzale suggested that an aneurysmal ACoA could be misdiagnosed as a duplicated ACoA (Barboriak and Provenzale, 1997).

Kaplan (1956) suggested that the name “PCA” should be used only to refer to the distal part of the vessel, which begins after the PCoA joins, whereas the proximal part of the artery where it originates from the BA should be called the mesencephalic artery.

Akgun et al. (2013) found anatomical variations to be more common on the left side, whereas the findings of Qiu et al. (2015) and Given and Morris (2002) revealed the opposite (more common on the right). Caldemeyer (1998) claimed that some anatomical variations were more frequent on the right, whereas others were present equally on both sides, even as Van Raamt et al. (2006) found both sides to be equally affected.

Variations vs. Gender, Age and Population

The findings of Kondori et al. (2017) in Iran and Shaikh and Sohail (2018) in Pakistan suggest that there is no relationship between age or gender and anatomical variations; however, these studies did not measure blood vessel diameters. In Egypt, though Afifi et al. (2011) found gender-specific differences in anatomical variations in the COW that were not statistically significant, Maaly and Ismail (2011) concluded that the COW tended to be complete in women and young male subjects, whereas it was incomplete in older people, which was contrary to the findings of (Afifi et al., 2011). In a study conducted in the Netherlands, Hartkamp et al. (1999) found a relationship between anatomic variations and gender as well as age.

Li et al. (2011) claimed that posterior collateral circulation was more common in the Chinese than in the Japanese or Western populations. In addition, incomplete collateral circulation was observed more frequently in the posterior circle than in the anterior circle.

Of the 2246 subjects they examined, Qiu et al. (2015) found 28 cases of unilateral duplicated PCA, wherein one extends from the BA and the other extends from the ICA, with no connection between them (Qiu et al., 2015). Although they suggested that this anatomical variation was found only in the Chinese population, earlier in 2008, Kapoor et al. (2008) were one of the first to describe a similar anomaly on the basis of their cadaveric study conducted in India.

The complete COW was observed in 12.45% of subjects by Qiu et al. (2015) and Chen et al. (2004). Hartkamp et al. (1999) found that a greater proportion of participants younger than 40 years (75%) had a complete anterior circle than those in older age groups (65%). Maaly and Ismail (2011) found that complete circulation was more common in female subjects (52.8%) than in male subjects (42.6%), which was supported by the findings of (Afifi al., 2011) (75% in female subjects and 70% in male subjects).

Blood Vessel Diameter

The centripetal and proximal vessels supplying the COW, which include the ICAs and BA, were larger in older participants, whereas the distal part of the arteries, which supply the brain centrifugally, were smaller (Maaly and Ismail, 2011). Glagov et al. (1987) referred to this phenomenon of enlarged centripetal vessels as "compensatory enlargement in reaction to decreased cardiac output and decreased wall elasticity or atherosclerosis, which increase with age".

Teaching Points for Clinical Practice

The aim of this paper is to show the relationship between anatomical variation from one side with age, gender, race, geographic region, and comorbidity from another side. A traveling physician to work abroad may face some of these anatomical variations or in case of a foreign patient visiting a local physician (i.e. an African, an Asian, or a Latino patient visits a European physician in Europe and vice versa). A rare anatomical variation in the United States could be a common finding in China and contrariwise. For example, a healthy Indian patient could have a narrower diameter of the blood vessels of COW below the average vessels' diameter worldwide. A sick patient could have anatomical variation as a result of that disease. Finally, not all the absent blood vessels on an MRI or a CT scan means these vessels do not exist during surgery.

Conclusion

The aim of this review was to amalgamate the findings of various angiographic studies, examining the various factors associated with anatomical variations in the COW. Relations to age, gender, race, geographical region, and comorbidities were noted. The prevalence was described for every single variation. A detailed understanding of these variations is pivotal to specialists of various fields. Future avenues of research directed at ameliorating the detectability of small blood vessels (<3 mm diameter) by MRA and CTA are warranted to advance our understanding of these critical variations.

ABBREVIATIONS

ACA, anterior cerebral artery
BA, basilar artery
COW, circle of Willis
CT, computed tomography
ICA, internal carotid artery
MRA, magnetic resonance angiography
MRI, magnetic resonance imaging
PCA, posterior cerebral artery
PCoA, posterior communicating artery

REFERENCES

AKGUN V, BATTAL B, BOZKURT Y, OZ O, HAMCAN S, SARI S, AKGUN H (2013) Normal anatomical features and variations of the vertebrobasilar circulation and its branches: an analysis with 64-detector row CT and 3T MR angiographies. Sci World J, 2013: 620162.

AUGUSTE KI, WARE ML, LAWTON MT (2004) Nonsaccular aneurysms of the azygos anterior cerebral artery. Neurosurg Focus, 17: E12.

BARBORIAK DP, PROVENZALE JM (1997) Pictorial review: magnetic resonance angiography of arterial variants at the Circle of Willis. Clin Radiol, 52: 429-436.

BHATTACHARYA JJ, LAMIN S, THAMMAROJ J (2004) Otic or mythic?. ANJR Am J Neuroradiol, 25: 160-162.

BOŻEK P, PILCH-KOWALCZYK J, KLUCZEWSKA E, ZYMON-ZAGÓRSKA A (2012) Detection of cerebral artery fenestrations by computed tomography angiography. Neurol Neurochir Pol, 46: 239-244.

CALDEMEYER KS, CARRICO JB, MATHEWS VP (1998) The radiology and embryology of anomalous arteries of the head and neck. AJR Am J Roentgenol, 170: 197-203.

CHEN HW, YEN PS, LEE CC (2004) Magnetic resonance angiographic evaluation of Circle of Willis in general population: A morphologic study in 507 cases. Chin J Radiol, 29: 223-229.

DE GAST AN, VAN ROOIJ WJ, SLUZEWSKI M (2008) Fenestrations of the anterior communicating artery: incidence on 3D angiography and relationship to aneurysms. AJNR Am J Neuroradiol, 29: 296-298.

DIMMICK SJ, FAULDER KC (2009) Normal variants of the cerebral circulation at multidetector CT angiography. Radiographics, 29: 1027-1043.

DODEVSKI A, TOSOVSKA LAZAROVA D, MITRESKA N, ALIJI V, STOJOVSKA JOVANOVSKA E (2014) Posterior cerebral artery-variation in the origin and clinical significance. Pril (Makedon Akad Nauk Umet Odd Med Nauki), 35: 163-168.

EL-BARHOUN EN, GLEDHILL SR, PITMAN AG (2009) Circle of Willis artery diameters on MR angiography: an Australian reference database. J Med Imaging Radiation Oncol, 53(3): 248-260.

GIVEN CA, MORRIS PP (2002) Recognition and importance of an infraoptic anterior cerebral artery: case report. AJNR Am J Neuroradiol, 23: 452-454.

GLAGOV S, WEISENBERG E, ZARINS CK, STANKUNAVICIUS R, KOLETTIS GJ (1987) Compensatory enlargement of human atherosclerotic coronary arteries. N Engl J Med, 316: 1371-1375.

GOLDSTEIN JH, WOODCOCK R, DO HM, PHILLIPS CD, DION JE (1999) Complete duplication or extreme fenestration of the basilar artery. AJNR Am J Neuroradiol, 20: 149-150.

HAFEZ KA, AFIFI NM, SAUDI FZ (2007) Anatomical variations of the circle of Willis in males and females on 3D MR angiograms. Egyptian J Hospital Med, 26: 106-121.

HARTKAMP MJ, VAN DER GROND J, VAN EVERDINGEN KJ, HILLEN B, MALI WP (1999) Circle of Willis collateral flow investigated by magnetic resonance angiography. Stroke, 30: 2671-2678.

JIMÉNEZ-SOSA MS, CANTU-GONZALEZ JR, MORALES-AVALOS R, GARZA-CASTRO O, QUIROGA-GARZA A, PINALES-RAZO R, ELIZONDO-RIOJAS G, ELIZONDO-OMAÑA RE, GUZMÁN- LÓPEZ S (2017) Anatomical variants of anterior cerebral arterial circle. A study by multidetector computerized 3D tomographic angiography. Int J Morphol, 35: 1121-1128.

KAPOOR K, SINGH B, DEWAN LIJ (2008) Variations in the configuration of the circle of Willis. Anat Sci Int, 83: 96-106.

KARATAS A, COBAN G, CINAR C, ORAN I, UZ A (2015) Assessment of the circle of Willis with cranial tomography angiography. Med Sci Monit, 21: 2647-2652.

KOLBINGER R, HEINDEL W, PAWLIK G, ERASMI-KÖRBER H (1993) Right proatlantal artery type I, right internal carotid occlusion, and left internal carotid stenosis: Case report and review of the literature. J Neurol Sci, 117: 232-239.

KOMINAMI M, YAMADA N, IMAKITA S, UCHIDA R, KURIBAYASHI S, KIMURA K, TAKAMIYA M (1999) MR angiography of steno-occlusive lesions of intracranial arteries: a comparative study between turbo MRA and conventional MRA. Nihon Igaku Hoshasen Gakkai Zasshi, 59: 504-509.

KONDORI BJ, AZEMATI F, DADSERESHT S (2017) Magnetic resonance angiographic study of anatomic variations of the circle of Willis in a population in Tehran. Arch Iran Med, 20: 235-239.

KRABBE-HARTKAMP MJ, VAN DER GROND J, DE LEEUW FE, DE GROOT JC, ALGRA A, HILLEN B, BRETELER MM, MALI WP (1998) Circle of Willis: Morphologic variation on three-dimensional time-of-flight MR angiograms. Radiology, 207: 103-111.

LATH N, TANEJA M (2008) Bilateral congenital hypoplasia of the internal carotid arteries. Hong Kong J Radiol, 11: 129-131.

LESLEY WS, DALSANIA HJ (2004) Double origin of the posterior inferior cerebellar artery. AJNR Am J Neuroradiol, 25: 425-427.

LI Q, LI J, LV F, LI K, LUO T, XIE P (2011) A multidetector CT angiography study of variations in the circle of Willis in a Chinese population. J Clin Neurosci, 18: 379 -383.

LOUKAS M, LOUIS RG JR, CHILDS RS (2006) Anatomical examination of the recurrent artery of Heubner. Clin Anat, 19: 25-31.

LUH GY, DEAN BL, TOMSICK TA, WALLACE RC (1999) The persistent fetal carotid-vertebrobasilar anastomoses. AJR Am J Roentgenol, 172: 1427-1432.

MAALY MA, ISMAIL AA (2011) Three-dimensional magnetic resonance angiography of the circle of Willis: Anatomical variations in general Egyptian population. Egypt J Radiol Nucl Med, 42: 405-412.

MOKIN M, KASS-HOUT T, KASS-HOUT O, DUMONT TM, KAN P, SNYDER KV, HOPKINS LN, SIDDIQUI AH, LEVY EI (2012) Intravenous thrombolysis and endovascular therapy for acute ischemic stroke with internal carotid artery occlusion: A systematic review of clinical outcomes. Stroke, 43: 2362-2368.

MUJAGIĆ S, KOZIĆ D, HUSEINAGIĆ H, SMAJLOVIĆ D (2016) Symmetry, asymmetry and hypoplasia of the intracranial ICA on magnetic resonance angiography. Acta Med Acad, 45: 1-9.

OELERICH M, SCHUIERER G (1997) Primitive hypoglossal artery: demonstration with digital subtraction-, MR-and CT angiography. Eur Radiol, 7: 1492-1494.

OLIVEIRA GDP, SOARES NLR, OLIVEIRA GDP, VALE BP (2014) Bilateral internal carotid artery agenesis: a case report. J Vasc Bras, 13(4): 336-339.

OSBORN AG (1999) Circle of Willis. In: Osborn AG (ed). Diagnostic cerebral angiography, 2nd edn. Lippincott Williams & Wilkins, Philadelphia, pp 105-116.

PADGET DH (1948) The development of the cranial arteries in the human embryo. Contrib Embryol, 32: 205-261.

PATRUX B, LAISSY JP, JOUINI S, KAWIECKI W, COTY P, THIÉBOT J (1994) Magnetic resonance angiography (MRA) of the circle of Willis: a prospective comparison with conventional angiography in 54 subjects. Neuroradiology, 36: 193-197.

QIU C, ZHANG Y, XUE C, JIANG S, ZHANG W (2015) MRA study on variation of the circle of Willis in healthy Chinese male adults. Biomed Res Int, 2015: 976340.

RUMBOLDT Z, CASTILLO M, SOLANDER S (2003) Bilateral congenital absence of the internal carotid artery. Eur Radiol, 13: L130-L132. https://doi.org/10.1007/s00330-002-1742-2.

SAIKIA B, HANDIQUE A, PHUKAN P, LYNSER D, SARMA A (2014) Circle of Willis: Variant forms and their embryology using gross dissection and magnetic resonance angiography. Int J Anat Res, 2: 344-353.

SHAIKH R, SOHAIL S (2018) MRA-based evaluation of anatomical variation of circle of Willis in adult Pakistanis. J Pak Med Assoc, 68: 187-191.

TAŞAR M, YETIŞER S, TAŞAR A, UĞUREL S, GÖNÜL E, SAĞLAM M (2004) Congenital absence or hypoplasia of the carotid artery: radioclinical issues. Am J Otolaryngol, 25: 339-349.

TEKALE V, AMBIYE M (2016) A study of circle of Willis by MR angiography. Int J Anat Res, 4(3): 2542-2546.

TOMSICK TA, LUKIN RR, CHAMBERS AA (1979) Persistent trigeminal artery: unusual associated abnormalities. Neuroradiology, 17: 253-257.

TRIPATHI M, GOEL V, PADMA MV, JAIN S, MAHESHWARI MC, GAIKWAD S, GUPTA V, CHANDRA PS, MEHTA VS (2003) Fenestration of the posterior communicating artery. Neurol India, 51: 75-76.

UCHINO A, SAWADA A, TAKASE Y, KUDO S (2001) Persistent primitive olfactory artery: diagnosis with MR angiography. Clin Imaging, 25: 258-261.

VAN RAAMT AF, MALI WP, VAN LAAR PJ, VAN DER GRAAF Y (2006) The fetal variant of the circle of Willis and its influence on the cerebral collateral circulation. Cerebrovasc Dis, 22: 217-224.

YENIÇERI IÖ, ÇULLU N, DEVEER M, YENIÇERI EN (2017) Circle of Willis variations and artery diameter measurements in the Turkish population. Folia Morphol, 76: 420-425.

ZAMPAKIS P, PANAGIOTOPOULOS V, PETSAS T, KALOGEROPOULOU C (2015) Common and uncommon intracranial arterial anatomic variations in multi-detector computed tomography angiography (MDCTA). What radiologists should be aware of. Insights Imaging, 6: 33-42.

ŻURADA A, GIELECKI JS (2007) A novel formula for the classification of blood vessels according to symmetry, asymmetry and hypoplasia. Folia Morphol, 66: 339-345.