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The Development of Cerebrovascular Diseases in Patients with Anatomical Variants in the Circle of Willis

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Abstract

Introduction: Cerebrovascular disease (CVD) is the second leading cause of death worldwide. Cerebrovascular disease includes several clinical-pathological entities, namely: ischemic and hemorrhagic stroke, transient ischemic attack, brain aneurysm, small vessel disease and vascular dementia, but the most common form of cerebrovascular disease is stroke. Ischemic stroke accounts for 87% of all strokes, while 10% are intracerebral hemorrhages and 3% are subarachnoid hemorrhagic strokes. The circle of Willis (CoW), even though it may present certain variations at times, it is genuinely composed of three cerebral and two communicating arteries.

Material and method: The study was based on multiple searches of PubMed, Google Scholar and SpringerLink. Using the following keywords: "circle of Willis, variations, cerebrovascular disease", "and circle of willis, variants, stroke"and"circle of Willis, variations, and aneurysm. We inspected 100 abstracts found on the mentioned topic, with the selection of only 30 full-text studies, written in English language most in connexion to our scientifical purpose, published over the last 20 years (the period between 2004-2024). This permitted the realization of a thorogh descriptive review on the interconnection between anatomical variants of the CoW and CVD.

Results and discussion: It seems that anatomical variants of fenestration of Anterior Communicating Artery (AcoA) represent a predictive risk factor of death for hemorrhagic stroke because aneurysms can develop at this level. Hypoplasia of the A1 segment of the Anterior Cerebral Artery (ACA) affects the CoW functionality, and thus becomes a risk factor for acute ischemic stroke. Most of these patients have occlusive strokes of small vessels, especially within the striatum, respectively at the supratentorial level. Many authors have suggested an increased risk of ischemic stroke in the presence of CoW variations. There is an increased risk of infarction, particularly in the thalamic region, associated with hypoplasia of Posterior Communicating Artery (PCoA).

Conclusion: A more thorough knowledge of the implications of the anatomical variations in the development of both ischemic or hemorrhagic stroke and aneurysms could be of help in the neurology field for the understanding of some out of ordinary clinical or particular signs and symptoms in the case of CVD, thus becoming of crucial importance for clinicians.

Keywords: Circle of Willis; Anatomical variations; Stroke; Aneurysm; Cerebrovascular disease

Introduction

Cerebrovascular disease (CVD) is the second leading cause of death worldwide. Cerebrovascular disease includes several clinical-pathological entities, namely: ischemic and hemorrhagic stroke, transient ischemic attack, brain aneurysm, small vessel disease and vascular dementia, but the most common form of cerebrovascular disease is stroke [1]. Ischemic stroke accounts for 87% of all strokes, while 10% are intracerebral hemorrhages and 3% are subarachnoid hemorrhagic strokes [2]. The circle of Willis (CoW), even though it may present certain variations at times, it is genuinely composed of three cerebral and two communicating arteries. Many authors have described the CoW as a heptagon comprising: the Anterior Communicating Artery (ACoA) (anteriorly), two Anterior Cerebral Arteries (ACAs) (right and left), two Posterior Communicating Arteries (PCoAs) (right and left) and two Posterior Cerebral Arteries (PCAs) (right and left). In what anatomical variations in the Circle of Willis are concerned, there have been researchers that divided the circle of Willis in two parts: one anterior (composed of the ACoA and the two ACAs) and another posterior (composed of the two PCAs and the two PCoAs). A typical CoW would comprise all of its component arteries, whereas an atypical circle of Willis would present asymmetry in the diameter or shape

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of its composing vessels. Most commonly encountered anatomical variations in the CoW are hipoplasia, fetal type artery, duplication or triplication, fenestration, absence and azygos type artery [3],[4].

In what the correlation between stroke and anatomical variations is concerned, in a retrospective study realized on almost 300 patients with acute stroke that underwent cerebral RMI investigation, there were analyzed the implication of aplasia and hipoplasia of the segments A1 of ACA and P1 of PCA and the aplasia or hipoplasia of the Vertebral Artery (VA) in the development of the CVD. The authors found an incomplete CoW in 34 % of the investigated patients with stroke and there was also noted a poorer disease prognosis in these patients than in the ones presenting a complete or typical CoW[5].

Regarding the correlation between intracranial aneurysm and anatomical variations of the CoW, the latter contribute significantly to the development of CVD of this kind [6]. In a recent Romanian study there was presented the case of a patient with aneurysm of the ACoA associated with multiple anatomical variants located both on the anterior and on the posterior part of the CoW, more exactly the hipoplasia of the right ACA and the bilateral hipoplasia of the PCoAs [7].

A recent study reported that the number of hypo plastic or absent arteries in the Circle of Willis increases with age, which affects the capacity o the anastomotic structure and becomes a risk factor for CVD with advancing age [8]. Also, a group of Chinese researchers analyzed the CoW configuration and the morphological appearance of the vascular wall of the carotid arteries using MRI to identify a possible correlation between the two elements. They found a statistically significant correlation between the presence of anatomical variants at the level of the anterior part of the CoW and the presence of atherosclerosis complicated with plaque hemorrhage in the internal carotid arteries [9]. Another study conducted by American and Chinese researchers investigated the correlation between the presence of anatomical variants at the CoW level and the distribution of atheroma plaques at the Middle Cerebral Artery (MCA) level. They confirmed that anatomical variants of CoW were present in patients with atherosclerosis at the MCA level. In addition, these authors also reported a different localization of atheroma plaques according to the presence or absence of CoW variants [10].

However, there are also conflicting studies, which state that although hipoplasic arteries are identified from the fetal period or at birth, there is an increasing prevalence of hypo plastic arteries with age and in association with ischemic heart disease, which may suggest that some arteries would may undergo hypotrophic remodeling of the wall throughout life, possibly in vascular disease [11].

Material and Method: The study was based on multiple searches of PubMed, MEDLINE, Google Scholar and SpringerLink. Using the following keywords: "circle of Willis, variations, cerebrovascular disease", "and circle of willis, variants, stroke"and"circle of Willis, variations, and aneurysm. We inspected 100 abstracts found on the mentioned topic, with the selection of only 30 full-text studies, written in English language most in connexion to our scientifical purpose, published over the last 20 years (the period between 2004-2024). This permitted the realization of a thorogh descriptive review on the interconnection between anatomical variants of the CoW and CVD.

Results and Discussion

Correlations between the localization of ischemic /hemorrhagic stroke and the type of anatomical variant of the AcoA

A study by two Colombian researchers analyzed 50 CoWs and found the greatest variability of this anastomotic structure in the arteries of the anterior circulation, but another study conducted in Chile did not identify the presence of any anatomical variant at the AcoA level, although the A1 segment of the ACA showed hypoplasia in 8.3% of cases [12,13].

A mixed group of Hungarian and Dutch researchers analyzed the correlation between the collateral function of the anterior and posterior communicating arteries of the CoW, assessed by duplex transcranial ultrasound, and the presence of atheroma plaques at the level of the Internal Carotid Artery (ICA) [14]. The obtained results demonstrated the fact that patients with ischemic stroke had a non-functional anterior collateral pathway, probably through hypoplasia or absence of AcoA, which was associated with the presence of severe atherosclerotic stenosis at the ICA level. The same aspects were also reported by another more recent study who concluded that the lack of integrity of AcoA and PCoA is statistically significantly associated with atherosclerotic plaque complications from the ICA [9]. In addition, patients with AcoA aplasia/absence and ischemic stroke have a poorer prognosis of recovery rate and even have a tendency towards death, as we identified in the present research [13].

It seems that anatomical variants of fenestration AcoA represent a predictive risk factor of death for hemorrhagic stroke because aneurysms can develop at this level. At the same time, the anatomical variants of AcoA, in the form of hypoplasia, fenestration and absence of the vessel, represent a predictive factor of mortality risk for multiple, infra- and supratentorial ischemic strokes.

There are also reports of associations between the presence of anatomical variants of AcoA and the development of aneurysms at the level of the anterior AcoA-ACA complex and their rupture, which often leads to the death of those patients [15].

Correlations between the location of hemorrhagic / ischemic stroke and the type of anatomical variant of ACA

Of all ischemic strokes, those located in the territory of the ACA constitute only 0.6–3% and are correlated with anatomical variations of the A1 segment of ACA. The most frequent abnormalities of ACA are agenesis/absence, hypoplasia and duplication [16]. A1 segment hypoplasia is an uncommon variant of CoW. The frequency of this congenital variation is 1–13% as derived from angiograms and autopsy reports in various experimental studies [17].

The A1 segment of the ACA is a major supplier of anterior collateral blood flow. This segment is also a source for numerous penetrating striatal arteries that supply the anterior hypothalamus, the septum pellucidum, and the anterior and inferior portions of the striatum [17].

Hypoplasia of the A1 segment of the ACA affects CoW functionality and thus becomes a risk factor for acute ischemic stroke. Most of these patients have occlusive strokes of small vessels, especially within the striatum, respectively at the supratentorial level, as we also identified in the present research. Such strokes occur because of poor collateral capacity, especially when the arteries entering the striatum show lesions of arteriolosclerosis or hypertensive hyalinosis. There is also poor clearance of thromboembolism within the striatum when there is defective collateral circulation. Ischemic stroke related to hypoplasia of the A1 segment is usually tolerable, manifesting predominantly with sensory-motor deficit contralateral to the hypoplasia of the A1 segment [17].

The A1 segment of the ACA can show variations of up to 15% in cerebral MRI angiographic analyses. The effects of the presence of this

anatomical variant are identified either predominantly in the form of ipsilateral lacunar striatal infarcts (in about 70% of the analyzed cases), or in the form of striatal infarcts as a result of the occlusion of penetrating arteries in the striatal area [18]. Also, two cases of bilateral cerebral infarction in the territory of the ACA were reported; in which MRI angio identified unilateral hypoplasia of the A1 segment of the ACA. The authors concluded that unilateral A1 hypoplasia is a significant predisposing factor for this rare type of ischemic stroke [19]. A group of authors from India also reported that most of their cases (64.06%) with hypoplasia of the A1 segment of the ACA were diagnosed with ischemic stroke in the territory associated with the hypo plastic artery as a result of irrigation reduced ipsilateral or bilateral striatal areas [20].

In general, arterial "fenestration" is described as that cerebral artery doubled in one part of its trunk by the presence of two independent channels, which have their own tunica intima and their own tunica media, and sometimes even a tunica adventitia of their own, and after the corresponding course, the two channels join and reform the original artery. Fenestration of the A1 segment of the ACA may occur due to the absence of fusion of the primitive plexiform anastomosis between the ACA and the primitive olfactory artery, normally present at the 18–43 mm embryonic stage [21].

Some findings on fenestrations of the A1 segment of the ACA in the literature have indicated controversies regarding their pathophysiological and clinical significance. Some have shown that ACA fenestration causes ACA aneurysms; others did not find fenestration of the A1 segment to be associated with ischemic stroke, nor to represent a "weak point" for aneurysm development, especially if the diameter of the ACA does not vary in its different parts [21].

Correlations between location of hemorrhagic/ischemic stroke and type of anatomical variant of PCoA.

Abnormalities identified in the posterior part of the arterial polygon of Willis result either from the persistence of vessels that should normally disappear during embryonic development, or from the absence of certain vessels that should have been present at birth [22]. The presence of effective posterior communicating arteries is a vital factor for stroke patients, as these vessels link the anterior to the posterior cerebral circulation, providing a powerful source of plasticity in cerebral hemodynamics [23].

Hypoplasia of the posterior communicating artery (PCoA) is a congenital variation found in 6–21% of the general population [24]. Some authors state that PCoA hypoplasia becomes a risk factor for ischemic stroke only in the presence of ipsilateral ICA occlusion, but others demonstrated that PCoA hypoplasia appears to contribute to the risk of cerebral ischemia in the form of ipsilateral thalamic lacunar infarcts, with or without the occipital lobe involvement, even in the absence of ICA occlusion [24]. Many authors have suggested an increased risk of ischemic stroke in the presence of CoW variations. There is an increased risk of infarction, particularly in the thalamic region, associated with hypoplasia of Posterior Communicating Artery (PCoA) [25].

In a recent Romanian article, there were analyzed the medical causes of death in patients with bilateral PCoA hypoplasia. The obtained data allowed the authors to conclude that extensive stroke can be correlated with bilateral hypoplasia of the PCoA, especially if there is also an associated systemic pathology, as well as occlusion of an important artery that supplies the brain, such as the ICA or the basilar trunk. The pathophysiological mechanism could be that the reduction in PCoA diameter is associated with a reduction in cerebral blood demand because the volume of blood flow is inversely proportional to the length of the artery and directly proportional to its diameter [26]. Thus, the shorter and wider the PCoA, the more efficient the transmission of blood to the nerve tissue dependent on that artery will become. Conversely, the longer and narrower the lumen of one or both PCoAs, the weaker the irrigated area of the brain will be [27].

It appears that some individuals may develop another collateral circulation in the case of a non-functional PCoA, but this situation is highly variable between individuals.

Patients with bilateral paramedian thalamic lesions without other lesions outside the thalamus were more likely to have hypoplastic P1 segments or unilateral or bilateral absences. Hypoplasia of the ipsilateral vertebral artery (VA) adds an additional risk factor to the presence of a hypoplastic PCoA because it increases arterial pressure in the contralateral VA in conditions where the patient has hypertension. Regardless of age, the presence of a single aplastic PCoA artery does not cause stroke if there are no associated risk factors (hypertension, atherosclerosis, stress, etc.). A stress-marked life can affect both the atherosclerosis formation and the cardiovascular system. Tensional, anxious, depressive and conflictual states can trigger both hyper and hypodynamic reactions at a cardiovascular level such as changes in the rate, rhythm, force and magnitude of heart contraction, modifications in the pumping of the heart and within the peripheral vascular resistance [28].The presence of anatomical variants at the level of CoW can impact the trajectory of microembolic and therefore lead to infarcts in more unusual, distal areas of the brain [29].

In the context of occlusion of large arteries or severe stenosis, communicating arteries become crucial. In this context, the caliber of communicating arteries is inversely proportional to the risk of stroke, because the smaller these communicating arteries, the lower the ability to compensate for reduced or lost flow [11]. Although hypo plastic arteries can be found at birth, there is an increasing prevalence of hypo plastic arteries with age and in association with ischemic heart disease, suggesting that some hypo plastic arteries in adults may undergo hypo trophic wall remodeling, possibly in the context of vascular disease [11]. The clinical significance of the anatomical variants of CoW is revealed especially in the case of an atypical stroke model.

Correlations between the location of hemorrhagic / ischemic stroke and the type of anatomical variant of PCA

The prevalence of ischemic stroke in the territory irrigated by PCA is not higher than 10%. Areas irrigated by the PCA include: the paramecia midbrain, the medial and postero-lateral thalamus, the occipital lobes, and the parietal and posterior areas of the temporal lobes [30].

The fetal type anatomical variant of the posterior communicating artery is associated with PCA hypoplasia and these vascular aspects have been noted to cause ischemic stroke in the territories irrigated by the posterior circulation, respectively supratentorial in the occipital region, and infratentorial, especially in the presence of ICA atherosclerosis. Unilateral partial fetal type PCoA means the presence of a hypo plastic ipsilateral PCA P1 segment connecting the ICA and AB, which may represent a risk factor for paradoxical right hemispheric ischemic stroke if the patient has systemic atherosclerosis complicated with ulcerations and calcifications and high tensional values (31).

The occurrence and evolution of ischemic stroke in the territory of the PCA depend on the functionality of the ICA and Basilary Artery (BA). Thus, the infarct area is correlated with the thrombosed major artery [30]. Therefore, supratentorial (capsulo-thalamic and lobar)

ischemic stroke occurs in ICA occlusion, and infratentorial (bulbo-pontine) stroke occurs in BA occlusion, as the two vasculatures do not communicate due to the greatly reduced lumen of the P1 segment of a hypoplasic PCA, comparatively to a normal one.

Conclusion

There are quite a few studies in literature that reveal the incidence of anatomical variants of the CoW in the general population, but most of these focus mainly on either just the anterior or posterior part of the circle, not analyzing the arterial polygon in its integrity. In this context, there is needed a better understanding of the anatomical variations of the CoW, in order to prioritize an individualized treatment for patients with CVD. A more thorough knowledge of the implications of the anatomical variationsof the CoW in the development of either ischemic or hemorrhagic stroke could be of help in the neurology field for the understanding of some out of ordinary clinical or particular signs and symptoms in the case of CVD, thus becoming of crucial importance for clinicians. A CT angiography with 3D reconstruction in patients with communicating artery aneurysms could be a useful tool for identifying intracranial aneurysms and associated anatomical variants of the polygon of Willis.

Acknowledgment

None

Conflict of Interest

None

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