Original Article

Evaluation of the Frequency of Migraine and CVA Patients Based on Circle of Willis Morphological Variations in MRA Images

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Abstract

Background: The Circle of Willis (CoW) forms a critical collateral route for the compensation pathway at the basal cistern of the brain. This study aims to determine if migraine headaches and cerebrovascular accidents (CVAs) are associated with the prevalence and patterns of CoW arterial variations seen in the three-dimensional time-of-flight magnetic resonance angiography technique in patients.

Materials and Methods: A cross-sectional study was undertaken by a systemic search of electronic databases in the Imaging Center, Abadan's Taleghani Hospital, Iran, from March 2020 to March 2022. Data on the prevalence of variations in patients who presented for screening for migraine and CVA were extracted and analyzed with Student *t*-test and the Chi-square method.

Results: Findings show complete CoW has been visible in 20.19% of our patients. The anterior part of the CoW was almost intact in all patients. The posterior part of CoW was mostly bilaterally hypoplastic (31.73%) or bilateral aplastic (29.81%) and in some rare cases unilaterally varied. In migraine patients, CoW was rarely in its classic form (15%) and was varied bilaterally in 72.5% of the cases. In CVA patients, CoW was in its complete vascular structure in 23.08% and bilaterally varied in 46.15% of all cases.

Conclusions: Overall, migraine and CVA are associated with anatomical variations in the posterior portions of the CoW. Further larger prospective trials are needed to determine the true prevalence of CoW variations and their pathological significance.

Keywords: CoW, CVA, magnetic resonance angiography, migraine

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Introduction

Migraine as a risk factor for ischemic stroke is the most common neurological disease in the world. The prevalence of migraine in Iran was recorded as 15.1%, and this amount is higher in women than in men.[1] Evidence indicated that cortical spreading depression (CSD) can activate the migraine headaches.[2] It would be suggested that arterial variants might pose different hemodynamic challenges to brain blood flow, which may be trigger migraine.[3] The Circle of Willis (CoW) is the collateral network for preserving satisfactory brain perfusion, revealing considerable morphological variations.[4] It includes the anteriorly located internal carotid and the posteriorly vertebrobasilar arterial system. The CoW consists of a symmetrical arterial circle, with a single AcomA and bilateral PcomA, which usually have smaller diameters than the pre-communicating segments of the posterior cerebral artery (PCA). The posterior communicating artery (PcomA), a

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branch of internal carotid artery which serves as an important anastomotic channel between anterior and posterior cerebral flows, is of more pathophysiological importance.[5] Each PcomA passes postero-medially and anastomose at the confluence between pre- (P1) and post-communicating (P2) portions of ipsilateral PCA. The PcomA sometimes extends as PCA, named fetal PCA (f-PCA), with a complete absence of P1 segment.[6,7] Fetal PCA incidence may be unilateral or bilateral, and in these circumstances, the PcomA is bigger than the usual. The communication between the internal carotid and vertebro-basilar system via PcomA is crucial for CNS vasculature.[6,7]

Until now, to find out the different variations of the brain vascular ring and its branches, various methods including dissection, surgery, radiological angiography, magnetic resonance angiography (MRA), and Doppler ultrasonography have been used.[8-12]

Due to the importance of knowing the relationship between CoW variations and some vascular diseases clinically, studies have been conducted in this field, although these studies have been limited in Iran. In this regard, we used non-invasive three-dimensional time-of-flight MRA (3D-TOF-MRA) method as a quite sensitive diagnostic modality in the detection of pathological lesions or normal intracranial vasculature variants in southwest Iranian patients and investigated their relationship with age and gender. Recognition of such modifications is essential in the assessment of cerebro-vascular disease and its associated treatments.

Materials and Methods

A total of 104 patients were selected for the current study between March 2020 and March 2022. They were referred for screening with MRA for cerebral ischemic stroke (CIS), migraine, less hearing sense, dim vision, and mild focal neurological loss in the Taleghani Hospital Imaging Center Abadan, southwest of Iran. All the subjects experienced 3D TOF-MRA utilizing a 1.5 Tesla MRA system (GE Healthcare, Milwaukee, WI, USA), and imaging factors were included: a repetition time (TR) of 30 milliseconds, an echo time (TE) of 2.7–3.1 milliseconds, a flip angle of 20°, a field of view (FOV) of 200 mm, a slice thickness of 1.4 mm, and an imaging time (TA) of approximately 4.50 minutes. The examination was supervised and evaluated in the departments of anatomy of Abadan University of medical science. All the captured images were converted, applying a maximum intensity projection (MIP) algorithm to produce an angiogram-like image.[8] The reconstructed MRA images were again interpreted to identify the CoW variations and hypoplastic or aplastic arteries, with or without the fetal PCA. Hypoplastic arteries were considered <1 mm in diameter.[6] Besides variations of CoW, hypoplasia or aplasia of other cerebral arteries and its branches was also mentioned. To define a reciprocal acute ischemic lesion, diffusion weighted imaging (DWI) was applied. A distribution and size assessment of DWI hyperintense lesions were employed for topographic localization. DW images were obtained in the axial plane utilizing a single-shot echo-planar and spin-echo pulse sequence based on research previously reported by Chuang *et al*.[13]

Statistical analysis

The data were analyzed with Statistical Package for Social Sciences software (IBM SPSS Statistics for Windows, Version 24.0. IBM Corp., Armonk, NY, USA) and reported as mean ± standard deviation (SD). The statistical dependencies between age and sex were calculated utilizing the Student *t*-test. The differences between the male and female arterial hypoplasia were evaluated in relation to the side employing the Chi-square test. Conditional logistic regression with univariate analysis was used to determine ORs and 95% CIs to assess the independent effects of possible risk factors. Probability values of $P > 0.05$ were considered statistically significant.

Results

The 104 participants included 59 males (56.7%) and 45 females (43.3%).

The average age of male participants in the study was 44.42 ± 14.88, and female participants (44 ± 14.8) were in the age group of 10 to 79 years.

Among these, 12.5% of people with a differential diagnosis of stroke (CVA), 38.46% of people with a differential diagnosis of migraine headache, and 49% of people with other differential diagnoses such as double nose, vertigo, and so on were subjected to MRA [Figure 1].

In this study, hypoplasia and aplasia of ACA, PCA, and AcomA were rarely seen; that is why only PcomA is discussed in the statistical analysis. In the statistical population under our study, complete CoW, bilateral hypoplasia, and bilateral aplasia were seen in 21 (19.20%), 33 (31.73%), and 31 (29.81%) people, respectively. One side hypoplasia alongside with aplasia on

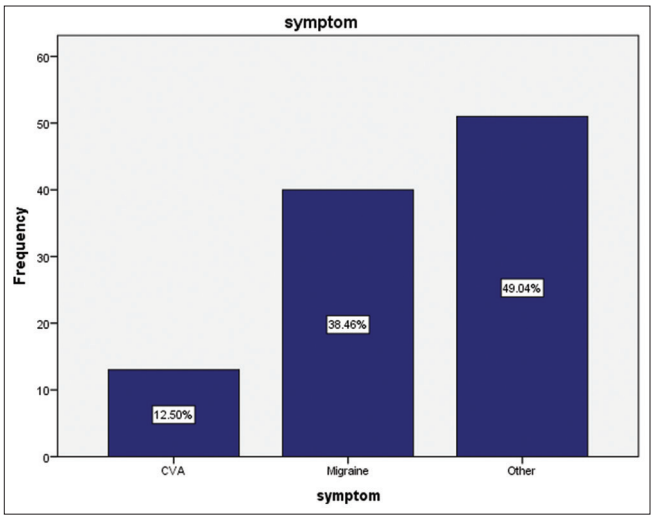

Figure 1: Under study patients distribution based on clinical symptoms

the other side was seen among females (n = 6, 5.77%). Left unilateral hypoplasia was seen in men (n = 1, 0.96%). Right unilateral aplasia, left unilateral aplasia, and right unilateral aplagia were seen in two and one females (2.88% and 1.99%) and seven men (6.73%), respectively [Figure 2].

According to the statistical analysis, the distribution of CoW variations was different according to gender [Figure 3].

Using the Chi-square test, it was found that the distribution of aplasia is significantly more in men than in females (P value ≥ 0), while the left and right side aplasia had no significant relationship with gender (P value ≤ 0.461); right hypoplasia showed a significant relationship with gender (P value = 000).

According to the statistical analysis, the distribution of CoW variation was different based on clinical symptoms. Among the 21 people who had a complete CoW, 3, 6, and 12 people came with stroke, migraine headaches diagnosis, and other diagnoses, respectively. Among the 33 people who had bilateral hypoplasia, 1, 15, and 17 people were diagnosed with stroke, migraine headaches, and other differential diagnoses, respectively. Among the 31 people who had bilateral aplasia, 5, 14, and 12 people were diagnosed with stroke, migraine headaches, and other differential diagnoses. Among the 6 people with hypoplasia and aplasia simultaneously, 1, 5, and 5 people were diagnosed with migraine headaches, stroke, and other differential diagnoses. One person had unilateral left hypoplasia with a stroke. 3 people had unilateral right hypoplasia with differential diagnoses. Out of 2 people with left unilateral aplasia, 1 had a migraine headache, and the other hada stroke. Out of 7 people with right unilateral aplasia, 2, 3 and 3 people had stroke, migraine headaches, and other differential diagnoses, respectively.

Among the 33 people who had bilateral hypoplasia, 20 were female and 13 were male. The person who had unilateral left hypoplasia was male. Out of 3 people with unilateral right hypoplasia, 2 were female and 1 was male.

Using the Chi-square test, it was found that there is no significant relationship between clinical symptoms and aplasia of the CoW (P Value ≥ 0.053), while changes in hypoplasia in people with a history of cerebrovascular disorders and migraine had a significant relationship (P value ≤ 0.028). Aplasia changes on the right showed a significant relationship with clinical symptoms (P value = 000). The changes of aplasia on the left side did not show a significant relationship with clinical symptoms (P value ≤ 0679) [Figure 4].

Discussion

It has been confirmed that hemodynamic changes during fetal life can play a significant role in determining the final structure of the CoW. During the embryological development of cerebral arteries, a complex process involving regressions and anastomoses of the primitive vessels take place and may result in a wide range of individual variations from normal anatomy, including persistent fetal forms, hypoplasia, or aplasia of the arterial segments, duplications, or fenestrations of the arteries or persistent carotid-basilar anastomoses.[14]

Van Overbeek concluded that the rapid growth of the occipital lobe in the embryonic period would have a significant effect on the final shape of the CoW, especially in the posterior part.[15] Some researchers believe that hemodynamic changes are not limited to the fetal period, and there is a possibility that the shape of the CoW will change in the first decade of life after birth.[16] Many other factors can also be involved in the formation of arterial changes; in some cases, the changes are pathological and are of great importance in the clinic.[17] In this regard, studies have been conducted to investigate the relationship between changes in the CoW and some neurovascular problems. For example, a clinical study[13] showed that PcomA aplasia or hypoplasia can increase the risk of stroke in internal carotid artery occlusion cases.

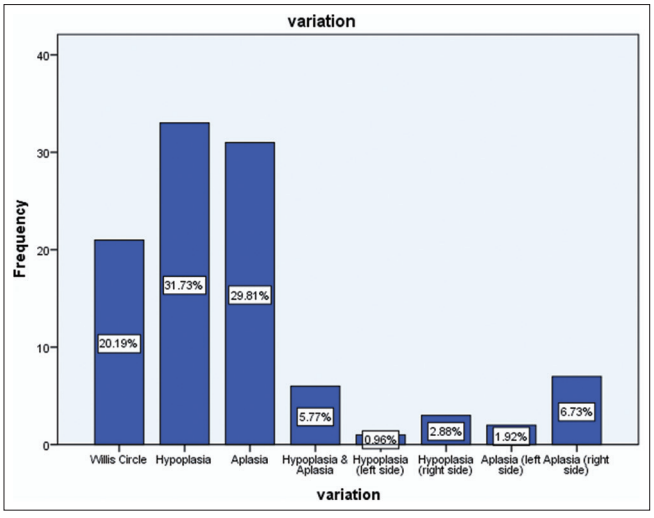

Figure 2: Under study patients distribution based on CoW variations

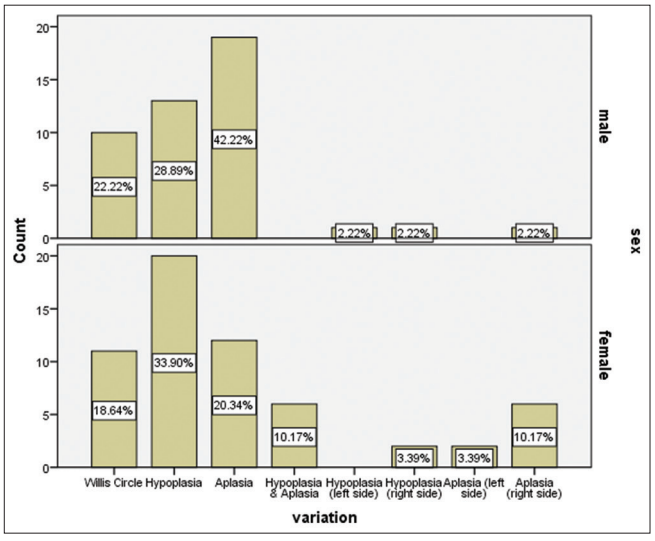

Figure 3: Distribution of CoW variations based on gender

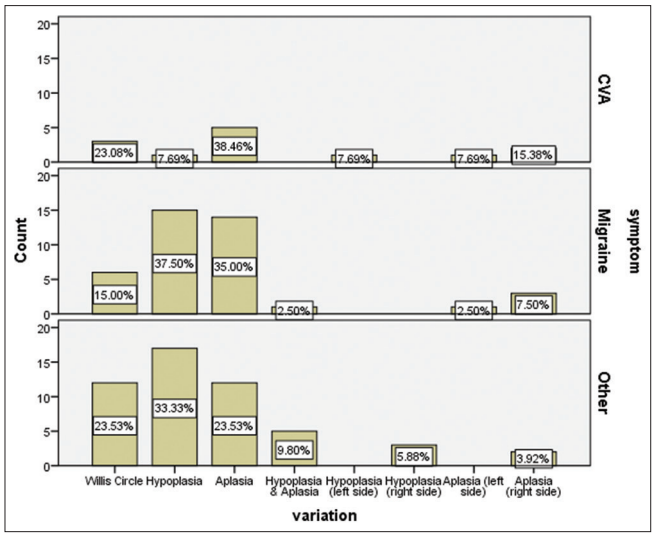

Figure 4: Distribution of CoW variations based on clinical symptoms

Haghighimorad *et al*.,[18] in a study, examined 298 patients in two groups with and without stroke; among them, 63 patients had hypoplasia or aplasia of the fetal posterior cerebral artery FPcoA (Fetal PcoA) and 231 patients had hypoplasia or aplasia of the posterior communicating artery (PcoA). The findings of this study also indicate that in stroke patients, the majority of the studied population had aplasia or hypoplasia of PcomA and only 23.08% had a complete CoW.

In the population under our study, major changes were in the posterior part of the CoW, and just 20.19% of our statistical population had a complete CoW, which is consistent with Kondori *et al*.[19] study, and results are entirely similar to each other. They investigated the CoW anatomical variations of the CoW in Tehran resident population and concluded that the CoW could be seen in a perfect and complete form in a small percentage of the population.

Khalesi *et al*.,[20] in investigation of anatomical CoW changes in 57 cases of the human brain, showed that 29.8% of all samples had a normal anatomical condition and 3.3% of the arteries of the CoW originated from an abnormal place, the most common of which was related to the left posterior cerebral artery, which originated from the internal carotid artery. Dr. Khalesi's data are largely different from our study data, which is probably due to the different statistical population and his different survey methods.

In another study, variations of the CoW in patients suffering from atherosclerosis checked out and compared the blood supply of the anterior and posterior parts of the ring in terms of function. They reported cases of low function of the PcomA artery and also the fetal form of this artery.[21] The data of the present study also indicate that most of the statistical population had dysfunction in PcomA, and according to the dysfunction of the artery in cases of hypoplasia and aplasia, the findings are completely consistent with the above study.

The findings of our research and other studies indicated that the vascular ring of the brain is a variable anatomical structure. This hypothesis confronts us with the question of what is the cause and origin of this phenomenon and when is the time of emergence and stabilization of variations.

According to results from the current study with other similar studies, cerebral angiography can be considered a reliable way for the natural diagnosis of variations, but autopsy and anatomy, if possible, are necessary to confirm the results.[22]

In a study conducted in 2018 by Hamming *et al*.[23] on changes in the CoW and migraine in ischemic stroke patients, among the 646 studied samples with stroke, 52 had a history of migraine headaches, and among them, 45 people (87%) had an incomplete CoW, of which 85% had an incomplete circle in the CoW posterior part. In this study, among the 40 people who had migraine headaches, only 15% had a complete CoW and 85% had a disorder in the posterior part of the CoW.

In a 2011 study by Cavestro regarding anatomical changes in the CoW and brain damage in migraine patients, they concluded that there is a strong connection between changes in the CoW and migraine. The changes are significant in migraine patients with aura, especially in the posterior part of the CoW, which indicates the induction of critical pressure due to blood flow disturbance.[24] In the current study, due to the small size of the statistical population and, on the other hand, the lack of access to the patient's complete history, we have not been able to investigate this issue, which is suggested in future research in this field with the cooperation of neurologists and collecting related information. To patients, a more comprehensive relationship between the type of headache and changes should be found. In a 2013 study by Brett Cucchiara and his colleagues regarding the relationship between incomplete CoW and migraine headaches with aura, among the 170 studied samples, 56 people had migraine with aura, and of this average, 73% had ring changes.[25] In this study, it is especially found that the occurrence of changes in the posterior part of the CoW and in the PcomA blood supply area due to blood supply disorders can be the cause of migraine headaches in people with posterior changes.

Although co-incidental occurrence of the migraine could not be excluded, we thought that the migraine headaches might be triggered by transient decreases in CBF due to the presence of the incomplete posterior CoW. On the other hand, this possibility may also be associated with increased risk of stroke particularly in advanced ages. Therefore, being aware of these aberrations is important for an accurate evaluation and management of the ischemic areas in the setting of stroke especially when the unexpected involvements of arterial territories are present. Moreover, such variations should always be considered and evaluated before endovascular/neurosurgical interventions to prevent complications.

Conclusion

Finally, it seems that conducting studies with accurate sampling and measurement in different regions can answer the question

of whether there is a difference between different races, and at the same time, it seems that conducting a study on changes in the CoW are more useful during life.

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Author's contributions

Investigation and data collecting: Ehsan Khatavian; Writing, original draftpreparation, editing: Forouzan Absalan, Alireza Eftekhari Moghadam and Milad Jalilian; Data analyzing: Fatemeh Maghsoudi.

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Conflict of interest

All authors certify that this manuscript has neither been published in whole or in part nor is it being considered for publication elsewhere.

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