



 Research Article

ASSOCIATION BETWEEN CHRONIC PRIMARY HEADACHES AND CIRCLE OF WILLIS ANOMALIES IN MAGNETIC RESONANCE ANGIOGRAPHY

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ABSTRACT

Primary chronic headaches affect a substantial portion of the population, being predominant contributors to headache-related disability. Magnetic Resonance Angiography has emerged as a valuable diagnostic tool in examining the visibility of posterior communicating arteries in primary chronic headaches. Study at AKFA Medline University Hospital, involved 53 patients who were subjected to comprehensive neurological evaluations, assessed headache severity and frequency, and advanced imaging procedures. Six participants were excluded due to concomitant illnesses. According to 47 patients (M:F= 20:27) reported chronic headaches: n=41 (87.2%) showed no Posterior Communicating Artery visualization and n=6 (12.8%) showed Posterior Communicating Artery visualization. The mean age of participants was 42.3 ± 13.4 . Alterations in the standard structure of the Circle of Willis might influence the frequency and intensity of headache symptoms. There has been a noted correlation between irregularities in the Circle of Willis with patients experiencing headaches, and a possible genetic involvement. More research is needed to understand the mechanisms.

KEYWORDS

Primary chronic headache, Chronic migraine, Chronic tension type headache, MRA, Posterior communicating arteries, Circle of Willis.

INTRODUCTION

The brain relies on blood flow through cerebral vascular networks. The posterior communicating

artery (PCom) is important for this process. MRI angiography [1] shows an interesting blood circulation

pattern in the PCom. Around 35% of people have a hypoplastic PCom, which affects our understanding of chronic headaches [2] and their relationship with cerebral anatomy [3,4].

Moreover, the PCom supplies blood to a portion of the thalamus, a significant relay station for sensory information in the brain. It is worth noting that the PCom exhibits unique features, including an infundibulum and an uncommon occurrence where the anterior choroidal artery originates from it [2].

Numerous studies have shown that individuals with migraines often have abnormalities in their cerebral blood flow regulation, especially in the posterior circulation of the CW [5,6]. Ibrahim et al. conducted a study on Sudanese migraine sufferers and control volunteers to further investigate this connection. They used three-dimensional Magnetic Resonance Angiography (MRA) to examine the cerebral arterial system of 46 migraine sufferers and 100 control volunteers. The results indicate a significant presence of flawed CW in those with migraines, particularly in the posterior circulation where incomplete, hypoplastic, and fetal-type variations are common [7]. Chronic migraines have various mechanisms, including neuronal hyperexcitability, cortical spreading depression related to trigeminal nerve activation, and aura [8].

Central sensitization, a process where the central nervous system becomes more sensitive to stimuli, is thought to play a significant role in migraine pathophysiology [9]. The phenomenon encompasses modified handling of sensory information in the brainstem, specifically in the trigeminal nucleus caudalis [10,11]. The trigeminovascular pathway, consisting of the trigeminal nerve and its connections, is essential for migraines. Activation of this pathway results in the release of neuropeptides such as CGRP

[12], initiating a sequence involving heightened nitric oxide production and sensitization of the trigeminal nerves [13].

The research paper titled "A Comprehensive Investigation of the Anatomical Variations of the Circle of Willis in Adult Human Brains" [14] discloses that the most common anomaly found in normal brains is the narrowing of one or more blood vessels within the Circle of Willis. Around 24% of cases demonstrated either underdeveloped or slender vessels, which aligns with similar findings from previous studies (Alpers et al. - 27% [15], Kamath - 24% [16], Fetterman and Moran - 23% [17]). Primarily, these irregularities affected the posterior communicating arteries, and instances of improperly formed circular segments of the posterior cerebral artery were also observed in this examination.

In light of the findings that chronic tension-type headaches (CTTH) similarly affect the visualization of posterior communicating arteries, as observed in migraine cases, it's evident that CTTH may also be linked to cerebral vascular anomalies [18].

Linking these mechanisms to the non-visualized posterior communicating arteries, it's possible that anomalies or developmental variations in these arteries, as part of the Circle of Willis, could lead to altered cerebral blood flow. This altered CBF may contribute to primary chronic headaches susceptibility and the pathophysiological processes involved in migraine and CTTH, including trigeminal nerve activation and central sensitization. In cases where the posterior communicating arteries are not visualized or are hypoplastic, there might be an increased likelihood of disrupted CBF, potentially exacerbating the processes of trigeminal nerve sensitization and leading to more severe headache symptoms. This disruption in CBF could be a contributing factor to the heightened

neuronal excitability and increased sensitivity to sensory stimuli observed in migraineurs.

METHODS

This study was designed to investigate variations from the customary structure of the Circle of Willis that could potentially contribute to the frequency and intensity of headache symptoms. The research was carried out at the AKFA Medline University Hospital (Uzbekistan) with proper instruction and direction of neurologist. Individuals were enlisted and examined during the period of January 2022 to November 2023.

At first, our research examined a total of 1450 individuals who were diagnosed with chronic headaches lasting for more than 5 years. Out of this group, 1397 participants were eliminated since they either did not undergo Magnetic Resonance Angiography (MRA) or experienced secondary headaches. Consequently, we were left with a final sample size of 53 participants who fulfilled the requirements for being categorized as having 'primary chronic headache' according to the guidelines specified in the International Classification of Headache Disorders (ICHD) [12].

The clinical features of each participant were recorded in a thorough manner, with specific attention given to the traits and occurrence rate of their headache episodes. The research involved a group of 53 participants (23 males, 30 females) who underwent extensive neurological examinations and pain evaluations using the Numerical Rating Scale (NRS) and frequency of headache attacks. NRS revealed that patients frequently reported a pain intensity of at least 7 out of 10, with occurrences averaging no less than 15 times per month had PCom non-visualisation (74.5%) on MRA. Nonetheless, six out of the 53 individuals in the study were later disqualified due to additional medical

conditions. As a result, our sample size decreased to 47 participants (M:F=20:27).

The inclusion criteria for this study consisted of individuals between the ages of 18 and 68 ($M = 42.9 \pm 13.8$), who had been experiencing more than 15 ($M = 15.3 \pm 1.41$) headache episodes per month for a minimum of three years. Additionally, participants needed to meet the primary headache criteria outlined in the International Classification of Headache Disorders, Third Edition (ICHD-3) [12], without any accompanying secondary comorbidities. Individuals who had secondary headaches and coexisting conditions such as hypertension or carotid artery disease (11.3%) were not included in the study due to exclusion criteria.

RESULTS

In this study, a correlation was observed between the frequency ($M = 15.3 \pm 1.41$) of headaches and non-visualization of the Posterior Communicating artery (PCom) ($M = 0.872$). Among patients experiencing headaches (87.2%) at least 15 times per month, a notable prevalence of PCom non-visualization was documented. Intriguingly, this pattern appeared more prominently in patients with a familial history of chronic primary headaches, exemplified by a case involving a mother and her daughter, both presenting with primary chronic headaches and PCom non-visualization. Out of the total patient cohort, only 12.8% exhibited 'typical circles' in cerebral angiography. The remaining 87.2% demonstrated some form of hypoplasia. Predominantly, anomalies were located in the posterior communicating segment of the Circle of Willis (85.1%).

Occurrence of headaches ($M = 87.23 \pm 0.337$) and the non-visualisation of PCom ($M = 85.11 \pm 0.360$) in our sample consisted of $n=41$ patients reporting headaches

(87.2%) and n=6 patients not experiencing headaches (12.8%). Regarding PCom non-visualisation, n=40 patients (85.1%) did not have PCom visualisation, while n=7 patients (14.9%) did. The patients in our study had a high average occurrence of headaches, with a mean value of 87.2%. This implies that a significant majority of the patients reported headaches with high intensity (NRS=7/10).

The patient study predominantly consists of middle-aged individuals, with a slightly higher proportion of females (56.6% vs 43.4%). The most common symptoms reported are headaches (87.2%), with a less significant number of patients also experiencing dizziness (34.04%). The majority of patients did not have PCom visualisation. The headache characteristics are diverse but often involve pulsatile pain and referral to the eyes, indicating a potential commonality in the underlying cause or symptom expression.

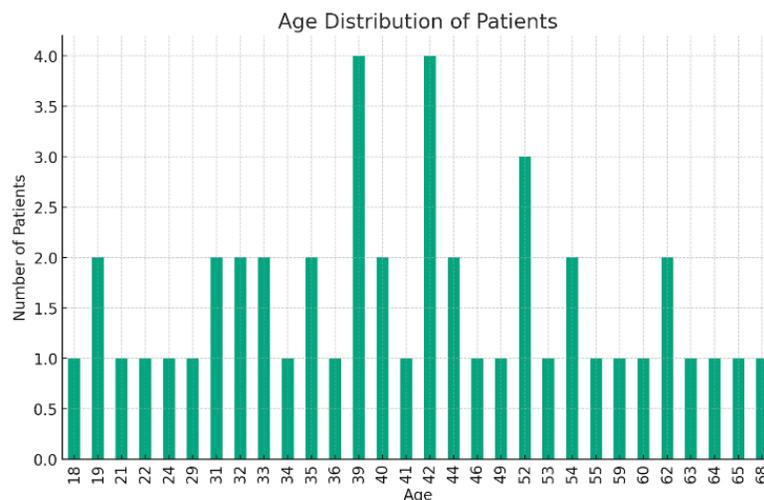


Figure 1

Figure 1: Age distribution of the patients.

The distribution appears relatively uniform across a wide age range, with a slight concentration in middle-aged adults (most prominently in the 30-40 and 50-60 age groups).

Age ($M=42.28 \pm 13.44$, $SD=0.337$, $df=92$, $CI=-2.2629$ to -1.9771 , $t\text{-statistic}=-29.473$) distribution of patients (Figure 1) clarifies the demographic spread of the sample with a noticeable concentration among middle-aged adults, particularly in the 30-40 and 50-60 age brackets. This bias towards middle age may be an indication of specific demographic trends in the

population or could suggest a higher prevalence of the condition under examination within these age groups.

In addition to analyzing the age distribution of patients, there are interesting familial patterns that indicate a potential genetic link between primary chronic headaches and PCom non-visualization. A particularly noteworthy example involves a 62-year-old female patient who not only presented with PCom non-visualization alongside chronic headaches but also reported a similar condition in her daughter

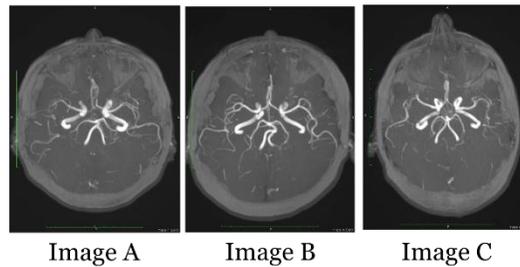


Figure 2

Figure 2: Image A: MRI of the 62-year-old female patient with chronic headaches and PCom non-visualization (mother). Image B: MRI of the patient's daughter, presenting with similar condition of chronic headaches and PCom non-visualization. Image C: An example MRI image showing a clear case of PCom non-visualization for comparison.

This occurrence within the same family suggests that there may be a hereditary factor contributing to the development of PCom non-visualization and its association with primary chronic headaches. The diversity of our sample, mostly consisting of individuals in their middle years, enhances the context of our discoveries. The slight focuses on the factors that

contribute to PCom non-visualization and chronic headaches, advocating for a more sophisticated approach that takes into consideration both genetic and demographic elements.

The headache types were classified according to thorough patient accounts, which encompassed symptoms such as throbbing pain in the fronto-temporal region $n=1$ (2.86%), throbbing pain that worsens with specific movements, pain in the temporal $n=12$ (34.29%) and occipital $n=7$ (20.00%) areas, sensations of pressure $n=3$ (8.57%) and tingling $n=2$ (5.71%), among others. Figure 3, was partitioned to signify the number of patients with and without PCom visualization for each respective headache type.

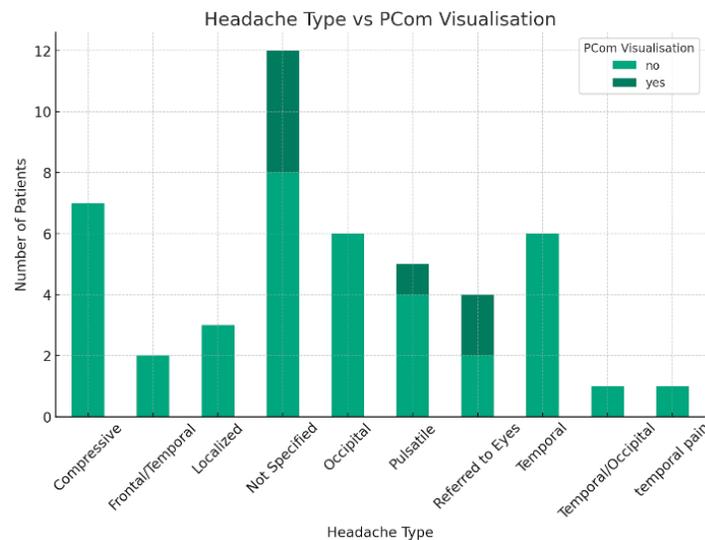


Figure 3

Figure 3: relationship between different types of headache characteristics and PCom visualisation status. Each bar represents a specific headache type, categorized broadly from the detailed descriptions provided. The bars are divided to show the count of patients with and without PCom visualisation for each headache type.

It was noted that specific headache attributes including throbbing pain at the back of the head and pain in the temples that spreads to the eyes n=6 (17.14%) were more common in patients who did not have visible posterior communicating arteries (PCom). For instance, patients who lacked PCom visibility, reported throbbing pain in the front and sides n=2

(5.71%) of their heads as well as other similar symptoms. Conversely, there were patients, who had visible PCom, experienced a throbbing headache without such specific location. This discrepancy in headache characteristics based on PCom visibility suggests a potential underlying physiological relationship.

The findings of our research highlight a potential connection between the presence of headaches and the visualization status of PCom (Figure 4), although it falls short of establishing a direct cause-and-effect relationship. The majority of patients who experienced headaches (41 out of 47, accounting for 87.2% of the sample) did not show PCom visualization.

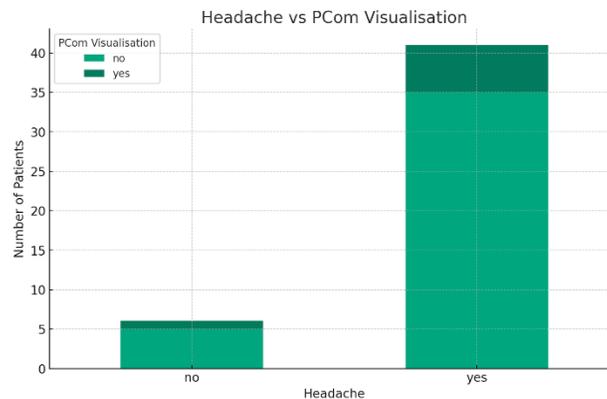


Figure 4

Figure 4: correlation between the presence of headaches and PCom visualisation. A significant majority of patients with headaches (30 out of 34) did not exhibit PCom visualisation. This trend was also observed, albeit to a lesser extent, among patients who did not report headaches (10 out of 13). This finding could suggest a limited direct correlation between headache presence and PCom visualisation. However, the data does not conclusively establish causality but rather indicates a possible trend that could be explored in further studie

CONCLUSION

Our study investigated the potential correlation between primary chronic headaches and the non-visualization of the Posterior Communicating artery (PCom). Notably, the study revealed a familial occurrence of chronic primary headaches and PCom non-visualization in a mother-daughter pair, hinting at a genetic predisposition towards these conditions. This familial pattern, alongside the age distribution concentrated in the middle-aged demographic, underscores the necessity for a nuanced approach in understanding the etiology of chronic headaches. The headache characteristics varied, but a considerable number of patients reported symptoms that were

pulsatile in nature, often involving the temporal and occipital regions, and in some cases, referred pain to the eyes. These specific symptoms were more frequently reported by those with PCom non-visualization, suggesting a possible anatomical and physiological basis for the headaches experienced. While the data points toward a correlation between chronic headaches and PCom non-visualization, a direct causative link remains to be established. Our study's findings provide a foundation for future research to delve deeper into the genetic, demographic, and anatomical factors at play.

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