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Short communication

Association of migraine headaches with anatomical variations of the Circle of Willis: Evidence from a meta-analysis



AND NEUROSURGERY

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ABSTRACT

Background: Several studies have attempted to investigate whether variations in the Circle of Willis (COW) are more common in migraine patients and whether the subsequent changes in perfusion may contribute to the pathomechanism of migraine. However, studies are not in agreement as to whether or not there is an increased prevalence of COW variations in migraineurs. *Objective:* To determine if migraine headaches are associated with variations in morphology of the COW. *Methods:* A systemic search of the major electronic databases was performed for articles studying the association of variations in the COW and migraine. Data on the prevalence of variations in patients with migraine were extracted and pooled into the meta-analysis. *Results:* A total of four articles (n = 807 patients) were deemed eligible for the meta-analysis. Migraine, regardless of subtype, was found to be associated with variations in the COW (OR = 2.27, 95%CI 1.53–3.38, p < 0.0001). An incomplete posterior circle (OR = 2.60, 95%CI 1.79–3.76, p < 0.00001) was found to be more strongly associated with migraine than an incom-

plete anterior circle (OR = 2.01, 95%CI 1.15–3.53, p = 0.01). In sub-group analysis, migraine with aura was found to be associated with both an incomplete posterior (OR = 3.55, 95%CI 2.25–5.59, p < 0.00001) and an incomplete anterior circle (OR = 2.35, 95%CI 1.20–4.62, p = 0.01). Migraine without aura was found only to be associated with an incomplete posterior circle (OR = 2.10, 95%CI 1.39–3.17, p = 0.0004).

Conclusions: Migraine is associated with anatomical variations in both the anterior and posterior portions of the COW. However, larger prospective trials are needed to determine the true prevalence of variations and their pathological significance.

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1. Introduction

Chronic migraine is a common, disabling illness whose mechanism of pathogenesis remains to be discovered. Studies have shown that migraines are associated with increased risk of both ischemic [1] and hemorrhagic stroke [2], suggesting a potential vascular role in the etiology of this condition. Furthermore, it has been suggested that variations in the anatomical structure of Circle of Willis (COW), an important source of collateral blood flow in the brain, may contribute to the pathomechanism of migraine [3,4].

Anatomical variations in the COW may alter blood flow to regions of the brain, resulting in local ischemia during periods of increased metabolic demands, thereby increasing the risk of triggering a cortical spreading depression [3]. However, a recent conflicting hypothesis from Borgdorff and Tangelder [4] suggests that anatomical variations in the structure of the COW do not, in the majority of cases, result in significantly decreased cerebral perfusion. The authors propose that such variations may cause an increased shear stress in small vessels of the COW, thereby triggering migraine through a platelet-mediated serotonin release.

A review of the literature demonstrates that a consensus on the association of migraine and anatomical variations of the COW has not been clearly established. Disagreement exists between studies and there appears to be a difference in the association of variations between migraine with aura (MwA) [3] and migraine without aura (MwoA) [7]. We sought to analyze all the available studies in order to determine if an association between migraine and COW variants exists.

2. Methods

A systematic search of PubMed, Scopus, EMBASE, Science Direct, Web of Science, and the Cochrane Library was performed to identify articles that studied variations in the Circle of Willis in patients with migraine. The search terms included but were not limited to: migraine, Circle of Willis, Willis Polygon, circulus arteriosus cerebri, anterior cerebral artery, posterior cerebral artery, variations, anomalies, and incomplete. No date limit or language restriction was set. All articles reporting the incidence of variations in the Circle of Willis in both migraine patients and controls were included. The relevant data were extracted and statistical analysis was performed using RevMan 5.2 with a random effects model to account for heterogeneity between the studies.

Results

The search identified 850 articles that were screened by title and abstract for potential eligibility and 6 articles were further assessed by full-text for eligibility in the meta-analysis. One study was excluded due to absence of controls [8], and one letter to the editor with no relevant data was also excluded [9]. A total of 4 articles were included in the meta-analysis (Table 1). Of these, 3 articles studied COW variations in both MwA and MwoA, and 1 studied COW variations only in MwoA. Results from the analysis are summarized in Fig. 1.

In analysis of migraineurs (n = 807), regardless of sub-type, an incomplete COW was found to be significantly associated with migraine as compared to controls (OR = 2.27, 95%CI 1.53–3.38, p < 0.0001). Variations in both the anterior circle and the posterior circle were found to be more common in migraineurs. A stronger association was found with an incomplete posterior circle (OR = 2.60, 95%CI 1.79–3.76, p < 0.00001) than an incomplete anterior circle (OR = 2.01, 95%CI 1.15–3.53, p = 0.01).

In the sub-analysis, a strong association was found between an incomplete COW and patients with MwA (n = 435) as compared to controls (OR = 3.33, 95%CI 2.15–5.15, p < 0.00001). MwA was associated with both an incomplete anterior circle (OR = 2.35, 95%CI 1.20–4.62, p = 0.01) and an incomplete posterior circle (OR = 3.55, 95%CI 2.25–5.59, p < 0.00001).

The sub-analysis of patients with MwoA (n = 661) found that MwoA was also associated with an incomplete COW (OR = 1.97, 95%CI 1.40–2.78, p = 0.0001), especially an incomplete posterior circle (OR = 2.10, 95%CI 1.39–3.17, p = 0.0004). However, unlike MwA, MwoA was not found to be significantly associated with an incomplete anterior circle (OR = 1.81, 95%CI 0.97–3.38, p = 0.06).

4. Discussion

Despite the disagreement in the literature, our analysis found that variations in the COW are more prevalent in migraineurs. Both incomplete anterior and incomplete posterior circles were found to be associated with migraine headaches. Specifically, the posterior variations were more strongly associated with migraine than the anterior variations, across both migraines with and without aura. This may not be surprising, as many of the brain regions suspected to be involved in the pathogenesis of migraine, might be more likely to be affected by changes in posterior circulation. An incomplete posterior circle was also more common in patients with MwA, supporting the hypothesis proposed by Cucchiara et al. [3] that it may contribute to the cortical spreading depression common in these patients, although the role that such variations may play in the pathogenesis of migraine requires further study.

These anatomical variations in the vasculature of the brain may account for the reported increased risk of both ischemic [1] and hemorrhagic [2] stroke in migraineurs. COW variations may result in alterations in cerebral hemodynamics and perfusion, or changes in the structure of the vessel itself, increasing the risk of stroke. Interestingly, an incomplete COW was more prevalent in MwA, and may explain why the reported risk of ischemic stroke is higher in MwA than in MwoA [1].

In our analysis, we included all studies available in the current literature, with the exception of studies that did not include a control group or included data that were not peerreviewed. The meta-analysis was limited by several differences amongst the included studies. In the study by Ezzatian-Ahar et al. [7], only MwoA was studied and the authors reported finding no significant differences in the prevalence of anatomical variations in patients versus controls. However, the study was limited by its retrospective case–control design, Download English Version:

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