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Migraine with aura increases the risk of stroke

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Abstract

Migraine—in particular, migraine with aura—seems to confer an increased risk of ischemic stroke and might also be linked with other cardiovascular events. Findings from a new meta-analysis support the former association; however, insufficient data exist to conclude whether this type of headache increases the risk of nonstroke cardiovascular disease.

Some individuals with migraine experience transient focal neurological symptoms, which are usually visual in nature, just before or during headache attacks. These symptoms are collectively known as aura and can also include sensory, aphasic and/or motor disturbances.[1] Considerable evidence has been published linking migraine—particularly migraine with aura—with an increase in the risk of ischemic stroke. Some studies have gone further and suggested a broader relationship between migraine and cardiovascular disease (CVD). The determination of the extent to which migraine is a marker or a risk factor for CVD is important from a public health viewpoint, as migraine affects ≈18% of women and 6–7% of men, with approximately one-third of these people experiencing migraine with aura.[2] Furthermore, the possible link between migraine and CVD has immediate relevance to clinical practice. Physicians need to know whether to counsel their patients with migraine in relation to the risk of cardiovascular events. Moreover, the level of this risk might influence decisions regarding triptan prescription, as these drugs are contraindicated in patients with CVD. Investigators have now attempted to evaluate the link between migraine and CVD and, thus, address the public health-care and clinical considerations surrounding this possible association.[3]

Schürks and colleagues conducted a structured review and meta-analysis of studies linking migraine with CVD. Of the 25 studies that met the investigators' inclusion criteria, 13 had been published after the last meta-analysis of this field. The cases included in the meta-analysis came from various sources, encompassing small hospital-based case–control studies, large medical data bases with patients identified via diagnostic codes and/or

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Competing interests

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migraine-specific medication use, and large longitudinal and cross-sectional population-based studies.

The CVD outcomes considered by Schürks *et al.* Included stroke, myocardial infarction, angina pectoris, and death due to CVD. Where possible, these outcomes were analyzed separately by aura status. Possible associations between migraine and CVD were also analyzed according to sex, as some studies have suggested that the risk of stroke in people with migraine might be higher in women than in men. Secondary analyses included meta-regression by age, use of oral contraceptives, and smoking.

In line with earlier findings, Schürks *et al.* showed that individuals with migraine had nearly a twofold increase in the risk of ischemic stroke (pooled relative risk [RR] of 1.73) over people without migraine. This risk seemed to be higher in women with migraine (pooled RR = 2.08) than in men with such headaches (pooled RR = 1.37), although the difference between these risk values was not significant. The meta-analysis also suggested that the risk of ischemic stroke in people with migraine seemed to be notably high in individuals aged <45 years (pooled RR = 2.6), with women below this age particularly at risk (pooled RR = 3.7). When patients were stratified by aura status, the risk of ischemic stroke conferred by migraine seemed to be primarily attributable to migraine with aura. In the presence of aura, the risk of ischemic stroke doubled (pooled RR = 2.2), whereas in cases of migraine without aura, this risk did not rise above baseline (pooled RR = 1.2).

In contrast to the effect on stroke, migraine did not seem to increase the risk of myocardial infarction or death due to CVD. Only one study included in the meta-analysis measured the effect of aura status on the risk of these outcomes. In this women-only study, individuals who experienced migraine with aura (but not without aura) were reported to have approximately a twofold increase in the risk of myocardial infarction, angina, or death due to CVD over people without headache.[4] Thus, an association between migraine with aura and an increase in the risk of nonstroke CVD or cardiovascular mortality is still plausible, but will remain unproven until additional evidence can be provided from population-based studies that examine outcomes by aura status.

The link between migraine and ischemic stroke seems to be solid; however, the clinical implications of this association are still unclear. Risk-reduction counseling, in relation to traditional risk factors for stroke, is probably safe in patients with migraine. Indeed, in an editorial accompanying the meta-analysis, Loder suggests that such patients should be treated aggressively for modifiable CVD risk factors.[1] To our knowledge, however, every study of stroke in migraine that has adjusted for CVD risk factors at baseline has found that such factors have not appreciably affected the migraine–stroke association. These findings indicate that the mechanism linking migraine and ischemic stroke might be independent of traditional CVD risk factors. One study even found that the risk of stroke in women with migraine who experienced aura seemed to be most pronounced in individuals with the lowest risk factor profile for a cardiovascular event.[5] A possible contributory role for traditional CVD risk factors in individual migraine patients with aura cannot be excluded. Furthermore, the ways in which risk factors have been measured in studies to date might not have been sufficiently sensitive to influence the associations between CVD and migraine.

The meta-analysis by Schürks *et al.* Suggests that the risk of ischemic stroke in people with migraine is higher in women than in men, and is particularly high in young women. These findings have, however, been largely driven by the results of early and small hospital-based case–control studies, which might be more prone to selection bias than longitudinal population-based studies. Thus, clinicians should not assume, at least not for the time being, that only young women with migraine merit counseling.

Several clinically important questions flow from the body of evidence linking migraine with ischemic stroke. First, should migraine history be included as part of stroke risk assessment algorithms?[6] Before this question can be answered, we believe that further research is needed to determine exactly how much migraine adds to the risk score in such predictive algorithms. Second, should anticoagulants be considered in some or all patients with migraine who experience aura, even in the absence of other risk factors for stroke? In our opinion, this question can only be answered following a carefully designed clinical trial of such drugs in individuals with migraine.

As stated earlier, insufficient data exist to include or exclude a link between migraine with aura and either nonstroke CVD or cardiovascular mortality. To resolve whether a link exists, well-designed studies that examine CVD outcomes in migraine by aura status are needed. Such studies would ideally include a more-detailed assessment of migraine aura than has been conducted previously. The international Classification of Headache Disorders standardized diagnostic criteria for migraine with aura require only two lifetime attacks of such headaches.[7] Nevertheless, the frequency of aura might be related to the risk of stroke or CVD.[8,9] As most studies conducted to date have failed to adequately capture information relating to the frequency of aura, the true risk of stroke in migraine could be higher than has been reported to date, although this as sertion remains to be proven.

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