Migraine with aura has been associated with a slightly elevated stroke risk. However, the association between migraine and subclinical cerebrovascular disease is limited to a few predominantly white population studies. In the Northern Manhattan Study (NOMAS) and a racially/ethnically diverse population-based urban cohort, we hypothesized that migraine is associated with white matter hyperintensity volume (WMHV) and silent brain infarction (SBI).

Methods

Study Participants

NOMAS includes 3289 participants followed prospectively to determine stroke incidence, risk factors, and prognosis. The study is approved by the Institutional Review Boards of Columbia University and the University of Miami, and participants provided written informed consent. Details of the study have been published previously. From the entire NOMAS cohort, we excluded 378 participants with history of meningitis, head trauma, or radiation to rule out secondary headache.

Baseline Evaluation

Baseline data on demographics, socioeconomic factors, medical history and medication use, vascular risk factors, family history, and other health-related information were collected. Participants recruited after 1998 were interviewed about their migraine history (some participants enrolled between 1996 and 1997 were reinterviewed), as previously described.

MRI Substudy

All participants aged >55 years remaining clinically stroke-free were screened for recruitment into the brain MRI substudy (n=1091). Protocols to determine WMHVs and SBI have been described.

Statistical Analysis

Data on migraine were available for 1380 participants, of whom 546 had MRI data available. The unadjusted associations between migraine and WMHV and SBI were examined, using linear regression for WMHV and logistic regression for SBI. Multivariable-adjusted regression models were constructed.

Conclusions

Migraine may be a risk factor for subclinical brain infarction. Prospective studies are needed in race/ethnically diverse populations.
Results

Table 1 shows the distribution of the demographic and vascular risk factors in the study population across migraine categories. Covariates included in the fully adjusted models were age, sex, race/ethnicity, insurance status, high school completion, smoking, mild-to-moderate alcohol use, diabetes mellitus, hypertension, and body mass index. Among those with MRI data, the frequency of migraine was 19% (n=546), 6% with aura, 13% without aura. The prevalence of self-reported migraine was 17%.

Years between baseline and MRI ranged from 2 to 11 (mean±SD, 5.7±1.5; median, 5.4). Fifty-six participants (10%) had SBI, of whom 15 also had migraines and only 2 had aura (which prevented further analysis of the effects of migraine with aura separately). The mean (±SD) WMHV was 0.65 (±0.84; interquartile range, 0.20%–0.71%; median, 0.34 total cranial volume). Table 2 shows the relationship between migraine overall and the 2 outcomes. Migraine overall was associated with >2-fold greater odds of SBI after adjusting for covariates. The association between migraine without aura and SBI was even stronger (model 2; odds ratio, 2.6; 95% confidence interval, 1.3–5.5). The Figure shows the percentage of participants with an SBI stratified by migraine status and age categories. Infarcts were found most commonly in the white matter (13%), cerebellum (10%), and frontal cortex (7%). There was no association between migraine status and WMHV in either unadjusted or fully adjusted models.

Discussion

We found that participants with a self-reported history of migraine were more likely to have SBI, whereas there was no association between migraine and white matter lesion load. The association between migraine and SBI was independent of cardiovascular risk factors and was significant in the subgroup with migraine without aura. Migraine seems to be an important stroke risk factor for younger individuals; however, we have shown that migraine may also be an important risk factor even for much older populations (Table 2). We did not find race/ethnic differences in the odds of SBI by migraine diagnosis. Unexpectedly, we found no associations between WMHV and migraine or its subgroups. Perhaps the group difference in WMH was not detected because of the high burden of other cardiovascular risk factors in our racially diverse older cohort.

The strengths of this study include the large stroke-free population-based race/ethnically diverse older cohort that includes a large proportion of Hispanic participants, who are typically under-represented in studies of migraine. However, because of the cross-sectional design, we are unable to infer a causal or temporal association between migraine and SBI. Migraine was identified by self-report although the details of the history of headache allowed classification as migraine without selection bias. The questionnaire was not systematically validated; however, the questions were based on the International Classification of Headache Disorders-2 criteria. Our definition of visual auras confined to visual changes, such as spots, stars, lines, and flashing lights, is a restrictive one. However, we do not think that this was a significant problem.

Table 2. The Northern Manhattan Study: Association of Migraine With WMHV and SBI

<table>
<thead>
<tr>
<th>Migraine vs No Migraine</th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
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<tbody>
<tr>
<td>WMHV: β (P value)</td>
<td>–0.12945 (0.21)</td>
<td>–0.16258 (0.09)</td>
</tr>
<tr>
<td>SBI: OR (95% CI)</td>
<td>1.65 (0.87–3.11)</td>
<td>2.07 (1.03–4.17)</td>
</tr>
</tbody>
</table>

Unadjusted model: univariate; adjusted model: controlling for age, sex, race/ethnicity, insurance status, high school completion, smoking, mild-to-moderate alcohol use, diabetes mellitus, hypertension, body mass index, and the time from baseline to MRI. CI indicates confidence interval; OR, odds ratio; SBI, silent brain infarction; and WMHV, white matter hyperintensity volume.
because the prevalence of migraine aura in our sample size was representative when historically compared, and nonvisual migraine symptoms are much less common.

Although the risk of ischemic stroke in people with migraine is considered small, the potential for more aggressive measures of risk factor reduction in individuals with migraine found to have SBI and other vascular risk factors needs consideration. Larger prospective multiethnic studies are necessary to elucidate the potential for SBI accumulation as a biomarker for subclinical cerebrovascular disease in individuals with migraine.

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Disclosures

None.

References

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