

LITERATURE REVIEW

Migraine May Be an Important Risk Factor for Cardiovascular Diseases

In a population-based study, migraine was associated with venous thromboembolism, atrial fibrillation, myocardial infarction, and stroke.

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Migraine is associated with increased risk of myocardial infarction, ischemic stroke, hemorrhagic stroke, venous thromboembolism, and atrial fibrillation or atrial flutter, according to a study published online ahead of print January 31 in *BMJ*. The results suggest that “migraine should be considered a potent and persistent risk factor for most cardiovascular diseases in both men and women,” the researchers said.

Prior studies have found that migraine is associated with ischemic stroke and ischemic heart disease, especially among women and patients with migraine with aura. Convincing epidemiologic evidence of an association between migraine and other cardiovascular events has been lacking, however, said Kasper Adelborg, MD, PhD, of the Department of Clinical Epidemiology at Aarhus University Hospital in Denmark, and colleagues.

To study cardiovascular morbidity associated with migraine, Dr. Adelborg and colleagues conducted a nationwide, population-based cohort study. The study included patients from all Danish hospitals and hospital outpatient clinics between 1995 and 2013. The researchers used Cox regression analysis to assess comorbidity-adjusted hazard ratios of cardiovascular outcomes.

Their analysis included 51,032 patients with migraine and 510,320 people from the general population matched on age, sex, and calendar year. Median age at migraine diagnosis was 35, and 71% of the participants were women.



Kasper Adelborg, MD, PhD

Incidence per 1,000 People

Patients with incident migraine had greater absolute risk of most cardiovascular outcomes, compared with the general population, across most follow-up periods. After 19 years of follow-up, the cumulative incidences per 1,000 people were greater among migraineurs, compared with the general population, for myocardial infarction (25 vs 17), ischemic stroke (45 vs 25), hemorrhagic stroke (11 vs 6), peripheral artery disease (13 vs 11), venous thromboembolism (27 vs 18), atrial fibrillation or atrial flutter (47 vs 34), and heart failure (19 vs 18).

Migraine was associated with myocardial infarction (adjusted hazard ratio [HR], 1.49), ischemic stroke (adjusted HR, 2.26), and hemorrhagic stroke (adjusted HR, 1.94), as well as venous thromboembolism (adjusted HR, 1.59) and atrial fibrillation or atrial flutter (adjusted HR, 1.25). Migraine was not meaningfully associated with peripheral artery disease or heart failure. “The associations, particularly for stroke outcomes, were stronger during the short term (0–1 years) after diagnosis than the long term (up to 19 years),” the researchers said. In addition, associations were stronger in migraine with aura than in migraine without aura, and in women than in men. In a subcohort of patients with additional data, the associations persisted after additional adjustments for BMI and smoking.

The absolute risk of cardiovascular outcomes was low, which was expected, given the young age of the study population, the researchers noted. Although the investigators adjusted for a range of potential confounders, other unknown or residual confounding (eg, by physical activity) is possible.

Multifactorial mechanisms may explain the observed increased risk of cardiovascular disease in migraine, and different mechanisms may be involved in specific cardiovascular outcomes. Migraine and cardiovascular diseases may share genetic, inflammatory, vascular, endothelial, electrical or depolarizing, or coagulable factors, the researchers said. In addition, migraineurs often use NSAIDs, which are associated with increased risk of cardiovascular events. It is also possible that immobilization due to migraine attacks may increase the risk of venous thromboembolism.

Reducing Risk

“Although the magnitude of the increased cardiovascular risk associated with migraine was fairly small at the individual level, it translates into a substantial increase in risk at the population level, because migraine is a common disease,” Dr. Adelborg and colleagues said. Migraine increasingly is recognized as an important cardiovascular risk factor to consider in clinical practice, and the recently developed QRISK3 algorithm, which predicts 10-year risk of cardiovascular disease in men and women ages 25 to 84, is the first cardiovascular risk-stratification tool to incorporate migraine.

“Ultimately, it will be important to determine whether prevention strategies in patients with migraine can reduce the burden of cardiovascular disease in patients with this common disorder,” the

researchers said. “Current migraine guidelines do not recommend use of aspirin and clopidogrel in the prophylaxis of migraine, but clinicians should consider whether patients at particularly high risk of cardiovascular diseases would benefit from anticoagulant treatment.”

The present study and prior research provide “plenty of evidence that migraine should be taken seriously as a strong cardiovascular risk marker,” and data indicate that migraine is associated with “a measurable risk of cardiovascular death,” said Tobias Kurth, MD, Professor of Public Health and Epidemiology and Director of the Institute of Public Health at the Charité-Universitätsmedizin Berlin, and colleagues, in an accompanying editorial. Strategies to reduce the risk of cardiovascular disease in patients with migraine are urgently needed and long overdue, they said.

Suggested Reading

Adelborg K, Szépligeti SK, Holland-Bill L, et al. Migraine and risk of cardiovascular diseases: Danish population based matched cohort study. *BMJ* <<https://www.ncbi.nlm.nih.gov/pubmed/29386181>> . 2018 Jan 31 [Epub ahead of print].

Kurth T, Rohmann JL, Shapiro RE. Migraine and risk of cardiovascular disease. *BMJ* <<https://www.ncbi.nlm.nih.gov/pubmed/29386182>> . 2018 Jan 31 [Epub ahead of print].

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