

Migraine and Stroke

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Over the past 40 years multiple studies and meta-analyses have firmly established an independent association between migraine and stroke, but the link is multi-faceted. The ways in which these two conditions may be connected included:

- Migraine aura symptoms (e.g. hemiplegia, hemianopia, transient monocular blindness, aphasia) mimic stroke, and stroke symptoms (e.g. headache, sensory march) mimic migraine.
- Stroke occurs during the course of a typical attack of migraine with aura. This is known as migrainous infarction, and is a rare condition.
- Transient brain ischemia or minor hemorrhage may trigger cortical spreading depression, causing a migraine aura-like event. This is known as symptomatic migraine, and is likely an under recognized occurrence.
- Migraine and stroke share a common cause, for example a right-to-left cardiac shunt (patent foramen ovale), which allows for increased serotonin into the cerebral circulation (causing migraine) and shunting of emboli from the venous to arterial circulation (causing stroke).
- Migraine is associated with silent stroke (stroke-like lesions seen on MRI without symptoms of stroke) and with white matter hyper intensities on T2 and T2 FLAIR without hypo intensities on T1 MRI images.
- Migraine is a risk factor for stroke, i.e., stroke occurs more frequently in persons who have or have had migraine, even remote from an attack.

What is the risk of stroke with migraine? The yearly risk of stroke in women with migraine is about 3 times what it is for women without migraine, but the absolute risk of migraine-related stroke is low. It is estimated that 13 strokes per 100,000 women are tied to migraine rather than to another diagnosis. This means that out of 28 million women in the U.S. with migraine, the number of stroke per year related to migraine diagnosis is about 3,600. In the U.S. the annual number of strokes from all causes is about 800,000 (split fairly evenly between the sexes). This means that migraine is the cause of about 1 percent of the total strokes affecting women.

Who with migraine is at risk? The main type of stroke associated with migraine is ischemic stroke but persons with migraine also have an increased risk of hemorrhagic stroke. The main type of migraine associated with stroke is migraine with aura, a subtype affecting about 25% of individuals with migraine. Women with aura are 3 times more likely to have stroke than women without migraine, controlling for other factors. Women with aura are also at higher risk of stroke than men with aura. Somewhat counter-intuitive is the fact that 1) young migraineurs (i.e. <45 years old) are at greater risk for migraine-related stroke than are older persons with migraine, and 2) migraine and stroke are more commonly linked in persons without traditional stroke risk factors (e.g. hypertension, diabetes mellitus hyperlipidemia). Factors that are more common in migraine-associated stroke are presence of PFO and of thrombophilia (in particular pregnancy and use of combination contraceptives). Recently, it has been reported that persons with migraine, particularly migraine with aura, are at greater risk of peri-operative stroke.

Mechanisms linking migraine and stroke

Vascular. Atherosclerosis, the most common cause of stroke in the general population is not enhanced in persons with migraine, and is likely not a prominent cause of migraine-related stroke. Stroke occurring during the migraine with aura attack may be due to enhanced vasospasm of one or more arteries or due to vasoconstriction of the microcirculation during

aura/cortical spreading depression. Cervical artery dissection is more common in persons with migraine, and the precipitating event may be minor trauma to the artery (vertebral or carotid). The most common presenting symptom of dissection is head and neck pain, and may be overlooked in persons with migraine. There is growing evidence of endothelial activation during and between migraine, which leads to increases in inflammation, coagulation, and eventually decreased vascular reactivity. There is evidence that endothelial involvement may be systemic rather than restricted to the cerebral circulation.

Genetic causes of the migraine-stroke association have also been uncovered, such as Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). This condition is clinically characterized by migraine with aura, recurrent subcortical ischemic infarcts, mood disorders, progressive dementia and diffuse white matter abnormalities in MRI. The mutations are in the *NOTCH3* gene and lead to small vessel noninflammatory, nonamyloid, and nonatherosclerotic arteriopathy with degeneration of the surrounding vascular smooth muscles cells.

Hypercoagulability. A hypercoaguable state may be caused by genetic, acquired (e.g., antiphospholipid syndrome), or lifestyle factors (e.g., cigarette smoking). High estrogen states as seen with pregnancy and use of combined contraceptive also predispose to clotting. A study of 1000 young persons with stroke showed that those with migraine with aura were over twice as likely to have at least one factor causing hypercoagulability as those with migraine without aura, or no migraine at all. For some persons, use of daily aspirin prevents aura.

Cardiological causes. About 25% of persons have a patent foramen ovale (PFO) between the right and left atria, resulting in a conduit for clots forming in the venous circulation to reach the arterial circulation. Wide variation of results from studies investigating the frequency of PFO in persons with migraine (range: 15 to 90%), and of migraine in persons with PFO (range: 16 to 64%) have clouded the potential role of PFO as a link between migraine and stroke. Clinical trials of PFO closure have not proven that this is an effective way to prevent migraine.

Migraine and Heart Disease

Most of the studies examining migraine and vascular disease have naturally focused on stroke. There is, however, also strong evidence that migraine increases the risk of heart disease, such as myocardial infarction (heart attacks) and angina. The link between migraine and heart disease has been uncovered in men and women over a range of ages. Most recently the large (23,000 women) Nurses' Health Study, which enrolled persons, ages 25 to 42 years old, about 20 years earlier, showed that migraine increases the risk of stroke, coronary events, and related death by about 50%. In several other study populations the risk of ischemic heart disease was doubled. The mechanisms are unknown but likely involve inflammation, coagulation, and dysfunction of endothelial lining of the arteries.

Recommendation to lower migraine-related ischemia:

- Maintain a healthful diet and good hydration.
- Avoid cigarette smoking.
- Minimize conventional vascular risk factors such as high blood pressure, high cholesterol and diabetes.
- Avoid use of estrogen containing contraceptives, especially in aura, or in smokers or persons with a personal or family history of blood clots (see Fact Sheet on Oral Contraceptives and Migraine).
- Consider therapies which repair/maintain a healthy endothelium, including regular exercise and use of certain preventives (i.e. lisinopril, candesartan, and statins).

- In persons with aura consider trial of low dose aspirin, after addressing safety concerns.
- Avoid chiropractic manipulation of the neck, in order to decrease the risk of cervical artery dissection.
- In persons with a history of heart disease or stroke, or with hemiplegic or basilar migraine, avoid triptans and ergotamines.

References

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