Stroke in Women
An Evolving Topic
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See Go Red for Women section.

Stroke in women is a major health issue that has long been neglected but is now attracting more and more attention.1 Many aspects of stroke are similar in men and women, including clinical presentation, neuroimaging data, main subtypes, and acute treatment. The major conventional risk factors are also the same.2 There are, however, some gender differences and specificities in stroke epidemiology, etiologies with specific causes, risk factors, and preventive treatments, as well as differences in the social impact.

One third of strokes occur among individuals <65 years of age,3 but stroke in women is an ongoing epidemic because of the sharp increase in stroke incidence with increasing age, the rapidly aging population, and the greater longevity of women. Projections indicate that the prevalence and incidence of stroke will increase by 2020 in both genders, but that these increases will be 30% higher in women than men, a figure driven by the age group >85.4 It should also be noted that the social impact of stroke is greater in women because women have poorer functional outcome after stroke with more physical and cognitive impairment, more depression, more limitations in active daily living, and lower quality of life.5 Furthermore, many older women, particularly in wealthy countries, are socially isolated: 8 million women versus 2.7 million men in the United States.6

Earlier in life, causes and risk factors for stroke differ widely according to gender and age; however, after menopause, the main causes of stroke are similar, including large artery atheroma, small vessel disease, and cardiac disease. Postmenopausal hormone use has been associated with a small but statistically significant increase in the risk of stroke in observational studies7 and randomized, controlled trials such as the Women’s Estrogen for Stroke Trial8 and the Women’s Health Initiative.9,10

The risk of stroke was increased for estrogen plus progestrone and estrogen alone, corresponding, however, to a relatively low absolute risk increase of 8 per 10 000 women per year.

In women before menopause, although rare, stroke remains a potentially devastating occurrence during pregnancy and the postpartum period. This has specifically been a problem for women with multiple pregnancies11 and eclampsia.12 During the postpartum period, risk of ischemic and hemorrhagic stroke is markedly increased,12 and further studies are needed to identify women who are at particular increased risk after pregnancy. Migraine may be one of these factors.13 Rare but characteristic types of stroke during the postpartum period are cerebral venous thrombosis and postpartum angiopathy (postpartum reversible vasocostriction syndrome), which should be kept in mind when women report headache, seizures, or/and focal deficits after pregnancy.1

The numerous studies devoted to oral contraceptives and stroke have shown that oral contraceptives containing a high content of estrogen greatly increase the risk of stroke (relative risk around 4), both ischemic and hemorrhagic, whereas oral contraceptives with low estrogen content “only” double the risk of ischemic stroke with a low absolute risk (additional 4 per 100 000 women per year).14 Another specific risk factor for stroke in young women is migraine with aura.15,16 Although the absolute risk increase is again considerably low, this risk is particularly high for women with migraine with aura who smoke and/or use oral contraceptives, an association that has been confirmed with very recent data.17 Also intriguing is the fact that the association between migraine with aura and ischemic stroke is particularly strong for women with a rather healthy vascular risk status.18 Women in this age group are also preponderant for rare causes of stroke, including Takayasu arteritis, fibromuscular dysplasia, Susac syndrome (small infarcts of the cochlear, retinal, and encebral tissue), antiphospholipid antibody syndrome, systemic lupus, Sneddon syndrome, and reversible cerebral vasocostriction syndrome. These uncommon causes of stroke require specific diagnostic procedures and should be kept in mind when younger women present with stroke.

With regard to treatment, many studies have been devoted to acute stroke care, with conflicting results about gender differences in pre- and in-hospital delay, likelihood in receiving thrombolysis, and frequency of complications such as pneumonia, urinary tract infections, and depression.5 With regard to preventive treatment, the most striking gender difference is the differential effect of low-dose aspirin in the primary prevention of ischemic stroke, indicating a significantly decreased risk in women with no clear benefit in men.19 However, because numerous secondary prevention trials of aspirin do not show a gender difference for recurrent stroke or other ischemic vascular events20 and because dosing of aspirin and follow-up time differed in primary prevention...
trials of men and women, the reason for this apparent gender difference remains unclear.

Our understanding of stroke in women has been substantially improved over the last decades. Some risk factors have consistently been linked to increased risk of stroke in women and one cannot emphasize enough that smoking is a major contributor of stroke among young women, particularly if women have migraine with aura and use oral contraceptives. Many open questions in epidemiology, clinical etiology, and outcome of stroke among women remain, however. Substantial efforts by the American Heart Association/Stroke Association with their Go Red for Women campaign have been started and will continue to improve the awareness of cardiovascular disease and stroke in women and will help induce new research efforts.

Future clinical and population-based research in stroke should include specific a priori hypotheses and detailed data collection allowing causal inference of stroke risk factors in women. Because of different risk factor distributions and health behaviors in Africa and eastern European countries as well as Asian countries, specific emphasis should be given to gender differences in stroke occurrence in these regions. Implementation of substudies in large stroke registries will allow specific collection of clinical, laboratory, and brain imaging data helping to unveil mechanisms of increased risk of stroke for women. Because stroke is a rare event among younger women, collaborative efforts are needed to identify subgroups of women at particular increased risk. Such collective efforts are also needed to evaluate genetic determinants of stroke in women as well as potential gene–environment interactions.

Disclosures

None.

References


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