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Sex and Gender in Stroke

What is Stroke?

During a stroke, the blood supply to the brain is cut off or reduced. The reduction in or lack of blood supply results in a deprivation of oxygen and nutrients to the brain, thereby killing brain cells. There are various causes of stroke. The first type is caused by a blocked artery, which is called an ischemic stroke. The second type occurs when blood vessels leak or burst, called a hemorrhagic stroke. Finally, a transient ischemic occurs when the blood flow is temporarily disrupted, sometimes referred to as a mini stroke. The complications resulting from a stroke can range from temporary to permanent disabilities, including but not limited to: issues speaking or swallowing; memory loss or difficulties thinking; emotional issues; pain; paralysis or muscle movement loss; and behavioural changes and difficulties caring for oneself. In the EU, strokes cost over 38 billion Euros annually.^{1,2}

How Big is the Problem?

In Europe stroke is the second leading cause of death; it accounts for 1/3 of CVD death in women and 1/4 of CVD death in men. Annually, stroke results in nearly 110,000 deaths people ages 75 and under in the EU, accounting for 8% of male deaths and 11% of female deaths. This rate increases with age. Women, due to their greater longevity, are at higher lifetime risk of stroke than men, and women die from stroke at a higher rate than men do.³

Why Sex and Gender Matter: Biological Differences

Women and Stroke

There are various gender and sex differences in stroke. The Framingham Heart Study demonstrated that women were older than men on average for the first stroke. In addition, women had higher rates of stroke over the age of 85 and generally across their lifetime than did men.⁵ Similarly in 2007, another study found that women aged 45 to 54 had a higher rate of stroke than men of the same age, although the reason for this finding are not fully understood. However, it has been established that contraceptives with hormones, hormone replacement therapy, experiencing migraines and pregnancy lead to an increased risk of stroke in women under the age of 65.⁶

Furthermore, women are more likely than men to inherit the risk of ischemic stroke. People who had a stroke as well as having family history of stroke were two to three times more likely to be female than male, though, like other sex and gender differences, the reason for this finding is unknown.⁷ Moreover, gender differences are prevalent not only in the presentation of stroke, but also in the outcomes, most notably in the complications stemming from stroke. Women have higher rates of disability and institutionalisation following stroke than do men.⁸

Men and Stroke

Overall, there has been a decline in the mortality and morbidity from cardiovascular disease (CVD) generally and stroke specifically in men over the recent decades. However, stroke remains a major health issue for men, accounting for 8% of male death, about 200,000 men, in the EU annually. For men under the age of 65, stroke accounts for about 28,000 deaths of those under the age of 65 each year, about 4% of premature deaths. Like CVD broadly, there are major disparities in mortality and morbidity across EU Member States with Bulgaria, Macedonia and Romania having the highest rates of death from stroke. Greece and Portugal also have stroke mortality in men than does Western Europe.²⁶

Stroke and Hormones

The interaction between the female sex hormones—notably oestrogen and progesterone—is not fully understood. There is some indication that oestrogen on one hand may protect against stroke due to its effects on cholesterol, but on the other hand, it can increase the risk of blood clots and thus stroke.¹⁰ There is interaction between hormones and stroke. The increased risk of stroke in women has been linked to contraception use, Hormone Replacement Therapy (HRT) and pregnancy.

Stroke and Contraception

Oral contraception pills consist of a combination of oestrogen and progesterone. The use of oral contraceptives nearly doubles the risk of stroke in women. Pills with lower levels of oestrogen seem to have lower risk of stroke than oral contraceptive with more elevated levels. Women with other risk factors—such as high blood pressure, smoking, diabetes or older age—who use oral contraception are at particular risk of stroke.^{11,12}

Stroke and Hormone Replacement Therapy (HRT)

Hormone replacement therapy (HRT) is a treatment that replaces hormones that the body stops producing after menopause to reduce its symptoms producing to reduce the symptoms of menopause. High levels of estrogen prior to menopause was believed to have a protective effect for women with regard to stroke. However, studies have found that HRT increases the risk of stroke in women as it raises their blood pressure and increases the risk of blood clots. HRT increases the rate of ischemic stroke and severe strokes in women.^{13,14,15}

Stroke and Pregnancy

During pregnancy, hormone levels change and blood pressure can rise. As a result, stroke risk is higher in pregnant women than in non-pregnant women, although the risk is relatively low in both cohorts. Specifically, about 3 in 10,000 pregnant women have a stroke during pregnancy compared to 2 in 10,000 who are not pregnant. The risk of stroke is elevated during the last three months of pregnancy and in the six weeks following labour.^{16,17} Moreover, there is a link between pre-eclampsia and stroke. Pre-eclampsia occurs in 5-8% of pregnancies. Pre-eclampsia develops when there is a problem with the placenta and results in high blood pressure, waste in the urine and high protein in the urine. Pre-eclampsia doubles the risk of stroke later in the woman's life. Diabetes and gestational diabetes also increases the risk of stroke as it damages blood vessels and can lead to a hardening of arteries.^{18,19}

Stroke and Migraine

Migraines occur in 15% of the population. During their reproductive years, women have migraines three times more often than do men. Migraines with aura double the risk of stroke. The risk of stroke in people with migraines is higher in women than in men. The risk is also elevated in women under the age of 45, for women who take the contraceptive pill and women who smoke.²⁰

Stroke Prevention

Women and Smoking

Smoking is more likely to cause CVD and stroke in women than in men and research suggests that mortality in smoking women is higher. The risk of CVD is especially high in women who started smoking before the age of 15.²¹ It appears that women's risk of CVD increases with the number of cigarettes smoked.²² Women who smoked have a 25% higher risk of CVD than smoking men.²³ Since on average women smoke fewer cigarettes than men, some research suggests that women who smoke might extract a greater quantity of carcinogens and other toxic substances from the same number of cigarettes.²⁴ Women who smoke and take birth control pills, increase several times their risk of heart attack, stroke, blood clots, and peripheral vascular disease compared to men.²⁵

Stroke Treatment in Women

In addition to sex and gender differences in the presentation and outcome of stroke, there are many gender differences in the clinical management of stroke. It is important to note that clinical trials have typically enrolled a fair proportion of women. However, for example, following acute strokes, women underwent less brain imaging, Doppler examination, echocardiogram, and angiography than men. Also, fewer women, particularly older women, received lipid lowering drugs and antithrombotics than men following a stroke to prevent reoccurrence. In addition, women presenting with stroke had greater delays in an emergency department than men.⁹

ABOUT THE EUGENMED PROJECT

Research addressing sex and gender (S&G) in biomedical sciences and health research is emerging as a novel and highly promising field. This interaction between S&G leads to different manifestation of diseases—such as infarction, heart failure, diabetes, rheumatic disease—in women and men.

Research in the area will lead to novel, better targeted and, therefore, to more efficient treatment strategies than the previous global approaches, creating additional opportunities for prevention and increased healthy life expectancy.

The EUGenMed Project is coordinated by Charité, Universitaetsmedizin Berlin in partnership with the European Institute of Women's Health and the University Maastricht. The Project is funded by the European Commission under the Seventh Framework Programme and began on October 1st 2013. The Project aims to create a multi-sectorial source of knowledge based on consensus of experts.

The EUGenMed Project will produce an innovative roadmap for implementation of S&G in in biomedicine and health, based on the generation of material and results from four workshops and the final project conference.

For more information, please visit the EUGenMed website: <http://eugenmed.eu>.



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