



Review

Sex differences in the presentation of stroke

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ABSTRACT

Stroke affects both men and women of all ages, although the condition is more common among the elderly. Stroke occurs at an older age among women than among men; although the incidence is lower among women than among men, as women have a longer life expectancy their lifetime risk is slightly higher. Ischemic stroke is the most common type of stroke; and reperfusion treatment is possible if the patient reaches hospital early enough. Thrombolysis and thrombectomy are time-sensitive treatments – the earlier they are initiated the better is the chance of a positive outcome. It is therefore important to identify a stroke as soon as possible. Medical personnel can readily identify typical stroke symptoms but the presentation of non-traditional stroke symptoms, such as impaired consciousness and altered mental status, is often associated with a significant delay in the identification of stroke and thus delay in or inability to provide treatment. Non-traditional stroke symptoms are reported to be more common in women, who are thereby at risk of delayed recognition of stroke and treatment delay.

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1. Introduction

Every year 15 million persons suffer a stroke worldwide [1]. Compared to men, women have stroke at an older age. Women have a longer life expectancy and the life-time risk is slightly higher in women as is the prevalence [1,2]. Lately, the stroke incidence has

started to decline in Western Europe, North America and Australia although there are indications that the risk is declining less, particularly in younger women [3–7]. However, in developing countries stroke incidence continues to rise in both men and women [1].

Acute treatment of ischemic stroke has changed dramatically during the last decades. Thrombolysis with the recombinant tissue plasminogen activator (rt-PA) alteplase has good evidence if given within 4.5 h of stroke-onset in patients without contraindications and the treatment is more effective the earlier it can be started [8,9]. Thrombolysis in ischemic stroke has in general been shown to have

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equal effects in men and women although there are studies indicating a lower risk of hemorrhagic complications in women [10]. For patients with large artery occlusion strokes mechanical thrombectomy is often needed to achieve reperfusion. As with thrombolysis, the earlier after stroke onset the treatment is started, the better. The positive effect of reperfusion treatment in suitable patients with ischemic stroke has been shown regardless of patient's sex and age [11–17]. Pooled analysis of all the published clinical stent retriever trials did not find any difference between men and women in the positive effect of thrombectomy in large arterial stroke [18]. Identifying stroke early to enable use of this time dependent treatments has made stroke presentation a focus. It has been shown that arriving to the emergency room as a stroke alarm increases the chance of thrombolysis regardless of patients' sex [19–22]. Symptoms of stroke, how they are described, and how the patient presents at the emergency room affect the delay between stroke onset and time to treatment. The earlier in the emergency chain-of-care stroke is identified, the lesser the delay becomes.

2. Methods

A search was performed in the PubMed database limited to the last 10 year period, 2006–2016. The terms “stroke”, “prodromal symptoms or presentation” and “sex or female” resulted in 721 publications. Papers about stroke, symptoms and/or presentation, gender, written in English, were included while case reports, papers concerning infants and pregnancies were excluded. The 721 manuscripts were first sorted by titles and abstracts after which 43 publications remained. Additional articles found through other sources during the search process were added to the findings.

3. Sex differences in stroke

Women are, in general, older at time of stroke onset and more women have impairment in activities of daily living (ADL), a higher co-morbidity, and are more likely to be living alone compared to men. This will affect both outcome of stroke and how the patients present in the emergency room. As a stroke patient rarely gets in contact with emergency medical services by him/her self [23], being alone at time of stroke onset usually increases the delay. Knowledge of stroke in the population also affects the delay to treatment. Several studies have shown a higher level of knowledge of stroke warning signs in women [24–27].

Women compared to men with stroke have more severe symptoms at arrival to hospital and a worse prognosis according to some studies, [19,28] but there are conflicting data [29,30]. In a meta-analysis of 36 population-based studies and three randomized clinical studies the overall hazard risk of case fatality of stroke was 1.13 for women compared with men. The hazard risk was higher for women in the RCT sub group of the meta-analysis (1.27) compared to that in the population based studies (1.12) [31]. One explanation to this may be the differences in age at stroke onset and how this difference is considered when comparing different aspects of stroke care.

The majority of strokes, 85% in an adult Caucasian population, are ischemic [32,33]. Ischemic strokes can be due to large- or small vessel disease, cardiac emboli, more rare causes, or be cryptogenic [33]. Cardioembolic stroke is in general associated with poorer outcome and this sub type is more common in women [34–38] which could be another explanation to the higher risk of poor outcome in women as compared to men.

Both intracerebral hemorrhages and subarachnoidal hemorrhages are included in hemorrhagic stroke. Around 10% of all strokes are intracerebral hemorrhages. Most, but not all, studies have reported the incidence of intracerebral hemorrhage to be

Table 1
Overview of symptoms reported to differ between men and women.

Stroke symptoms	Finding [reference]
Severity	Higher in women [19,28,37,49–51]
Non-traditional symptoms	More common in women [35,36,52–54]
Symptoms more common in women	Impaired consciousness [34,35,49–55] Altered mental status [23,35,52,53] Paralysis [49] Dysphasia [49,50,53] Generalized weakness [35,53] Dysphagia [49] Urine incontinence [49,50]
Symptoms more common in men	Dysarthria [50] Diplopia [53] Sensory loss [50,53] Ataxia [50,53] Balance/walking/dizziness [54]
Conflicting findings	Visual disturbance [50,53]

lower in women [39–42]. Subarachnoidal hemorrhage is the most uncommon type of stroke, comprising around 5% of the stroke population. Presentation is different from ischemic stroke and intracerebral hemorrhage and the most pronounced symptom is sudden onset of severe headache. Over all, the risk of subarachnoidal hemorrhage is estimated to be 1.2 times higher in women compared to men, the gender gap starting at ages above 55 years [43]. In younger persons, the risk is higher in men [43]. In Finland and Eastern Europe however, the risk has been shown to be higher in men in all ages [44]. A meta-analysis showed the risk to be somewhat higher in women using combined oral contraceptives and postmenopausal women although no increased risk for a history of use of combined oral contraceptives or hormone replacement therapy use was found [43]. Presence and location of cerebral aneurysms have been suggested as an explanation to the higher prevalence of subarachnoidal hemorrhage in older women [45,46]. In the rest of this review we will focus on ischemic stroke and intracerebral hemorrhages when discussing presentation of stroke.

Stroke is characterized as a sudden onset of focal symptoms caused by vascular disturbances in the brain [47]. Symptoms of stroke depend on which part and how large area of the brain is affected by the impaired circulation. Sudden onset of hemiparesis and speech impairment are classical symptoms of stroke that have been used in many campaigns to raise awareness of stroke [26].

In contrast to acute myocardial infarction, there is no strong evidence suggesting major differences in stroke symptoms between men and women [48]. Previous studies report conflicting data concerning sex differences and stroke symptoms with or without age adjustments [34,49]. Large artery occlusions which are more common in cardioembolic strokes have more severe symptoms such as decreased level of consciousness, aphasia, neglect and visual field disturbances [38].

The most commonly reported difference between men and women concerning stroke symptoms is a higher frequency among women of severe stroke [19,37,49–51] and decreased consciousness [34,35,37,49–51]. The presence of non-traditional stroke symptoms has also been found to be more common among women compared to men [35,36,52,53] (Table 1), similar to what have been described for myocardial infarctions [48]. Individual symptoms that have been reported to be more common among women are the following: altered mental status, paralysis, dysphasia, generalized weakness, dysarthria, diplopia, sensory loss, ataxia, visual disturbance, balance/walking problem or dizziness, dysphagia, and urine incontinence (Table 1). The inconsistent findings of sex differences in stroke symptoms could depend upon the sources used to gather description of symptoms, at what time the symptoms are gathered, and which population is studied.

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