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Gender Differences and Stroke Outcomes

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Stroke affects both men and women; however, the incidence rates and outcomes differ between the 2 genders. Age-specific stroke rates are higher in men, but women experience more frequent stroke events because of their long life expectancy, and high stroke incidence at older ages [1]. After stroke, women have poorer functional outcomes and lower quality of life than men. Various factors, including coagulation status, sex hormones, genetic backgrounds, social interactions, and lifestyle might independently or together help to explain gender differences in stroke. However, many questions remain unanswered.

In this issue of the *Neuroepidemiology*, Pu et al. [2] report their findings on the gender differences in outcomes among ischemic stroke (IS) patients with intracranial atherosclerosis (ICAS), obtained from the Chinese IntraCranial AtheroSclerosis Study (CICAS). Between October 2007 and June 2009, the authors used the results of a large prospective cohort study in 22 general hospitals and collected information from 1,335 IS patients with ICAS. They found no gender differences in outcomes among stroke patients with ICAS in China. Previous studies have suggested a marked geographical variation in the incidence, mortality, and prevalence of stroke in China [3]. The study by Pu et al. [2] is of clinical importance because CICAS covers a wide geographical area in China and is not restricted only to rural or urban areas. ICAS can have a large influence in China because its frequency is high [4] and it is associated with a high risk of recurrent stroke. Recurrent stroke is often more severe and disabling when compared to the first stroke. Previous studies have shown gender differences in outcomes among IS patients with ICAS. For example, a recent prospective study conducted at a single hospital in Turkey showed that female gender was associated with severity and poor outcomes among IS patients with ICAS [5]. However, nationwide or multicenter large studies on gender differences in outcomes among symptomatic patients with ICAS have rarely been reported. The Warfarin-Aspirin Symptomatic Intracranial Disease study, which was performed at 59 medical centers in North America and included 569 patients with symptomatic ICAS, showed that women had a significantly higher risk for IS and for the combined endpoint of stroke and vascular death [6]. These findings differ from those of the study by Pu et al. [2]. The difference may be not only due to the study design but also due to the background of the study population. ICAS rates are disproportionately higher in Asian patients than in white patients [4]. Moreover, a meta-analysis showed that female gender is associated with

ICAS in the Asian population [7]. Variations in risk factors among populations from different countries may explain differences in the ICAS incidence. The high rate in Japanese population is attributed to the high frequency of hypertension. However, in the Chinese population, the prevalence of hypertension, diabetes mellitus, and hyperlipidemia is not higher than those in white population; therefore, the excess burden of ICAS is unaccounted for in these populations [4]. It is important to determine whether this pattern of outcomes of symptomatic ICAS is present in other Asian countries. The absence of this pattern would provide further evidence of the heterogeneity of stroke outcomes among countries. Because of such heterogeneity, stroke prevention, and therapeutic strategies focusing on gender differences may be most effective if aimed at a national level rather than at a world level. Future nationwide investigations focused on gender differences are needed in many countries for comparisons with the study by Pu et al. [2].

The study by Pu et al. [2] may help to address the pathophysiology of symptomatic ICAS severity. The most common biological explanation for gender differences in stroke is the presence of sex hormones [1], and Pu et al. [2] discussed gender differences in stroke outcomes, with consideration of sex hormones. In addition, more attention should be paid to anatomical differences. In view of stroke severity in symptomatic ICAS, the major determinants of infarct volume in large-vessel acute stroke are the territory at risk, duration of obstruction relative to oxygen demand, and extent of collateral arteries. Gender differences in cerebral collateral circulation were recently examined in animal models [8]. The differences in human cerebral collateral arteries between men and women or among different races are unclear; however, anatomical differences, including those related to cerebral collaterals, might be additional factors for explaining sex or study differences, and this should be investigated in the future.

We need to develop a better understanding of gender differences in stroke incidence, presentation, prevention, and treatment effectiveness. Future research is needed to determine whether the pathophysiology of IS actually differs between men and women and to assess the approach for translating knowledge into specific strategies for the prevention and treatment of IS.

Disclosure Statement

The authors have no conflicts of interest.

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