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Editorial

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Sex differences in cerebrovascular disease and other complex disease

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Sex is a biologic feature with a great impact on biology of many disease. Not only in the incidence of diseases, sex-related differences exist in outcomes of many conditions such as autoimmune diseases, heart failure, coronary artery disease, and ischemic stroke [1-3]. Compared to men, women with heart failure generally have a reduction of 36% in the probability of all-cause mortality [3]; women also present approximately a 1/3 reduction of hazard ratio for one-year mortality after acute myocardial infarction [4] and slightly lower one-year mortality [5] after transient ischemic attack. Also, the pharmacology response is different among sexes. For instance, thrombolytic tissue plasminogen activator for ischemic stroke has a distinct sex-based efficacy [6]. The biology underlying observed sex differences has been harnessed to provide new insight into disease biology. For instance, the finding that women tend to have better traumatic brain injury outcomes than men [7] has led to the study of sex hormones to improve outcome after traumatic brain injury [8,9].

Regarding cerebrovascular disease, most studies on gender differences have focused on ischemic stroke [10], demonstrating that women have greater 28-day mortality after ischemic stroke [11,12] and poorer functional outcome at discharge [13]. The few studies that have explored sex differences specifically in ICH (intracerebral haemorrhage) are characterized by discrepancies attributable to different choices of study setting (population-based or hospital-based), study population (Asian or Western), inclusion criteria, and duration of follow-up results or focus on functional outcomes [14-18]. As a result, whether sex influences outcome after ICH remains unclear [19]. Our group has demonstrated women with ICH experience a lower risk of both expansion and early and late mortality, even after controlling for known risk factors [20].

Differences between sex mortality may also involve complications. Overall 1/3 of deaths can be attributed to post-stroke complications [21,22]. Common factors that influence outcome after cerebrovascular events include cardiological complications, venous thrombotic events (DVT), and infections [23]. Sex differences have been described for some of these outcomes, with pulmonary infections being particularly important [24].

The identification of patient populations at greatest risk for complications is the first step toward development of precision strategies to improve outcomes in the patient populations through prevention of complications. This is particularly important in diseases where therapeutics options are lacking.

Genetics is also well-suited to investigate the sex-specific architecture of common diseases and genetic-sex interaction has been widely explored [25,26]. In a recent review, 16 diseases and traits were associated with DNA polymorphisms with sex-dependent effects [25,27]. These studies highlight how genome predisposition to disease interacts with non-genetic factors that differ between males and females (such as sex hormones or anatomical differences) to initiate a response that eventually leads to the pathological trait. For instance, in cardiovascular disease, Genome Wide Association Study (GWAS) and sex-stratified approach has identified a metabolic pathway associated with coronary artery disease only in women [28] or with type II diabetes only in men [29].

Understanding the influence of biological sex in health and disease will give scientific bases to improve treatments with the rationale to eliminate the difference between the rate of complications among sexes.

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