Editorial Commentary

Does Aging Cause Women to be More Sympathetic Than Men?

Jens Tank

According to life expectancy tables, women outlive men. One possible explanation might be that women have less sympathetic drive than men and therefore are more energy efficient. What are the main gender differences in this regard? The major contributors protecting the cardiovascular system in women are sex hormones. In fact, estrogen enhances vascular dilatory mechanisms and baroreflex regulation in humans and in animals. Moreover, reduced sympathetic nervous system activity, augmented sympathetic inhibition, and higher cardiac vagal tone in women, compared with men, have all been described.1-5 Finally, the responsiveness to stressor stimuli may be diminished in women compared with men as well.1 In summary, despite the overall increase in sympathetic activity with aging, for any given age women seem to have less sympathetic drive than men.

The increase in cardiovascular risk with aging is more pronounced in women6 and women seem to be more susceptible to risk factors than men,7 even at younger age. Data from microneurography studies in a Japanese population support this hypothesis.8 Furthermore, Narkiewicz et al8 were able to show convincingly that the increases in sympathetic activity for every decade of life was higher in Caucasian women, compared with men based on resting MSNA measurements in a large number of subjects from two different populations (USA and Poland). Interestingly, the results were independent of body mass index and waist-to-hip ratio. This finding is important because, body fat distribution was shown to be related to MSNA in an earlier study.9 Moreover, the investigators also showed that menopause did not explain the differences. The authors hypothesize, based on their results, that these findings may explain the absence of cardiovascular benefit from hormone replacement therapy in postmenopausal women. Furthermore, the authors showed that the increase in blood pressure per increment of MSNA was actually greater in women over the age of 40 years, than in similarly aged men. This finding may explain the higher propensity of women at that age to develop hypertension, compared with men. Therefore, one might suggest, that aging makes women at least in some aspects more sympathetically driven than men.

Narkiewicz et al8 and others3,4 describe lower MSNA in young women compared with men up to the age of about 40 to 50 years based on mean group values. This state-of-affairs might not apply to individual cases and prospective studies of individual cases may be more relevant in order to predict the development of hypertension. One limitation of microneurography is that MSNA is measured locally at the lower leg. Several studies have shown that the distribution of sympathetic activity to different target organs plays a key role in the pathogenesis of cardiovascular diseases.10 Thus, higher sympathetic activity at the peroneal nerve may not provide information about the sympathetic drive to the heart, to the kidneys, or to adipose tissue. Autonomic imbalance is of special interest in the pathogenesis of hypertension, obesity, heart failure, and clinical autonomic disorders. For example, imbalance between sympathetic activation of the heart and the vasculature has been described in patients with orthostatic intolerance, also termed postural tachycardia syndrome (POTS).11 Similar abnormalities occur in healthy subjects who are treated with drugs inhibiting the norepinephrine transporter.12 The disproportional stimulation of the heart appears to contribute directly to the orthostatic tachycardia and might be deleterious in the long term. A similar mechanism may contribute to cardiovascular risk. Given the much greater prevalence of POTS in women than men, and the overall reduced tolerance to fluid shifts2,13 gender itself might have an influence on the central distribution of sympathetic drive. The exact mechanism by which the heart rate response is enhanced and the MSNA response is attenuated in women compared with men remains unknown. The importance of stress responses puts the physiological relevance of MSNA measured at rest under question. The resting condition does not contain information about the responsiveness of the autonomic nervous system to external or endogenous stimuli. MSNA at older ages is similar in men and women, as is mean arterial pressure. However, the increased ratio between the change in MSNA and the change in mean blood pressure in women compared with men suggests that the pressor response to MSNA is more efficient in women than in men, or less attenuated with aging. Data about gender differences in the response of MSNA to changes in blood pressure and vice versa are lacking. Therefore, studies of the sympathetic baroreflex mediated vasomotor control versus baroreflex mediated heart rate control including measurements of sympathetic activity would be important to further elucidate the impact of gender on the distribution of sympathetic traffic. The results of the microneurography studies should encourage us to perform further studies in this area. As a result, we
might be able to more effectively manage our patients of either gender.

References

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