CLINICAL IMPLICATIONS

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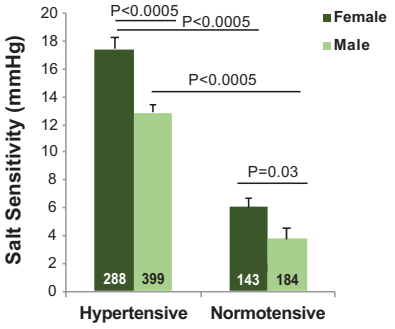
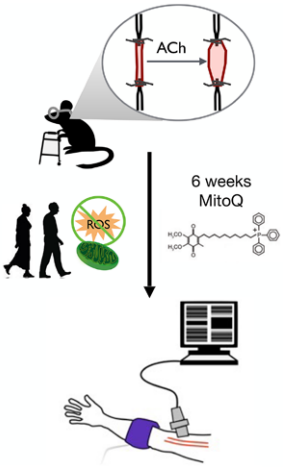
Biological Sex Modulates Aldosterone Levels (p 1083)



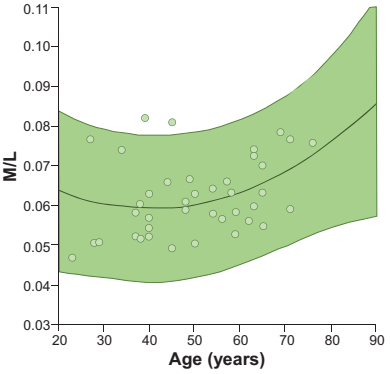
Sex differences in cardiovascular disease exist, with women being at greater risk than men for some hypertension-related cardiovascular diseases such as increased left ventricular hypertrophy. Salt sensitivity of blood pressure, the change in systolic blood pressure between high- and low-salt diet, is a risk factor for cardiovascular morbidity and mortality. In this study of 1592 normotensive and hypertensive individuals who participated in the Hypertensive Pathotype Consortium, women had increased salt sensitivity of blood pressure and increased blood pressure and aldosterone responses to angiotensin II as compared with men. In an animal model of aldosterone-dependent cardiovascular injury, female compared with male rodents had increased cardiovascular injury with increased aldosterone levels; mineralocorticoid receptor blockade was equally effective in both sexes in preventing the damage. These sex differences likely contribute to the increased salt sensitivity of blood pressure and to increased aldosterone-mediated cardiovascular disease in women compared with men. Thus, as compared with men, women are likely to receive a greater cardiovascular risk reduction from mineralocorticoid receptor blockade.

MitoQ Treatment and Vascular Function With Aging (p 1056)



Advancing age is the primary risk factor for cardiovascular disease. The development of vascular dysfunction, including vascular endothelial dysfunction and stiffening of the large elastic arteries (aorta and carotid arteries), is a major mechanism of increased cardiovascular disease risk with aging. Excessive production of reactive oxygen species by mitochondria has emerged as a key driver of vascular dysfunction with aging. Results of preclinical studies from our laboratory demonstrate that 4 weeks of oral supplementation with the mitochondria-targeted antioxidant MitoQ ameliorates age-related endothelial dysfunction and aortic stiffening in mice. In this issue of *Hypertension* we report the successful translation of these preclinical findings to humans. We show that 6 weeks of supplementation with MitoQ is safe and well tolerated and improves vascular endothelial function in healthy late middle-aged and older adults. We present data from a unique functional bioassay suggesting that the mechanism of action for the improvement in endothelial function with MitoQ supplementation involves a reduction in mitochondrial reactive oxygen species-associated suppression of endothelium-dependent dilation. We also show that MitoQ treatment reduces aortic stiffness in individuals exhibiting age-related aortic stiffening and that MitoQ supplementation decreases plasma concentrations of oxidized low-density lipoprotein, a circulating marker of oxidative stress. Collectively, these findings indicate that mitochondria-targeted therapies such as MitoQ may hold promise for reducing mitochondrial-derived oxidative stress, improving vascular function and decreasing cardiovascular disease risk with aging.

Media/Lumen Reference Values in Small Arteries (p 1193)



Small artery remodeling is an early feature of target organ damage in hypertension and retains a negative prognostic value. The gold standard for its assessment, media/lumen ratio (M/L), can be obtained by tissue biopsies. In this article, a cohort of 291 individuals with or without cardiovascular risk factors was pooled from 4 Italian centers to establish age- and sex-specific reference values and to explore M/L relationship with risk factors. M/L reference values obtained in a sufficiently large healthy population are useful in pathophysiological studies to establish the impact of classical and emerging risk factors on the microvasculature as well as the effect of treatment. Indeed, not only blood pressure, but also body mass index, cholesterol, smoking, and blood glucose were associated with increased M/L, highlighting especially the role of metabolic factors in inducing microvascular damage. From a clinical perspective, microvascular alterations are increasingly recognized as crucial mechanisms of cardiovascular and cerebrovascular disease, and they can be reversed by appropriate treatment. A better comprehension of microvascular damage accrual with age and risk factors may thus help identify novel treatment targets. Furthermore, the identification of a different impact of risk factors on M/L in the 2 sexes suggests a possible explanation for the well-known sex differences in the pathophysiology of cardiovascular disease, thus opening a novel pathway to personalized medicine.

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