Arterial Stiffness and Risk of Heart Failure Subtypes (p 267)

Higher measures of arterial stiffness are associated with increased risk of atherosclerotic cardiovascular disease and mortality. However, the contribution of higher arterial stiffness toward risk of heart failure (HF) and its subtypes, HF with preserved ejection fraction and HF with reduced ejection fraction, independent of other established risk factors, is not well studied. In this study, we evaluated the association between arterial stiffness measured as carotid-femoral pulse wave velocity and risk of HF outcomes among participants of the Health ABC study (Health, Aging, and Body Composition). We observed that higher carotid-femoral pulse wave velocity was associated with greater risk of overall HF and its subtypes, HF with preserved ejection fraction and HF with reduced ejection fraction. However, these associations were attenuated substantially and not significant after adjustment for prevalent cardiovascular disease and its risk factors. These findings suggest that the higher incidence of HF outcomes among patients with higher carotid-femoral pulse wave velocity was associated with greater risk of overall HF and its subtypes, HF with preserved ejection fraction and HF with reduced ejection fraction. However, these associations were attenuated substantially and not significant after adjustment for prevalent cardiovascular disease and its risk factors. Future studies are needed to determine if aggressive risk factor modification may lower the risk of HF among individuals with higher carotid-femoral pulse wave velocity.

Uric Acid Lowering and Endothelial Function (p 243)

Hypertension represents a staggering public health burden. Elevated serum uric acid levels (>5.0 mg/dL) have been associated with endothelial dysfunction, a precursor mechanism in the development of hypertension. Lowering uric acid in a population at a higher risk of developing hypertension could potentially improve endothelial function and thereby prevent the development of hypertension. We conducted a randomized, double-blind, placebo-controlled trial in which 47, 49, and 53 overweight/obese, nonhypertensive participants received probenecid, allopurinol, and matching placebo, respectively. Neither probenecid nor allopurinol improved endothelial-dependent vasodilation (a measure of endothelial function) by brachial artery ultrasound (endothelial-dependent vasodilation 7.4±5.1% at baseline and 8.3±5.1% at 8 weeks with probenecid; 7.6±6.0% at baseline and 6.2±4.8% at 8 weeks with allopurinol; 6.5±3.8% at baseline and 7.1±4.9% at 8 weeks with placebo; Figure), despite effective uric acid lowering. Our findings do not support the hypothesis that uric acid is causally related to endothelial dysfunction, a potential mechanism for the development of hypertension.

(Pro)Renin Receptor and Fructose-Induced Salt Sensitivity (p 339)

Fructose is a principal source of added sugar in our diet, such as in sugar-sweetened beverages. The consumption of fructose in the human diet has dramatically increased, coinciding with the epidemics of obesity and metabolic syndrome. Experimental evidence demonstrates that high fructose (HF) intake induces salt-sensitive hypertension, but the underlying mechanism largely remains elusive. The goal of the present study was to examine the role of (pro)renin receptor in HF-induced salt-sensitive hypertension. We tested whether a xanthine oxidase inhibitor allopurinol and a (pro)renin receptor decoy inhibitor PRO20 attenuated the development of salt-sensitive hypertension after HF intake. Radiotelemetry demonstrated that mean arterial pressure was 10 mm Hg higher in rats from HF-fed group receiving high salt diet that contained 8% NaCl compared with the control group rats, and this increase was completely blocked by allopurinol or PRO20 treatment (Figure). HF intake induced urinary renin activity and renal expression of Na+ transporters such as NKCC2 and NHE3, all of which were blunted by allopurinol or PRO20. We conclude that (1) (pro)renin receptor–dependent activation of intrarenal renin–angiotensin system and renal Na+ transporters underlies enhanced salt sensitivity induced by HF intake, (2) the activity of intrarenal renin–angiotensin system may predict the development of hypertension in patients with HF intake, and (3) our study calls for future clinical evaluation of allopurinol and PRO20 for their antihypertensive action in patients with HF-induced salt-sensitive hypertension.
Clinical Implications

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