Salt sensitivity is defined as a significant decrease in blood pressure when dietary sodium intake is lowered. Salt-sensitive individuals have a higher risk for cardiovascular disease. The incidence of salt sensitivity increases with age, but the underlying mechanisms are not fully understood. A major player could be a sodium channel in the plasma membrane of vascular endothelium.

The epithelial sodium channel is known to regulate blood pressure via the resorption of Na⁺ and H₂O in the kidney. This protein has recently been identified in vascular endothelium where it mediates intracellular sodium influx followed by stiffening of the endothelial cell cortex. The fact that stiff endothelial cells lack normal function such as adequate nitric oxide release strongly indicates a role of endothelial sodium channels in salt sensitivity and salt-associated cardiovascular diseases.

In this issue of Hypertension, endothelial sodium channel is identified as the mediator of endothelial salt sensitivity with aging. Quantification of endothelial sodium channel in ex vivo aortae of young and old mice revealed an age-related increase in channel expression. Endothelial stiffening, strictly depending on extracellular Na⁺, was aggravated.

Spironolactone, an aldosterone antagonist, and amiloride, a sodium channel blocker, reduced aging-dependent endothelial salt sensitivity. These classical diuretics, traditionally used to interfere with electrolyte transport in the kidneys, are suggested for the treatment of salt-sensitive hypertension and salt-associated cardiovascular disease in the elderly.

Sympathetic activation represents a pathophysiological hallmark of human obesity, contributing to the elevated cardiovascular risk profile of this clinical condition. Bariatric surgery has been previously shown to exert favorable effects on cardiometabolic function, reducing body weight and improving insulin sensitivity. Whether sympathetic neural function is also favorably affected by the intervention, particularly in the long term, is still largely unknown. The present study assessed the long-term effects (1 year) of sleeve gastrectomy on muscle sympathetic nerve traffic directly, recorded via the micro-neurographic technique, and the relationship with concomitant cardiometabolic changes.

10 severely obese patients who underwent sleeve gastrectomy, we found that bariatric surgery decreased body mass index by an average of 10.8 kg/m² and muscle sympathetic nerve activity by 38% while improving baroreflex control of the circulation. These favorable neuroadrenergic and reflex effects (which were not detected in the control group not undergoing surgery) were accompanied by a sustained reduction in circulating plasma leptin levels and by an improvement in insulin sensitivity. Taken together, these findings provide evidence that weight loss induced by sleeve gastrectomy is accompanied by sympathetic inhibition, which may participate in the improvement in cardiometabolic risk profile observed after bariatric surgery.

Fibrosis is a pathological end point of both hypertensive and nonhypertensive heart disease and a significant contributor to cardiac dysfunction and failure. The inability of the myocardium to undergo coordinated healing from injury, because of irreversible cardiomyocyte loss and a disproportionate accumulation of (myo)fibroblasts, leads to focal scarring, endocardial and interstitial fibrosis, which abets myocardial stiffening, and abnormalities in coronary reserve and cardiac contractility. Because angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers have limited antifibrotic actions compared with their blood pressure-lowering effects, these frontline therapies are unable to effectively protect from scarring-related end-stage organ failure. Hence, novel strategies that target collagen turnover and organization, while augmenting the actions of ACEi and angiotensin receptor blockers, may offer greater potential benefits. The hormone relaxin has rapid cardioprotective and antifibrotic actions, disrupting transforming growth factor-β1 signaling and collagen synthesis by myofibroblasts experimentally, regardless of pathogenesis. Despite this, the effects of relaxin on scarring have never been compared with current frontline treatments. In this issue of Hypertension, Samuel et al demonstrated that serelaxin (recombinant human relaxin 2) was more efficacious than optimal enalapril (ACEi) treatment in a murine model of cardiomyopathy. Combining serelaxin and enalapril reduced cardiac fibrosis by at least double that of enalapril alone in both preventative and therapeutic strategies. Although studies in other models are required, the clinical implications of these findings are that serelaxin may not only be a better antifibrotic than ACEi for nonhypertensive heart disease, but in combination may also enhance the antifibrotic efficacy while retaining the blood pressure-lowering effects of ACEi in hypertension-related disorders.