Renal Denervation and Heart Failure


Overactivation of the sympathetic and renin-angiotensin-aldosterone systems is a key component in the physiopathology of heart failure. It initiates as a compensatory mechanism due to impaired pump function, but in the long term it becomes largely responsible for adverse ventricular remodeling and unfavorable outcome of these hearts. For this reason, drugs limiting overactivation improve the prognosis and reduce mortality. Although these are clearly beneficial consequences, pharmacological treatments are associated with a considerable number of collateral effects and a limitation in treatment adherence. It is thus necessary to look for new therapeutic options to achieve a sustained inhibition of the deleterious effects of elevated sympathetic activity.

The renal plexus surrounding the renal arteries consists of afferent and efferent nerve fibers that not only regulate local catecholamine release in the renal tissue, but also participate in the regulation of the systemic autonomic tone, including that of the cardiac nervous system. Catheter-based renal denervation has shown its ability to reduce local and systemic sympathetic activity in acute myocardial infarction.

In this interesting work, Sharp et al. performed 75-minute ischemia followed by reperfusion and 18-week echocardiographic follow-up in an experimental pig model. After 6 weeks, a group of animals was subjected to renal denervation using a radiofrequency multielectrode catheter following blood sampling for biochemical tests. At the end of the protocol, pathological and biochemical studies were performed and a decreased sympathetic activity was observed, evidenced by reduction in renal catecholamines. Another interesting finding was lower nephrilysin levels in the renal tissue, together with higher plasma B natriuretic peptide (BNP) levels. These results suggest an additional benefit due to greater BNP availability. Despite the lower sympathetic tone, the animals showed no evidence of decreased systolic or diastolic pressure, which indicates that the advantage of renal denervation is independent of hypotensive effects. The group with denervation also evidenced lower levels of plasma angiotensin I and II and better coronary artery relaxation compared with the control group. Moreover, histological studies demonstrated a marked reduction of myocardial fibrosis in the treated pigs, together with a favorable evolution of left ventricular function, corroborated by improved longitudinal strain and lower end-systolic volume.

Different studies have shown that the increase in efferent renal sympathetic tone has an important role in the volume expansion observed in heart failure, prompting greater release of renin and the subsequent increase of angiotensin II. Heart failure also leads to abnormal afferent sympathetic signals contributing to the efferent sympathetic overactivation which produces excess cardiac and systemic catecholamines, whose concentration is directly proportional to pump failure. Therefore, catheter-based radiofrequency ablation of renal nerves seems to be an attractive technique to reduce sympathetic tone with minimal collateral effects in the context of heart failure. Effectively, a significant decrease of sympathetic tone has been clearly documented with experimental renal nerve sectioning, and beneficial effects have also been shown in different cardiovascular diseases, including pump failure. Moreover, initial clinical trials have reported promising results in hypertensive patients and case studies have shown a positive response in arrhythmias. However, the Symplicity HTN-3 study was unable to demonstrate a significant ability to reduce blood pressure in hypertensive patients treated with renal denervation. This result indicates that the pathway to follow is not so simple and a deeper analysis of different study variables is required. The work by Sharp et al. provides very promising preclinical data. Yet, it is necessary to develop controlled clinical trials, to transfer this knowledge to the clinical setting and improve the outcome of patients, considering the analysis of different variables that might lead to new failures if they were not taken into account. Finally, greater morphological and physiological knowledge of renal innervation may contribute to improve the extent of denervation, reduce injuries and understand the possibilities of reinnervation that could elicit the long-term recurrence of the neurohumoral condition.