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Cardioneuroablation and the Downside of Parasympathetic Denervation of the Heart

Chung W, Masuyama K, Challita R, Hayase J, Mori S, Cha S, et al. Ischemia-induced ventricular proarrhythmia and cardiovascular autonomic dysreflexia after cardioneuroablation. **Heart Rhythm. 2023;20:1534-45. http://dx.doi.org 10.1016/j.hrthm.2023.08.001.**

The autonomic nervous system is strongly involved in the pathophysiology of some diseases that often represent a great challenge for clinical management. Such are the cases of the vasovagal syncope, the syncope caused by carotid sinus hypersensitivity, the functional bradycardias with autonomic components, and the atrioventricular block, among others.

Although vasovagal syncope is a benign entity, it is frequent and, in many cases, produces severe episodes associated with trauma and general risks from loss of consciousness. The causal mechanism of vasovagal syncope is not yet completely understood, but it is known that hemodynamic, neurohormonal and autonomic components are involved; hyperreactivity of cardioinhibitory and vasodepressor mechanoreflexes is the most accepted mechanism. In this context, cardioneuroablation has emerged as a promising treatment for the most severe cases, especially those with a strong bradyarrhythmia component due to parasympathetic hyperactivity. Despite some technical and anatomical localization differences, as is the case of ablation for some atrial fibrillations, cardioneuroablation consists of radiofrequency ablation of some epicardial ganglionated plexuses of the intrinsic cardiac nervous system. Several clinical studies have shown improvement in these patients. However, many important aspects of this procedure have not been fully studied, such as the correct identification of the ganglionated plexus to be ablated, the optimal approach for ablation, the histological effects, and the long-term consequences of disrupting the delicate autonomic balance that controls cardiovascular function.

Wei-Hsin Chung et al. performed an interesting and well-conducted study in an experimental model of percutaneous cardioneuroablation in pigs to demonstrate the histological and functional effects in the acute and mid-term stage. Incomplete disruption of the ganglia that comprise the left superior ganglionic plexus and the right atrial ganglionated plexus was enough to block the effects of right vagal stimulation on heart rate reduction and the effects of left vagal stimulation on PR interval prolongation. These effects persisted six weeks after the procedure. Importantly, vagal stimulation in denervated animals activated compensatory sympathetic mechanisms which led to an increase in heart rate, left ventricular systolic pressure and dP/dt (change in pressure during isovolumetric contraction). An altered reflex response in ablated pigs was also observed with sympathetic stimulation. The paradoxical autonomic response after cardioablation demonstrates that the effect may extend beyond autonomic control of the conduction system nodes and, furthermore, that the persistence of this dysautonomia may have a long-term impact on overall cardiovascular health. They also observed a significant increase in the incidence of ventricular arrhythmias induced by myocardial ischaemia due to occlusion of the left anterior descending artery at six weeks in the ablation group compared to the control group. The increased susceptibility to severe arrhythmias occurred in the context of impaired repolarization and dispersion of ventricular repolarization. A combined effect of local denervation, cardiac dysreflexia and altered repolarization dynamics may be responsible for the arrhythmias.

The intrinsic cardiac nervous system consists of a complex system of highly interconnected nerve fibres and ganglia, which form a subepicardial neural network and another subendocardial (purely fibrillar) one which finely regulate regional cardiodynamic functions. The epicardial plexus is divided into subplexuses based on their anatomy and function, although much is yet to be known. Intracardiac sympathetic, parasympathetic, afferent and interconnecting neurons, in turn, have a functional relationship in an ascending hierarchical stochastic system to the higher centres. The recruitment of each neural level takes place through a delicate balance that determines the autonomic tone and conditions the normal functioning of each cardiac activity. Moreover, it extends far beyond the boundaries of the heart to regulate the entire cardiovascular tree and the kidney function as well as to condition our behaviours and emotions. The degree of dysautonomia may determine the course of many cardiovascular diseases and condition the patients' prognosis. In this regard, the presence of paradoxical reflexes and autonomic imbalances following cardioneuroablation in this experimental model should at least be a warning sign.

In addition, the increased incidence of arrhythmias caused by a very brief ischemia is a reminder of the important role of the autonomic nervous system in the regulation of heart rate and electrical stability of the myocardial syncytium. It also reminds us of the protective role of the parasympathetic system, which activates cell survival pathways, reduces inflammatory and oxidative stress, and is anti-fibrotic and pro-angiogenic, among other effects. Undoubtedly, a large group of people suffering from syncope with severe manifestations require a response, and cardioneuroablation has emerged as a very interesting proposal with promising symptomatic results. However, more studies are needed not only to delve more deeply into the long-term local and systemic effects but also to better understand the pathophysiology of syncope with significant involvement of the autonomic nervous system to find more selective solutions..