

The Two Windows for Atrial Fibrillation in Heart Failure

Burashnikov A, Di Diego JM, Sicouri S, Doss MX, Sachinidis A, Barajas-Martínez H, et al. A temporal window of vulnerability for development of atrial fibrillation with advancing heart failure. **Eur J Heart Fail** 2014;16(3):271-80. doi:10.1002/ehf.28

Heart failure (HF) frequently coexists with atrial fibrillation (AF) and each of these syndromes can promote the other. Atrial fibrillation is present in approximately 5-50% of patients with HF and its prevalence increases with poorer HF-associated functional class. The temporal evolution of HF is complex and influenced by therapeutic interventions, so that the association between the vulnerability to develop AF and electrical, structural and hemodynamic alterations at different stages of HF is difficult to establish. Such relationships are more amenable to study in a ventricular tachypacing (VTP)-induced experimental model of HF, where the severity of HF progresses with VTP duration. In this sense, Burashnikov et al. proposed an original study to determine atrial and ventricular tissue vulnerability during the progression of HF induced by VTP in dogs, a model similar to HF observed in patients.

The authors used a VTP protocol (200-240 beats per minute) to study the “early” and “late” windows of HF (2-3 and 5-6 weeks, respectively) in dogs. Ejection fraction decreased over a period of 2-3 weeks VTP, though without further reduction up to 5-6 weeks. Conversely, atrial and ventricular dimensions increased over a period of 5-6 weeks VTP. These changes were accompanied by fibrosis, which was more extended in the atria. Increased heart rate, QRS and QTc prolongation and a significant increase in the P wave amplitude were associated to these structural changes in HF animals.

Isolated atria from HF dogs showed spatial heterogeneity in electrophysiological parameters. Sodium channel-mediated electrophysiological parameters-maximum rate of rise of the transmembrane action potential (V_{max}), diastolic threshold of excitation (DTE) and velocity of conduction- were reduced as HF progressed. In the atria of HF dogs, the effective refractory period (ERP) was determined both by changes in action potential duration (APD) as by post-repolarization refractoriness (PRR).

The ERP was longer with advancing HF due to an increase in PRR. Moreover, patches of non-excitability were observed in 7/9 HF animals in the first 2-3 weeks of evolution, while 8/8 animals presented these alterations at 5-6 weeks, partly due to the

development of fibrosis.

Pulmonary veins were more depressed than atrial preparations, both in “early” and “late” windows of HF. Thus, 5/9 pulmonary vein preparations from the “early” window and all from the “late” window showed no response to stimulation, and in those which showed activity, this was reduced. In the ventricles, APD and QT were prolonged, while V_{max}, DTE, PRR and conduction velocity were significantly altered. Non-excitability areas were also found in the ventricles. In perfused right atria, prevalence of AF induced by spontaneous and programmed electrical stimulation (PES) was significantly greater in the “early” than in the “late” window. Similarly, the vulnerable period, defined as the range of diastolic intervals during which a single extra stimulus induces AF, was higher in the “early” than in the “late” window.

Non-sustained ventricular tachycardia and ventricular fibrillation (VT/VF) could be induced using PES in the “late” but not in the “early” window of isolated left ventricular muscle preparations. The increased vulnerability of the ventricles to develop VT/VF in the “late” window was associated to increased transmural dispersion of repolarization, slower conduction and exacerbated structural remodeling. Conversely, right ventricular preparations did not develop arrhythmias, probably because repolarization was homogeneously prolonged.

In conclusion, the main finding of these authors is the identification of two windows of vulnerability (“early” and “late”) for the development of AF and a relatively “late” phase of vulnerability for the development of VT/VF during the progression of HF. The major risk for the development of AF during the “early” stage of HF is characterized by atrial structural and electrical remodeling. Reduction of AF vulnerability in the late stages of HF is associated to greater depression of electrical function and structural remodeling. The vulnerability of ventricular tissue to develop VT/VF appears only in late stages of HF, together with the development of ventricular structural and electrical remodeling.

Thus, the present findings provide a better understanding of the mechanism for the temporal occurrence of these chamber-specific arrhythmias (atrial - ventricular). The concept of a window of vulnerability for the development of AF could have clinical implications regarding the prognosis and treatment of patients with HF.