Lone atrial fibrillation - 2010

Dr. Andrés R. Pérez Riera

Ever since AF was first recognized in young people (so called "lone" AF) over 4 decades ago, there has been increasing focus on determining the underlying the pathophysiology of the condition. Although lone AF is presumed to be a highly heterogeneous disease, recent studies have identified novel risk factors for the arrhythmia such as:

1. ***Inflammation***
2. ***Oxidative Stress***
3. ***Obesity***
4. ***Sleep apnoea***
5. ***Alcohol abuse and other intoxications,***
6. ***Endurance Sports excessive sports practice. Long-term structural changes in the LA and increased vagal tone related to high intensity training are the main hypothesized mechanisms. The best therapeutic approach is still unknown*** **but radiofrequency catheter ablation can become the treatment of choice for this kind of patient*.***
7. ***Latent hypertension: nondipper sustained hypertensive patients have a two-fold greater risk of developing AF than dipper ones.***
8. ***Genetics.***
9. ***Cholinergic AF***

These insights may provide novel therapeutic targets for treatment of this challenging arrhythmia in young patients.

AF initiation may be due to both abnormal focal activity and to reentry. AF frequently occurs under conditions associated with atrial dilatation (stretch) or vagal hyperactivity. Atrial stretch may contribute to focal arrhythmias by inducing afterdepolarizations and to reentrant arrhythmias by increasing the atrial surface, by

shortening the refractory period and/or slowing the conduction velocity and by increasing spatial dispersion. Moreover vagal stimulation contributes to the maintenance of AF by decreasing the atrial refractory periods and increasing the inhomogeneity of refractoriness in the atria.

The acute increase in atrial pressure due to ventricular contraction can facilitate cholinergic AF initiation by induction of different electrophysiological changes in atrial myocardium such as triggered activity, slowing of conduction velocity and/or heterogeneous change in refractoriness. Conduction slowing during acute atrial stretch can promote the genesis of cholinergic AF.

Communication between neighboring myocytes is mediated by cardiac gap junctions that are composed of connexin proteins through which electrotonic current flows[1]. Because cell-to-cell coupling plays a critical role in propagation, repolarization, and arrhythmias[2] stretch-induced uncoupling leads to spontaneous atrial premature depolarizations triggering cholinergic AF. In the absence of adrenocholinergic stimulation, stretch-related AF (SRAF) is maintained by high-frequency focal discharges that generate fibrillatory conduction and wave breaks. In the presence of adrenocholinergic stimulation, SRAF dynamics is characterized by multiple high frequency rotors that are rendered unstable by spatially distributed focal discharges[3].

A greater abundance of Kir3.x channels and higher $I_{(K,ACh)}$ density in LA than RA myocytes result in greater ACh-induced speeding-up of rotors in the LA than in the RA, which explains the ACh dose-dependent changes in overall AF frequency and wavelet formation[4].

1. Delmar M. Gap junctions as active signalling molecules for synchronous cardiac function. J Cardiovasc Electrophysiol. 2000; 11: 118–120.
2. Rudy Y. Conductive bridges in cardiac tissue: a beneficial role or an arrhythmogenic substrate? Circ Res. 2004; 94: 709–711.
3. Yamazaki M, Vaquero LM, Hou L, Campbell K, Zlochiver S, Klos M, et al. Mechanisms of stretch-induced atrial fibrillation in the presence and the absence of adrenocholinergic stimulation: interplay between rotors and focal discharges. Heart Rhythm. 2009 Jul;6:1009-1017.
4. Sarmast F, Kolli A, Zaitsev A, Parisian K, Dhamoon AS, Guha PK, et al. Cholinergic atrial fibrillation: I(K,ACh) gradients determine unequal left/right atrial frequencies and rotor dynamics. Cardiovasc Res. 2003 Oct 1; 59: 863-873.