The Pathophysiology of Atrial Fibrillation

Ulrich Schotten, MD, PhD

The progressive nature of atrial fibrillation (AF) has been demonstrated by numerous experimental as well as clinical investigations. With time paroxysmal AF becomes persistent and the success rate of cardioversion of persistent AF declines. Electrical remodeling (shortening of atrial refractoriness) develops within the first days of AF and contributes to the increase in stability of the arrhythmia. However, ‘domestication of AF’ must also depend on other mechanisms since the persistence of AF continues to increase after electrical remodeling has been completed. Atrial dilatation is a promising candidate to serve as such a ‘second factor’. Progressive dilatation of the atria is enhanced by increased atrial mechanical load due to structural heart disease, increased compliance of the fibrillating atrium due to loss of atrial contractility or slowly progressing tachycardiomyopathy of the ventricles. Chronic atrial stretch induces activation of numerous signaling pathways leading to cellular hypertrophy, fibroblast proliferation and tissue fibrosis. The resulting electro-anatomical substrate in dilated atria is characterized by increased non-uniform anisotropy and macroscopic slowing of conduction, facilitating reentry in the atria. Electrical dissociation between muscle bundles promote epicardial breakthroughs and the occurrence of narrow wavefronts which further increase the stability of AF. Prevention of electro-anatomical remodeling by blockade of pathways activated by chronic atrial stretch therefore has become the focus of research on future strategies for the management of AF.