

Atrial fibrillation – from bench to community

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Abstract

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting approximately 4% of individuals aged 60-70 years and over 10% of individuals aged over 80 years. According to estimates, the prevalence of AF is expected to increase further in the coming years, reaching more than 17 million cases in Europe by the year 2050. The presence of the arrhythmia is associated with an important increase in morbidity and mortality, especially through heart failure and ischemic vascular events, and also with a significant alteration of the quality of life of these patients.

This worrying epidemiological context justifies the continuous interest of researchers in the field of AF. Even so, after more than a century of clinical and experimental research, AF remains an enigma difficult to solve:

- despite the more effective control of risk factors, the continuous aging of the population and the involvement of multiple risk factors, many of them probably still unidentified, cause a continuous increase in the prevalence of AF;
- although multiple risk factors for AF occurrence have been identified, the clinical risk scores developed so far have little ability to predict the occurrence of the arrhythmia and to date there are no specific biomarkers that allow the diagnosis of AF in patients with silent AF or outside the arrhythmic episode;
- despite the multitude of clinical and experimental studies conducted over several decades, the antiarrhythmic treatment of AF remains extremely disappointing, and the near future does not seem to bring major changes in this regard;
- although the prophylaxis of ischemic vascular events has made considerable progress with the advent of direct oral anticoagulants, the anticoagulant treatment remains far from ideal, the risk (and fear, more or less justified) of bleeding limiting the judicious use of these agents;
- a good part of these unsolved problems is the consequence of our still insufficient understanding of the pathophysiology of AF, the multitude of intricate mechanisms involved in the occurrence and progression of this arrhythmia, and the still incomplete understanding of how the hemostatic system can be manipulated to limit the risk of bleeding.

All these mysteries and others have placed AF at the top of my research interests. I started these studies more than 14 years ago, during my PhD, and have continued them since then without interruption, trying to approach the problem of AF from multiple angles and through as wide a range of clinical and experimental approaches as possible. Without pretending to be a work of great scientific value (the data of scientific value can be found in the papers published in scientific journals over the years), the present thesis aims to summarize the most relevant results obtained so far, to present the ongoing studies, and to reveal some of the future projects.

The studies carried out so far have been focused on identifying risk factors of AF, elucidating the pathophysiological mechanisms underlying AF in various clinical scenarios, developing new experimental models of AF, testing the effects of some molecules with antiarrhythmic potential, and evaluating the effects of a direct anticoagulant used in the prevention of ischemic events in AF patients outside the coagulation cascade. Other studies, aiming to clarify the molecular mechanisms involved in the occurrence of the arrhythmia, identify new biomarkers for the prediction and diagnosis of AF, and test the antiarrhythmic effects of new molecules are currently underway and will also be briefly discussed in this document. Other projects, focused on the evaluation of the involvement of some inflammatory pathways and the potential antiarrhythmic impact of their manipulation, are currently being designed and will be implemented in the shortest time. These will also be discussed briefly, within the limits of their confidentiality. Some of the major problems that remain to be solved in the field of AF will also be discussed and some new research directions that we are considering in the near future will be proposed.

As an integral part of a multidisciplinary team, with interests in multiple areas of cardiology, my research activity naturally extended beyond the field of AF. Thus, during the 11 years since the completion of my PhD, together with the team that I coordinate, we have carried out multiple other studies, especially in the field of ischemic heart disease, studies that will also be briefly presented in this document.