Editorial

# Atrial Fibrillation: A Symptom Treated as a Disease?

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Key words: **Atrial fibrillation, electrophysiology, ablation.**

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The incidence of atrial fibrillation in the general population is around 1-2% and increases significantly with age.[1-3] An interesting question that arises for such a common cardiac arrhythmia, one that has plagued researchers in the past, is whether atrial fibrillation is a distinct nosological entity or simply a symptom.

The word "symptom", like so many in the medical lexicon, has its origins in ancient Greek. Etymologically it is a compound of the prefix "syn", meaning with or together, and a form of the verb "pipto", meaning to fall. Interestingly, the same verb forms the root of the Greek word for corpse, "ptoma", which comes into English in the word ptomaine. For the ancient Greeks the word "symptom" meant an unpleasant happenstance; perhaps the nearest equivalent in English is the verb befall. The modern medical definition, a "perceptible change in the body or its function indicating injury or disease," came later.[4]

Advances in genetics have allowed us to discover a genetic predisposition and cases of familial atrial fibrillation that are related with disturbances of potassium ion channels.[5-9] In addition, important developments in modern electrophysiology have provided us with valuable information about a relationship between this arrhythmia and the pulmonary veins.[10-14] Can genetics and electrophysiology, though, lead us to a complete aetiological analysis of atrial fibrillation? So far, this question must be answered in the negative, since atrial fibrillation can be a symptom of a plethora of cardiac and non-cardiac diseases. The most significant risk factors for the development of atrial fibrillation have been found to be hypertension and heart failure. The elimination of these conditions from the general population would lead to a reduction in the incidence of atrial fibrillation by 14% and 10-13%, respectively.[15,16]

How, though, does a patient with end-stage heart failure, who has distended atria and is in sinus rhythm, differ from a similar patient who, despite the optimum treatment he is receiving for heart failure, suffers from atrial fibrillation? This question is complex and difficult to answer. One might suppose that the patient in sinus rhythm simply lacks ectopic foci in the pulmonary veins, but it would be wiser to await the results of clinical studies before jumping to such conclusions. In any case, cardiac ischaemia, myocardial inflammation, acid-base imbalance, disturbances of electrolytes, thyroid hormones and the autonomic nervous system, the toxic action of substances such as alcohol, and a multitude of other causes that may coexist, are all also known to cause atrial fibrillation.[17-21]

We must conclude, therefore, that atrial fibrillation should be treated as a symptom and that our therapeutic approach to it must be customised to each individual patient on the basis of a thorough investigation. In practice, of course, the determination of the aetiology of this particular cardiac arrhythmia is far from easy, despite the

eruption of knowledge we have seen over the last decade with regard to its pathophysiology. Thus, the term "lone atrial fibrillation", which was applied widely in the past, is used nowadays only to describe atrial fibrillation of unknown origin in patients with no organic heart disease.

One legitimate question that arises is whether the modern guidelines, medications and invasive methods available today really allow us to evaluate and treat atrial fibrillation as a symptom rather than as a nosological entity. In spite of progress over the last decade, our inability to come up with an aetiological approach to atrial fibrillation is highlighted by the fact that the guidelines still focus on the classification and treatment of the arrhythmia based on its duration (paroxysmal, persistent, permanent) rather than on its aetiology.[22]

Confusion also reigns with regard to the data from various techniques for pulmonary vein ablation. If we accept that paroxysmal atrial fibrillation, regardless of whether it occurs in a hypertensive patient or in one with heart failure, originates from the pulmonary veins and can be successfully treated by ablation, then we are viewing this arrhythmia more as a disease in itself rather than as a symptom. This is analogous to the way we see atrial flutter; however, regardless of the clinical characteristics of a particular patient the latter arrhythmia has been shown to be due in the majority of cases to a macro-reentry circuit and can be treated successfully with cavotricuspid isthmus ablation.

The case of atrial fibrillation is considerably more complex. Even though ectopic foci in the pulmonary veins play a central role in the pathophysiology of atrial fibrillation, foci have also been found in the superior *vena cava*, the coronary sinus, the *crista terminalis*, Marshall's vein, and the interatrial septum.[23-26] For persistent atrial fibrillation, most investigators agree that a further requirement is an atrial substrate capable of sustaining multiple reentry circuits.[27,28] Modification of this substrate appears to be an important element in the strategy of ablation for persistent atrial fibrillation.

It has also been proposed that ablation of regions with fragmented electrical activity, double potentials and low amplitude electrograms could be an effective treatment for patients with paroxysmal or persistent atrial fibrillation.[29] There has been considerable debate regarding the value of additional linear ablation lesions in the mitral isthmus, the posterior wall and the roof of the left atrium, which may increase the success rate at the cost of more complications.[30,31] It is therefore clear that clinical studies are needed in order to identify those patients in whom electrical isolation of the pulmonary veins should be augmented by linear lesions in the left or right atrium.

In the immediate future the development of systems for cardiac imaging, mapping and ablation can be expected to make pulmonary vein ablation safer and more effective. Prospective, randomised studies comparing antiarrhythmic medication with ablation techniques will be an essential step towards improving and refining our knowledge. While we await the conclusions of those studies, along with developments in genetics and molecular cardiology, it would be preferable for us to continue for the time being to treat atrial fibrillation as a symptom and not as a disease.

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