

COMMENTARY

Atrial fibrillation and the 4P medicine

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Although the paradigm of the 4P medicine - Predictive, Personalized, Preemptive, and Participatory - has been suggested several years ago, its application to atrial fibrillation is still far away. Given the increasing prevalence and incidence of this pathology it is the time to promote preventive strategies, by identifying the risk factors associated to life style and by incentivizing innovative diagnostic technologies. The promotion of the correct life style and of the use of diagnostic devices based on innovative and reliable technologies, represent a first step towards the full realization of the revolution of 4P medicine in atrial fibrillation.

Key words

- atrial fibrillation
- lifestyle
- medical devices

Atrial fibrillation (AF) is the most commonly arrhythmia encountered in clinical practice. The current estimate of the prevalence of AF in the developed world is approximately 1.5-2% of the general population. Although not lethal, it is responsible for considerable morbidity and mortality, since it is associated with a five-fold risk of stroke and a three-fold incidence of congestive heart failure.

This arrhythmia is a major cardiovascular challenge in modern society because of the difficulties associated to its diagnosis and treatment and the lack of understanding of its pathophysiological mechanisms. Although a number of valuable treatments have been devised in recent years that may offer some solution to this problem, little has been made to foster a preventive and predictive approach. Indeed, the current understanding of the pathogenesis of AF is incomplete and, as a consequence, we lack specific primary preventive strategy.

The risk of the development of AF in an individual patient is often difficult to assess, but increasing age, presence of valvular heart disease and congestive heart failure are all factors that increase the risk of AF. Despite established association between AF and other cardiovascular (CV) risk factors such as diabetes, dyslipidemia and smoking, in 30% of patients with AF no apparent heart disease or other possible causes of AF are recognisable and the condition is known as lone AF [1]. In addition to long-established risk factors for AF, such as hypertension, diabetes, metabolic syndrome, and alcohol intake, newer etiologies, such as excessive physical activity, elevated vitamin D levels (> 100 ng/mL) and, possibly, high doses of N3-PUFAs are being discovered. Thus, other risk factors for AF, connected to life style, can be identify [2], in order to define simply primary preventive strategy that may decrease the incidence of AF and its complications.

Factors increasing the prevalence of atrial fibrillation include the metabolic syndrome and its various components.

Obesity is associated with AF although the pathogenesis is not clear. Obesity is strictly linked to left atrial size and left atrial enlargement, precursors of AF. In a meta-analysis of 16 studies the obese subjects have a 49% increased risk of AF compared with nonobese subjects [3]. Weight loss programs may help to decrease the risk of new onset of AF. Moreover tighter control of hemoglobine A1c level in patients with type 2 diabetes mellitus may prevent development of AF. Other studies have demonstrated that lower levels of HDL-cholesterol reduce new onset of AF. Although statin therapy is still controversial, encouraging patients to increase their HDL-cholesterol through exercise, a healthy diet and increase omega-3 polyunsaturated fatty acids intake may help reduce risk of AF. However the role of omega-3 polyunsaturated fatty acids in the setting of AF is still controversial [4]. Although some studies demonstrate lower incidence of AF recurrence with omega-3 polyunsaturated fatty acids, others have shown an increased risk. Finally, a good control of blood pressure may prove valuable in prevention of AF. Another aspect more common in industrialized countries is the alcohol consumption. Physicians should encourage patients to limit their alcohol use to no more than 1 or 2 drinks per day, even lower in high risk patient, as a preventive measure for AF [5].

It is important to underline that although mild to moderate physical activity may help with weight loss, evidence suggests that extreme levels of intense exercise seem to increase the risk of AF. The risk of AF seems to begin to increase with durations of vigorous aerobic exercise longer than 40 minutes daily, and so this may be reasonable upper limit for those at high risk for AF [6].

Finally, contrary to popular belief, drinking moderate amounts of coffee and tea may have protective effects against development of AF [7].

Moreover excessive increase of vitamin D intake (> 100 ng/mL) may be associated with an increased risk of AF [8].

This analysis reinforces the need of successful primary prevention strategies that enable patients to adopt and maintain healthy diet and behavioral patterns as a mean to reduce future CV risk measures.

Another important aspect concerns AF detection, which is of utmost importance for the treating clinician because the potential adverse consequences of AF, such as stroke and heart failure, may occur before AF is diagnosed. Indeed accurate detection of asymptomatic AF episodes is of extreme importance for patient management and is crucial for guiding anticoagulation therapy. The intermittent and often asymptomatic nature of AF makes its diagnosis very difficult. Indeed, given the intermittent nature of both arrhythmic events and current monitoring methods, the ability of monitoring strategy to diagnose AF is highly dependent on whether or not the moment selected for monitoring coincides with the occurrence of AF episodes. The National Heart, Lung, and Blood Institute convened an expert panel on April 28 to 29, 2008, to identify gaps and recommend research strategies to prevent atrial fibrillation (AF) [9]. The panel reviewed the existing literature about AF and proposed several recommendations to foster AF prevention by indicating specific research strategies. One recommendation regarded the improvement of the detection of AF by evaluating the ability of existing and emerging methods and technologies to detect AF. The 2012 focused update of the ESC Guidelines for the management of atrial fibrillation do not mention the emerging technology to continuously monitor patients at risk for AF. As far as the AF screening is concerned, the guidelines "recommend that, in patients aged 65 years or over, opportunistic screening for AF by pulse palpation, followed by recording of an ECG to verify diagnosis, should be considered for the early detection of AF" [10]. According to the latest

survey of the European Heart Rhythm Association Research Network [11], the current practice of AF detection and monitoring is basically committed to implantable devices, either implanted pacemakers/defibrillators or specially tuned subcutaneous leadless rhythm monitoring devices.

Technically speaking, there are a number of solutions which could be more precise and reliable than pulse palpation and less invasive than implantable device, although almost equally accurate. The detection of AF is now made by some portable and self measurement systems for blood pressure or by portable ECG monitor, some performing ECG from the fingers. Also, the web offers a number of apps for smartphones (not yet certified/authorized) by which it is possible to estimate the pulse frequency by placing the index finger over the camera. Of course, care must be paid to the sensitivity of these methods in detecting AF, but both CE mark and FDA approval guarantee about this issue. Emerging technologies could thus help in implementing continuous monitoring by using proper clinical sensors (such as small dry/textile electrodes placed on the skin) and proper diagnosis by using sensible algorithm on dedicated integrated circuit. It is hopeful that such emerging technology would be incentivised, in order to propose AF noninvasive diagnostic methods more reliable and effective than pulse palpation.

Thus, AF prevention strategies should be based on the promotion of a correct life style and the diffusion of proper diagnostic methods. This approach requires the *participation* of individuals in a proactive way, shifting the AF management from a late curative paradigm to an early *preemptive* one, based on the *prediction* of AF consequences and to the *personalization* of the AF therapy (4P medicine).

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