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Editorial

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Risk factors promoting atrial fibrillation

Factores de riesgo que inducen la fibrilación auricular

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Atrial fibrillation (AF) is a chronic, progressive, degenerative, and multifactorial disease characterized by exacerbations and remissions of this arrhythmia.[1,2] It is the most common supra-ventricular tachycardia, affecting approximately 1.0% of the world's population;[2] in México, it is estimated that more than one and a half million people are affected.[3] Because this arrhythmia is associated with several components of the metabolic syndrome, nowadays considered a worldwide pandemic, such prevalence will increase within the following decades, resulting in a higher mortality rate.[1-4] At first, AF is mostly an isolated electrical disorder starting from rapid discharges mainly originating from the pulmonary veins; sustained rapid firing that provokes disorganization into fibrillatory waves that maintain AF, causing structural and functional atrial changes that promote fibrosis and atrial cardiomyopathy, which is the reason why the concept of AF generates more AF is more valid than ever.[1]

Non-modifiable and modifiable risk factors are responsible for producing and maintaining impaired circuitry within the cardiac atrium that contributes to the development of atrial fibrillation.[5] Gender and age are among the non-modifiable risk factors; unfortunately, elderly males will present a higher prevalence of atrial fibrillation than younger men or women, increasing by 8.48% in those over 80 years old.[3,5,6] Also, race and genetic mutations translated into ion channel impairment are associated with a higher prevalence of this arrhythmia. Caucasians have a higher risk for AF than the African ethnic group.[5] For example, a third of patients over 55 years of age with European ancestry will develop an AF episode.[4]

On the other hand, modifiable risk factors include ischemic disease, hypertension, heart failure, obstructive sleep apnea, dyslipidemia, type 2 diabetes mellitus, and obesity, all of which, through different pathophysiological mechanisms, lead to the generation of AF.[6] Inflammation, specifically, chronic inflammation is the common pathway within these risk factors that leads to atrial fibrillation due to the dysregulation of several pro-inflammatory proteins.[7] The high expression of these inflammatory markers, like cytokines or growth factors within cardiac tissue, leads to oxidative stress, myocardial apoptosis, fibrosis, and alteration of intracellular calcium concentration, resulting in the development of arrhythmogenic substrates in the atrium.[8]

Several studies have demonstrated that cardiomyocytes have an intrinsic inflammatory mechanism through proteins that are part of the NACHT-LRR- and pyrin domain-containing 3-inflammasome. Atrial cardiomyocytes synthesize many pro-inflammatory proteins and their respective receptors, stimulating different signaling mechanisms related to the surge of atrial fibrillation, such as the JAKs, STATs, MAPKs, and NF-kB pathways, which in turn upregulate the expression of genes encoding for inflammatory factors.[9] More importantly, it is well documented that modifiable risk factors trigger the pro-inflammatory signaling cascades mentioned above. For instance, within heart failure, connective tissue disruption, increment of left atrial size, ischemia, the reduction of electrical conduction, and the development of

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fibrosis due to the up-regulation of the renin-angiotensin system will promote the surge of atrial fibrillation.[10]

Interestingly, the correlation between dyslipidemia and AF is controversial because high levels of low-density lipoprotein and total cholesterol have not been singled out as a primary cause for AF development, but low concentrations of high-density lipoprotein, as well as high concentrations of triglycerides, are independently associated with the incidence of atrial fibrillation; the latter mainly because of the lack of high-density lipoprotein anti-inflammatory properties and the detrimental effects of hypertriglyceridemia within the cardiovascular system.[11-13] Also, advanced glycation end products present in diabetic subjects promote AF. According to Nayak et al.,[5] the circulating concentration of advanced glycation end products and their receptors link directly with the progression of paroxysmal to permanent atrial fibrillation through the pro-inflammatory pathway triggered by reactive oxygen species.

The relationship between AF and obesity is very complex because it modifies hemodynamic regulation, neurohumoral, metabolic inflammatory, and autonomic system functions and is considered a proinflammatory systemic state related to adipokine and cytokines dysregulation.[7,14] Pericardial fat and epicardial adipose tissue also induce an inflammatory immune response that leads to fat infiltration in the atrial myocardium, increasing fibrosis and favoring the onset and sustainment of AF.[14]

Nowadays, AF treatment aims to convert and maintain sinus rhythm (SR) at the earliest through the diagnosis. Because the control of all these risk factors leading to a chronic inflammatory process is not enough, an integral approach that includes the modification of such risk factors, the administration of anti-arrhythmic drugs, and a catheter ablation that will achieve the isolation of the pulmonary veins is necessary to prevent a high arrhythmia burn, in order to have an impact in the long-term follow-up, by retarding fibrosis and maintaining the patient in sinus rhythm as long as possible.[1,4]

In conclusion, atrial fibrillation is the most common arrhythmia affecting millions of people worldwide. Chronic inflammation is one of the main factors involved in its pathogenesis, producing dysregulation of different proteins. This alteration generates arrhythmogenic substrates within the myocardial atrium that promote atrial fibrillation.

To prevent the surge of this arrhythmia, in addition to the clinician's advice on modifying lifestyle and nutrition habits, many scientists have focused on identifying biomarkers that could accurately predict the appearance or recurrence of atrial fibrillation before and after catheter ablation of pulmonary veins.

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