EDITORIAL

Seven Reflections on a First Episode of Lone Atrial Fibrillation

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The term atrial fibrillation encompasses several types of tachyarrhythmias whose common denominator is a rapid generation of atrial impulses that, with greater or lesser regularity, are conducted to the rest of the atrial myocardium, resulting in irregular ventricular responses due to variable degrees of penetration of the atrioventricular (AV) node. Advances in the treatment of atrial fibrillation using catheter ablation techniques have been achieved despite the lack of a clear idea of the different etiological and pathogenic types of this arrhythmia. Until recently, in epidemiological and even pharmacological studies, patients with atrial flutter and fibrillation were grouped under a single umbrella. Fortunately, we now know that it is necessary to separate the two. Flutter is the most common type of tachycardia secondary to atrial macroreentry, and the variety most frequently detected can be cured by means of ablation of the lower right atrial isthmus, also referred to as the cavotricuspid isthmus. Certain types of atrial fibrillation can be cured or improved by means of catheter ablation techniques; however, to continue progressing, we will have to contemplate the horizon of atrial fibrillation in the absence of past prejudices. In this respect, it would be interesting to reflect on certain considerations inspired by the article published in this issue of Revista Española De Cardiología by Planas et al,[1] aimed at determining the frequency and the factors involved in recurrences following a first episode of primary atrial fibrillation.

First Reflection: What Do We Mean When We Refer to Lone or Primary Atrial Fibrillation?

Planas et al[1] define primary atrial fibrillation as that produced in the absence of structural or functional heart disease or any other known etiological factor. The term primary atrial fibrillation has been used in the medical literature as an equivalent to the more widespread lone atrial fibrillation.[2] Lone atrial fibrillation should be understood to be that occurring in individuals under 60 years of age which present no clinical or echocardiographic evidence of cardiopulmonary disease, including hypertension.[3] However, the work of Planas et al[1] includes patients ranging in age between 23 and 82 years (mean: 52±14 years). As indicated by guidelines recently issued jointly by the European Society of Cardiology, the American Heart Association and the American College of Cardiology, "Although atrial fibrillation may occur in the elderly without underlying heart disease, the changes in cardiac structure and function that accompany aging, such as increased myocardial stiffness, may be associated with atrial fibrillation."[3] We would venture to say that future definitions will be even more restrictive if our objective is to conclusively establish the recurrence rate, thromboembolic risks, associated electrical disturbances or therapeutic options. Actually, we should limit the scope of lone atrial fibrillation not only to that developed by individuals under 60 years of age with no demonstrable cardiopulmonary disease, as has typically been recommended,[4] but to those with no family history of atrial fibrillation or of compulsive participation in sports, and with normal diastolic, and systolic function.

In 1997, Brugada el al[5] identified, in three Spanish families, the first locus for familial atrial fibrillation on chromosome 10q22-24.[5] The molecular bases of familial atrial fibrillation are a matter of controversy, although genes encoding subunits of the potassium channels with increased function have been identified in patients with familiar arrhythmia, the development of which would be facilitated by the reduction of the duration of the action potential of the atrial cardiomyocytes and the duration of their refractory period. A molecular or genetic basis could contribute by up to 15% to the "cul-de-sac" of lone atrial fibrillation, although these estimations require more extensive study.[6] Moreover, lone atrial fibrillation, and even familial fibrillation, can occur in young patients with a short QT interval and risk of sudden death due to ventricular fibrillation.[7] In some of these cases, mutations have been identified in the potassium channels that increase the Ikr current and produce a heterogeneous shortening of the duration of the action potentials and atrial and ventricular refractory periods.[8]

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Another group of patients that should be segregated from the hodgepodge of lone atrial fibrillation is that constituted by individuals, especially men, who have been and are very active in sports, a circumstance that we now know is a clear risk factor for the development of atrial fibrillation in relatively young subjects with no structural heart disease.[9,10]

Finally, in the case of lone atrial fibrillation, diastolic dysfunction should be ruled out to the greatest possible extent. Haissaguerre and his team, in Bordeaux, were the first to point out that some patients with lone atrial fibrillation could have left ventricular diastolic dysfunction.[11] The contribution of this factor may be greater in older populations, an important reason for limiting the age for inclusion among lone atrial fibrillation patients to individuals under 60 years of age.

Second Reflection: Embolic Risk and Lone Atrial Fibrillation

None of the patients in the study of Planas et al[1] presented ischemic cerebrovascular complications of any type during follow-up. The study does not indicate whether or not the patients received some form of antithrombotic prophylaxis. However, in reality, although more than half of the patients included were over 50 years old, they probably presented low risk of embolism. As pointed out in the guidelines established by experts from both sides of the Atlantic, the need for anticoagulation depends on the thromboembolic risk profile. Anticoagulation with oral coumarin derivatives should be recommended in all patients presenting high risk of systemic embolism (previous embolism or rheumatic mitral valve disease) or having more than one factor indicative of moderate risk for thromboembolic phenomena, such as age of 75 years or more, hypertension, heart failure, left ventricular systolic dysfunction with an ejection fraction less than or equal to 35%, or diabetes.[3] Thus, in a strict sense, oral anticoagulation therapy was not indicated in the patients in this study.

Third Reflection: Relation Between the Symptoms During the Acute Episode and During Recurrences

Planas et al[1] observed a significantly higher incidence of palpitations during the acute episode among the patients who experienced recurrences, and the presence of syncope or presyncope among those who did not. As the authors correctly indicate, given the methodology employed, they could not rule out the possibility that some of the patients who did not notice palpitations during the acute episode could have had asymptomatic recurrences and been erroneously included among those who did not develop recurrences.

With regard to the relationship between syncope in the initial episode of atrial fibrillation and the absence of recurrences, the authors consider it to be due to a nonrecurrent episodic vagal phenomenology. The observation that syncope, followed by documented, apparently lone, atrial fibrillation in young patients may often be a benign association does not mean that there is no need to scrutinize the ventricular repolarization in search of a short QT interval, or look into a possible family history of sudden death.

Fourth Reflection: Hypertension and Atrial Fibrillation

The association between hypertension and the risk of atrial fibrillation is well known. In most of the studies dealing with nonrheumatic atrial fibrillation, 50% of the patients are hypertensive. However, to label atrial fibrillation as lone or primary, it is necessary to rule out the presence of hypertension or blood pressure controlled with antihypertensive therapy.[3,4] In the present study of Planas et al,[1] the systolic arterial pressure of their patients with and without recurrences was 132.8 (14.6) mm Hg and 132.5 (20.5) mm Hg, respectively, and the diastolic pressure was 79.5 (9.8), and 79.5 (12.3) mm Hg; thus, in reality, almost all these patients are hypertensive or prehypertensive given that, at the present time, blood pressures over or equal to 120/80 mm Hg are considered as a prehypertensive state and those over or equal to 140/90 mm Hg as stage 1 hypertension.[12] One of the problems with this issue lies in the inclusion of patients over 60 years of age since, according to the above definition, the prevalence of hypertension or a prehypertensive state would be 88% for the segment of the population aged 60 years and older.[13]

This constitutes an additional problem when it comes to analyzing the data from this study since, in series of patients with lone atrial fibrillation to be selected in the future, it will be necessary to exclude by hipertensive individuals meticulously.

Fifth Reflection: Alcohol Consumption and Risk of Recurrence

The fact that Planas et al[1] have observed a higher risk of atrial fibrillation recurrences after the initial episode of this arrhythmia in patients who consumed alcohol could appear to be reasonable. The problem arises when we take into account that this study excluded patients who drank moderate or substancial amounts of alcohol (over 40g of alcohol per day in men and over 20g per day in women) is taken into account. The authors considered regular drinkers to be those individuals who consumed wine, beer or spirits daily, in lesser amounts than those indicated above, and defined the remainder of their population as occasional drinkers or nondrinkers. The fact that regular, moderate alcohol consumption has been found in this study to be a risk, factor for recurrence of atrial fibrillation following an initial episode appears

to contrast with recent data from the Framingham Heart Study, according to which chronic intake of less than 36 g of alcohol daily does not increase the risk of developing atrial fibrillation.[14] The small sample size in the report by Planas et al[1] and the dispersion in the vital statistics in terms of age, arterial blood pressure, habits, etc., makes it difficult to adjust for possible confounding effects of some variables with respect to others. On the other hand, the two studies transmit different messages. In the Framingham study, moderate alcohol consumption was not a risk factor for the development of atrial fibrillation, whereas, in the study we are discussing here, moderate alcohol intake appeared to favor the recurrence of this arrhythmia after a first episode. Many cardiologists, among whom I include myself, recommend patients not to drink alcohol for one year after a first episode of atrial fibrillation and, although the bases are not very solid, Planas et al[1] provide an argument for continuing to act along the same lines, although we must admit that it would be of interest to have sounder evidence.

Sixth Reflection: Ejection Fraction and Risk of Recurrence

An original finding and, to some extent, unexpected finding in the study of Planas et al[1] was that recurrences occur more frequently and earlier in patients whose ejection fraction was higher in the echocardiographic study performed after the restoration of sinus rhythm. With a sample of this size, it is difficult to rule out a type II error; that is, that the variables that exhibit a statistically significant relationship, in reality, are of no true biological value. We refer specifically to the difficulty in ruling out the possibility that the higher ejection fraction may actually reflect trends related to higher arterial blood pressure, greater alcohol consumption, and/or higher incidence of obesity, factors that could truly be related to the probability of recurrence, more so than the ejection fraction in itself.

Seventh Reflection: the Rate of Recurrence After an Initial Episode of Atrial Fibrillation is 40% at Three Years

The rate of recurrence at three years could appear to be elevated, although it is similar to or somewhat lower than that found in series of patients who have had a first episode of atrial fibrillation when there is no restriction for their inclusion in relation to the presence of associated comorbidities.[15] Once again, it would be interesting to insolate true lone atrial fibrillation from that which appears to be lone, but is no, and, here, the comments concerning the first of these seven reflections should again be taken into account.

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