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Role of the P-wave high frequency energy and duration as noninvasive cardiovascular predictors of paroxysmal atrial fibrillation

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ABSTRACT

A normal cardiac activation starts in the sinoatrial node and then spreads throughout the atrial myocardium, thus defining the P-wave of the electrocardiogram. However, when the onset of paroxysmal atrial fibrillation (PAF) approximates, a highly disturbed electrical activity occurs within the atria, thus provoking fragmented and eventually longer P-waves. Although this altered atrial conduction has been successfully quantified just before PAF onset from the signal-averaged P-wave spectral analysis, its evolution during the hours preceding the arrhythmia has not been assessed yet. This work focuses on quantifying the P-wave spectral content variability over the 2 h preceding PAF onset with the aim of anticipating as much as possible the arrhythmic episode envision. For that purpose, the time course of several metrics estimating absolute energy and ratios of high- to low-frequency power in different bands between 20 and 200 Hz has been computed from the P-wave autoregressive spectral estimation. All the analyzed metrics showed an increasing variability trend as PAF onset approximated, providing the P-wave high-frequency energy (between 80 and 150 Hz) a diagnostic accuracy around 80% to discern between healthy subjects, patients far from PAF and patients less than 1 h close to a PAF episode. This discriminant power was similar to that provided by the most classical time-domain approach, i.e., the P-wave duration. Furthermore, the linear combination of both metrics improved the diagnostic accuracy up to 88.07%, thus constituting a reliable noninvasive harbinger of PAF onset with a reasonable anticipation. The information provided by this methodology could be very useful in clinical practice either to optimize the antiarrhythmic treatment in patients at high-risk of PAF onset and to limit drug administration in low risk patients.

1. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical practice, increasing its incidence with age [1]. It may appear as paroxysmal AF (PAF), featuring arrhythmic sequences that terminate spontaneously after some seconds, minutes, hours or even days. In contrast, persistent AF requires medical intervention for its termination, whereas permanent AF cannot be reverted back to sinus

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rhythm or its termination is not recommended [2]. Nowadays, it is well-known that AF provokes electrophysiological changes within the atria, such as electrical, contractile and structural remodeling, that reduce the probability of its termination [1,3]. Indeed, approximately between 15 and 31% of PAF patients progress to persistent or permanent AF during a time period between 4 and 8 years [4]. Although AF is not a rapidly lethal disease, it can involve very disabling complications, such as cardiac failure and atrial thrombosis, with the subsequent risk of a stroke [1,5]. Hence, once a PAF episode terminates spontaneously, the early prediction of the next episode onset is a relevant clinical challenge. In fact, a wide variety of works have tried to predict the onset of PAF from the surface electrocardiogram (ECG), because it provides a noninvasive and low-cost approach to study the heart function. To this respect, the early use of pacing and drug treatments may prevent the recurrence of a new PAF episode, thus yielding electrical stabilization and avoiding that PAF degenerates into permanent AF [1,4].

A normal cardiac activation starts in the sinoatrial node and then spreads throughout the atrial myocardium, thus defining the P-wave in the ECG [6]. Given that P-wave morphology may change when the atrial depolarization wavefront spreads in an abnormal way and/or presents accessory pathways, reentries or conduction delays [7], its noninvasive analysis has received great attention in recent years. Indeed, P-wave duration is today accepted as the most reliable noninvasive marker for atrial conduction characterization. Its prolongation has been associated with history of AF [8], development of arrhythmias after bypass surgery [9] and progression from paroxysmal to persistent AF [10]. However, it is worth noting that the P-wave prolongation is attributed to atrial structural remodeling rather than on AF itself. Indeed, previous works have shown that patients with lone PAF failed to demonstrate any remarkable P-wave prolongation [11]. Similarly, P-wave duration has not been predictive of new-onset AF in patients with congestive heart failure [12]. Therefore, this electrophysiological alteration has not been considered as an unavoidable requirement for AF development [13].

Within this context, several authors have studied different morphological aspects of the P-wave to quantify additional atrial conduction disturbances. Thus, the P-wave morphology has been characterized from its singular value [14] and wavelet [15] decomposition or by its hidden Markov [16], Gaussian [17] and high-order polynomial [18] modeling. Nonetheless, the P-wave spectral content estimation has proven to be an extremely easy and useful way to quantify atrial properties alteration [19,20]. Indeed, previous works have revealed that P-waves before the onset of PAF contain more high-frequency energy than normal ones [19,20]. Additionally, P-wave spectral analysis has been able to discern between PAF patients and healthy subjects from the sinus rhythm ECG [19,21–23], quantify the effect of low dose sotalol in PAF patients [24] and stratify the recurrence risk of arrhythmic episodes over a time period of one year in PAF patients [15]. However, it has to be remarked that all these approaches have required signal-averaged ECG recordings in order to avoid the background noise effect [25], thus hindering the possibility of quantifying the P-wave morphology variability over time.

Although not completely understood, the transition from sinus rhythm to AF is often associated with progressive atrial electrophysiological alterations that may cause discontinuous propagation of sinus impulses [26]. Such increasing abnormalities result in a nonuniform and anisotropic atrial conduction, which is thought to play a major role in the initiation of reentry and, therefore, in the onset of PAF [26]. This uncoordinated atrial activity reaches the atrioventricular (AV) node and can be conducted to the ventricles, thus leading to a fast and irregular heart rate [1]. Taking advantage of this heart rate alteration, some authors have tried to predict with some time in advance the onset of PAF. Thus, several methods estimating time, frequency and complexity features of the RR series can be found in the literature [27–29]. However, they have only shown ability to reveal changes few minutes prior to the onset of PAF. Another drawback of these schemes is their need of complex RR series parameters combinations to predict successfully the onset of PAF, thus blurring the clinical meaning of each single parameter within the classification approach. Similarly, the identification of a high number of premature atrial complexes in the ECG has proven to be a good predictor of imminent PAF onset [30]. However, it has also been reported that the presence of these ectopic beats decreases considerably as the distance to the PAF onset increases [27]. Hence, the prediction is only feasible few minutes before the arrhythmia starts, thus turning unachievable the application of any efficient prophylactic therapy [31].

In contrast to all the aforesaid works, the P-wave duration variability analysis over time has proved a significant ability to quantify atrial electrophysiological alterations up to one hour preceding the onset of PAF [32]. Thus, the hypothesis of the present study is that the P-wave spectral characterization variability over time could provide clinically relevant and new information about the onset of AF. Hence, the present study focuses on quantifying the P-wave spectral variability during the 2 h preceding the onset of PAF from single-lead ECG recordings. This analysis represents an initial step in the global aim to determine the earliest reliable anticipation able to predict the onset of a PAF episode through the noninvasive study of atrial electrical activity.

2. Methods

2.1. Study population

In this retrospective study, 46 patients suffering from idiopathic PAF were analyzed. None of them were under antiarrhythmic drug treatment at the time of the study and suffered from heart disease, hyperthyroidism or pulmonary disease. Moreover, echocardiographic analysis proved that any patient enrolled in the study had atrial enlargement, such as Table 1 shows. From the 24-h Holter ECG recording of each patient, expert cardiologists annotated AF episodes, defined by irregular ventricular response and absence of P waves [33]. The number of arrhythmic events per patient was 2.9 ± 1.8 in mean, with an average duration of 4.1 ± 2.2 h. The mean duration of the normal sinus rhythm intervals among arrhythmic episodes was 5.87 ± 3.42 h. From each patient, the longest sinus rhythm interval in the recording