P-wave Indices to Detect Susceptibility to Atrial Fibrillation

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Abstract

The aim of this work is to present different markers resulting from the analysis of a single ECG lead recorded during sinus rhythm. To this purpose, the ECGs from three populations were compared: healthy subjects, patients subject to paroxysmal AF selected for catheter ablation, under general anesthesia or not. In addition to standard temporal P-wave parameters (P-wave duration and PQ interval), an index of P-wave stability over time defined as the Euclidean distance between beat-to-beat P waves, and morphologic characteristics of biphasic P-wave, such as P-wave initial force and terminal force, were studied. Significant differences between the healthy and pathological groups were obtained for the considered parameters. Moreover, a classification of the two groups based on the joint analysis of P-wave duration and PQ interval was suggested. In parallel, the analysis revealed that there are no significant differences in parameters between the groups under anesthesia or not. In conclusion, this study provides valuable markers for the early recognition of patients at high risk for atrial fibrillation which may guide upstream therapy.

1. Introduction

Atrial fibrillation (AF) is the most common type of human arrhythmia, and this prevalence is increasing. The prediction of AF susceptibility has been investigated in different contexts for years. Most of these studies used the 12 leads of the electrocardiogram (ECG) [1–3], the signal-averaged ECG [4–8] or the Frank leads [9, 10]. Different electrocardiographic markers have been proposed for the assessment of risk for AF: R-R intervals, maximum P wave duration, P index (defined as the standard deviation of the P wave duration across the 12 leads [3]), P wave dispersion, and morphologic changes of the P waves. But none has really proved itself conclusive. In particular, P wave duration has been demonstrated as an insufficient marker for AF prediction [4]. Improvements in the methodology of P wave analysis may lead to useful ECG markers in various clinical settings and particularly in the assessment of risk for AF [11].

The aim of this work is to complete a previous study in [12]. The purpose is to determine whether parameters resulting from the analysis of the P wave in ECG recorded during sinus rhythm could be markers for paroxysmal atrial fibrillation (PAF) susceptibility. Indeed, our idea is to compare the ECG in sinus rhythm from three populations: healthy subjects (Group 1), patients subject to paroxysmal AF selected for catheter ablation, under general anesthesia (Group 2), or not (Group 3). In addition to standard P wave parameters (P-wave duration, PQ interval), an index of P-wave stability over time defined as the Euclidean distance between beat-to-beat P waves, and morphologic characteristics of biphasic P-wave, such as P-wave initial force and terminal force, are studied.

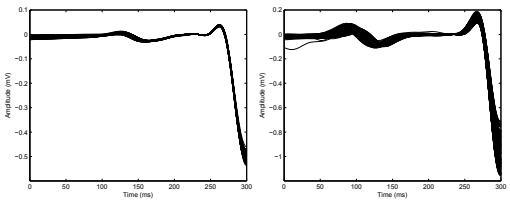
The remainder of the paper is organized as follows. In Section 2, the patient database, the data acquisition, and the analysis method are presented. The results on real ECG data are presented and discussed in Section 3. Finally, in Section 4, we conclude and suggest some perspectives.

2. Methods

2.1. Data

Tests were performed on 58 two-minute ECG recordings in sinus rhythm. The database included:

- Group 1: 30 ECGs from healthy men (Group 1) from the PTB database available on Physionet (healthy controls; sampling frequency 1 kHz);
- Group 2: 20 ECGs from male patients subject to PAF selected for catheter ablation (sampling frequency 977 Hz). The ECG signals were recorded while the patients were under general anesthesia just before catheter ablation;
- Group 3: 8 ECGs from male patients subject to PAF under normal resting conditions.



(a) (b)

Figure 1. Examples of segments including each expected P wave and its corresponding R wave in sequence for a control subject (a) and a patient subject to PAF of the Group 2 (b) in lead V1.

Patients who were in AF at the time of ECG-recording were excluded of our study. All patients underwent antiarrhythmic drug withdrawal at least 5 half-lives before the measurements. The characteristics of patients in the AF and no-AF groups are listed in Table 1.

Table 1. Comparison of the characteristics of control subjects and patients subject to paroxysmal AF

	Group 1	Group 2	Group 3
No. of patients	30	20	8
Age (years)	34 ± 13.3	57.5 ± 8.6	58.1 ± 7.0
Heart rate (bpm)	67.5 ± 12.6	51.1 ± 7.4	59.9 ± 6.27
BMI (kg.m^{-2})	–	25.6 ± 2.9	26.6 ± 3.7

2.2. Preprocessing

In order to remove the baseline, we applied to the real ECGs the preprocessing approach described in [12]. Several fiducial points were detected: the timing of the onset of the ventricular depolarization denoted as q_i, and R peaks locations t_k. In the following, only the lead V1, in which the baseline was removed, is considered because it exhibits the highest P wave amplitude. After R peak detection, a window was created (see figure 1): segments including each expected P wave and its corresponding R wave in sequence were formed by time locking them with the t_k. The length of the segments was fixed for all beats but depended on the subject: the left boundary of the segment was adjusted in order to ensure that the whole P wave was encompassed [13]. Premature atrial beats were removed from the analysis.

2.3. Analysis

Considering the above segments as our observations, several parameters were extracted from lead V1: P onsets, ends of P wave, P-wave duration, PQ interval, PR interval, center of gravity of the P waves, Euclidean distance between beat-to-beat resynchronized P waves. Besides, P wave morphologic characteristics such as area, duration and amplitude of the P-wave initial and terminal portions were measured in case of biphasic P-wave.

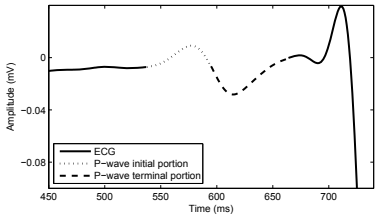


Figure 2. Example of the P-wave initial (dotted line) and terminal (dashed line) portions.

P onsets and ends were obtained using first and second derivative estimates of the ECG signal. The first and second derivatives were computed on the smoothed P wave. P wave delineation combined the slope characteristics as well as an amplitude criterion. Using a suitable threshold, the inflection points at the beginning and the end of the P wave were determined: when the second derivative vanished and changed sign, an inflection point was reached. P-wave duration was equal to the difference between the onset and the end of the P wave. The PQ interval was computed as the time between the beginning of the P wave and the Q wave (defined by q_i in the pre-processing step in section 2.2). The PR interval was defined as the time distance between the P onset and the following R peak t_k. The generalized Woody method presented in [13] permitted to determine the centers of gravity of the P wave. Considering a window around the wave of interest (*i.e.* excluding the Q and R waves) and after a resynchronization of the P waves with regard to centers of gravity, the beat-to-beat normalized Euclidean distance, an index of P-wave stability over time, was computed as:

$$ED_i = \frac{\sqrt{\sum_{i=1}^{N-1}(P_{i+1}[n-g_{i+1}] - P_i[n-g_i])^2}}{\sqrt{\sum_{i=1}^{N-1}(P_{i+1}[n-g_{i+1}])^2}}, \quad (1)$$

with $P_i[n-g_i]$ the i^{th} P wave resynchronized with regard to its center of gravity g_i.

Considering the recent study of Ishida *et al.* about the development of AF [14], P wave morphologic characteristics were measured in parallel to typical temporal P wave parameters when it was possible, *i.e.* when the P wave was biphasic in lead V1. For each beat, the boundary between the P-wave initial and terminal portions was determined as the point where the signal value was the average of the values at the P onset and end of P wave (see illustration in figure 2).

The duration, amplitude and area of P-wave initial and terminal portions were measured. The P terminal force was defined as the algebraic product of the duration and amplitude of the terminal P wave portion [15]. Similarly, the P-wave initial force was also computed.

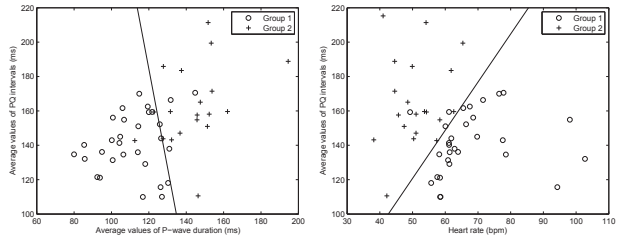
Table 2. Characteristics of ECG extracted from lead V1

Measurement	Group 1	Group 2	Group 3
Heart rate (bpm)	67.5 ± 12.6	51.1 ± 7.4	59.9 ± 6.27
P-wave duration (ms)	$111.5 \pm 15.8^{\sharp\S}$	$145.8 \pm 19.3^{\sharp}$	$139.9 \pm 21.8^{\S}$
PQ interval (ms)	$141.5 \pm 17.5^{\sharp\S}$	$165.4 \pm 25.6^{\sharp}$	$178.2 \pm 22.0^{\S}$
PR interval (ms)	$210.8 \pm 13.2^{\sharp\S}$	$244.2 \pm 28.9^{\sharp}$	$252.4 \pm 28.1^{\S}$
Variance of the beat-to-beat Euclidean distance	$2.42e^{-2\,\dagger}$	$1.38e^{-1\dagger}$	$3.50e^{-1\dagger}$

$^{\sharp}\ p < 0.0001 \quad ^{\S}\ p < 0.005 \quad ^{\dagger}\ p < 0.001$

Table 3. Measurements of P wave morphologic characteristics in lead V1. Symbol $\sharp$ means $p < 0.0001$

Measurement	Group 1	Group 2
Initial Portion		
Duration (ms)	$58.7 \pm 8.8^{\sharp}$	$78.1 \pm 8.7^{\sharp}$
Amplitude (mV)	$2.2e^{-2} \pm 6.4e^{-3\,\sharp}$	$6.3e^{-2} \pm 1.7e^{-2\,\sharp}$
Area (mV x ms)	$0.9 \pm 0.4^{\sharp}$	$3.1 \pm 1.4^{\sharp}$
Initial force (mV x ms)	$1.4 \pm 0.5^{\sharp}$	$5.1 \pm 1.8^{\sharp}$
Terminal Portion		
Duration (ms)	$52.4 \pm 9.5^{\sharp}$	$63.2 \pm 14.5^{\sharp}$
Amplitude (mV)	$-1.7e^{-2} \pm 7.8e^{-3\,\sharp}$	$-3.4e^{-2} \pm 1.0e^{-2\,\sharp}$
Area (mV x ms)	$-0.6 \pm 0.3^{\sharp}$	$-1.1 \pm 0.4^{\sharp}$
Terminal force (mV x ms)	$-1.1 \pm 0.5^{\sharp}$	$-2.3 \pm 1.1^{\sharp}$
No. of subjects where the P wave was biphasic	24/30	19/20



(a) (b)

Figure 3. Relationship between the averages of the PQ interval and the P-wave duration (a), the heart rate (b), for the first (o) and second ($+$) groups. The two groups can be correctly classified up to 88% in the first case (a) and up to 94% in the second case (b).

3. Results and discussion

ECG characteristics extracted from lead V1 are listed in Table 2. Means and standard deviations of each feature were computed for each group.

Before analyzing the results from the first and second groups, we studied the eight patients of the group 3 described in section 2.1. The comparison with the second group of patients under anesthesia revealed that the various temporal P wave parameters were not significantly different (see Table 2). We therefore conclude that anesthesia does not influence the investigated parameters.

Significant differences were observed between the first and second groups. The average P-wave duration, the average PQ interval and average PR interval were significantly longer in the group 2 than in the group 1. Changes in P-wave duration are mostly related to the substrate of the AF. In Table 2, we can observe that the extensions of P-wave duration and PR intervals of the first and second groups were of similar magnitude. This last remark suggests that the prolongation of the PR interval is not due to a QRS enlargement but primarily to the expansion of the P wave, *i.e.*, to the prolongation of intra-atrial conduction. This is confirmed by the similar extensions of PQ intervals and PR intervals between the different groups which are of similar magnitude.

The variance of the beat-to-beat Euclidean distance between P waves, a measure of P wave time variability *i.e.*, an index of P-wave stability over time, was higher for the group 2 than for control group 1. This may be indicative of intermittently disturbed conduction in atrial tissue in patients susceptible to AF. The relationship between the averages of the PQ interval and P-wave duration for the first and second groups is displayed in figure 3(a). Using P-wave duration and PQ interval parameters, the correct classification rate was on average 88% using Fisher's linear discriminant. The sensitivity, the specificity and the positive predictive value of the test were respectively equal to 86%, 90% and 82%. This result suggested that the combination of P-wave duration and PQ interval could lead to an effective detection tool for risk of AF.

Figure 3(b) shows the relationship between the average PQ interval and the heart rate for the first and second groups. Knowing that the heart rate decreases gradually with aging [16], and patients of the second group being older than those of the control group, lower heart rates were expected for the AF group. However differences in PQ intervals between the two groups were observed for similarly low heart rate. In accordance with our expectations, we observed that for a similarly low heart rate, the average PQ interval of the second group was higher than for the control group.

When ECGs displayed biphasic P-wave in lead V1, *i.e.*, for 24 subjects out of 30 in the control group 1 and for 19 patients out of 20 in the second group, the analysis of the P-wave initial and terminal portions was performed. The results of the P wave morphologic analysis are listed in Table 3. Significant differences were observed in morphology as

well as in P-wave initial and terminal portions. Indeed, whatever the portion of the P wave (initial or terminal), both duration, amplitude, area and force were significantly larger in the AF group (group 2) than in the control group. As these morphologic properties could be associated with an altered substrate or a modified pathway in the atria, in accordance with the study of Ishida *et al.* [14], the present study showed that an increased magnitude of P-wave initial force in lead V1 was associated with a higher rate of AF development. However, this marker can, of course, be used only when the P wave is biphasic.

4. Conclusion

In this paper, we proposed different P-wave markers, temporal or morphological, to detect predisposition to atrial fibrillation with only two-minute records and a single lead. However, our study presents several limitations. The main ones are the limited number of patients and the possible influence of anesthesia. However, we checked that no significant difference in the considered P wave markers exists between patients with or without anesthesia. The difference of age between the different groups can also be a limitation of the study. However, usually age is only moderately related to PR changes [17], therefore we can suppose that our results may still remain valid. On the other hand, there are to our knowledge no previous studies performed on the Euclidean variation of the P-wave in any age group. Subsequent larger studies are necessary to check if the age and the anesthesia in patients subject to PAF may influence the results.

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