

Susceptibility to Paroxysmal Atrial Fibrillation: A Study using Sinus Rhythm P Wave Parameters

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Abstract

Early recognition of patients at high risk for atrial fibrillation may help to minimize potential health risks. The detection of susceptibility to develop atrial fibrillation is thus a real clinical challenge. Whereas many studies have used the signal-averaged P wave, the aim of this work is to determine whether electrocardiographic parameters resulting from the analysis of the P wave in ECG recorded during sinus rhythm could be markers for paroxysmal atrial fibrillation susceptibility. Our idea was to compare the ECG in sinus rhythm from two populations: healthy people and patients subject to paroxysmal atrial fibrillation. In addition to standard P wave parameters (P width, P-R interval, . . .), the Euclidean distance between beat-to-beat P waves, which has been rarely addressed in this context, was studied on lead VI. Significant differences between the healthy and the paroxysmal atrial fibrillation groups were obtained for various parameters. Moreover, a classification of the two groups based on the joint analysis of P width and P-R interval was suggested. This proposed classification could lead to an effective identification of patients at risk to develop atrial fibrillation.

1. Introduction

Many studies have been performed on the assessment of the risk for atrial fibrillation (AF) over the recent years. The prediction of AF has been investigated in different contexts: in patients without apparent heart disease [1–11], in hypertensive ones [12, 13], in patients with coronary artery disease or undergoing coronary artery bypass surgery [14, 15] and in patients after cardiac surgery [16]. Most of these studies used the 12 leads of the electrocardiogram (ECG), the signal-averaged ECG [7, 8, 10, 16, 17] or the Frank leads [4, 9]. 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 [6]), P wave dispersion, and morphological 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 [7]. Improvements in the methodology of P wave analysis may lead to a useful ECG marker in various clinical settings and particularly in the assessment of risk for AF [18].

Therefore, the purpose of this investigation 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 two populations: healthy people and patients subject to paroxysmal atrial fibrillation. In addition to standard P wave parameters and P-R interval, the variance of the Euclidean distance between beat-to-beat P waves, which has been rarely addressed in this context, is studied.

The remainder of the paper is organized as follows. In Section 2, the study patients, the data acquisition, and the analysis method are presented. The results on real ECG data are presented in Section 3. Finally, we conclude and present some future directions in Section 4.

2. Methods

2.1. Data

Tests were performed on 42 two-minute ECG recordings in sinus rhythm. The database included 30 ECG from healthy men (non-AF group) from the PTB database available on Physionet (healthy controls ; sampling frequency 1 kHz), and 12 male patients subject to paroxysmal atrial fibrillation (AF group) from the Clinic Im Park in Switzerland (sampling frequency 977 Hz). The characteristics of patients in the AF and non-AF groups are listed in Table 1.

	non-AF	AF
No. of patients	30	12
Age (years)	34 ± 13.3	61 ± 8
Heart rate (bpm)	67.5 ± 12.6	53.2 ± 7.9
BMI ($\text{kg}\cdot\text{m}^{-2}$)	–	25 ± 2.7

Table 1. Comparison of characteristics of non-AF and AF patients

For the AF group, the ECG signals were recorded while the patients were under general anesthesia just before the catheter ablation in the Clinic Im Park in Zürich. 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 (including amiodarone).

2.2. Preprocessing

The root mean square (RMS) ECG signal was constructed using the eight independent components of the standard 12-lead ECG: the two limb leads (VR and VL) and the six precordial leads (V1 to V6). The RMS ECG signal $x_{RMS}[n]$ of a set of N ECG leads ($x_i[n]$ with $i = 1, \dots, N$) is defined as:

$$x_{RMS}[n] = \sqrt{\frac{1}{N} \sum_{i=1}^N x_i^2[n]}. \quad (1)$$

A derivative-based method was applied to the RMS ECG signal to detect ventricular complexes [19]. In the i^{th} cardiac cycle, the timing of the onset of the ventricular depolarization was denoted as q_i [20]. A baseline correction was applied to each of the eight lead signals by means of a cubic spline interpolation anchored to the onset points q_i identified in the RMS signal [21]. The fiducial point detection and the baseline correction were iteratively applied until no further changes in their timing were observed. The eight resulting ECG signals were smoothed by applying a low-pass finite impulse response filter (moving average window of 20 ms) [20]. Choosing the cubic spline interpolation points at the onset of the P waves instead of the Q waves [19] does not change the results presented in Section 3. In the following, only the lead V1, in which the baseline was removed, is considered because it exhibits the highest P wave amplitude. The first step in P wave signal extraction was to detect the QRS complexes. A threshold technique applied to this lead refined the estimation of the time occurrences t_k of the R waves, that are roughly the R peaks locations [22]. Once the R wave was found, it was used as a reference point. After R peak detection, a window was created (see Fig. 1): segments including each

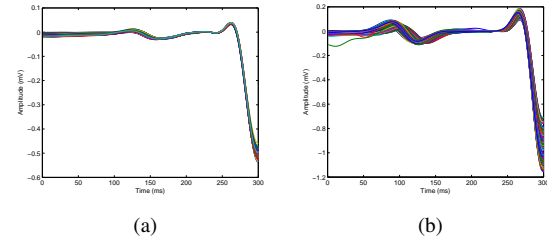


Figure 1. Examples of segments including each expected P wave and its corresponding R wave in sequence for a non-AF subject (a) and an AF patient (b) on lead V1.

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 [23]. 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 width, P-R interval, center of gravity of the P waves, Euclidean distance between beat-to-beat resynchronized P waves.

P onsets and ends were obtained using first and second derivative approximations of the ECG signal. The algorithm combines the slope characteristics as well as an amplitude criterion to define its decision boundaries. The first and second derivatives are computed on the smoothed P wave. Using a threshold technique, the inflection points at the beginning and the end of the P wave are determined: when the second derivative vanishes and changes sign, an inflection point is reached. P width is equal to the difference between the onset and the end of the P wave. The P-R interval is defined as the time distance between the P onset and the following R peak t_k . The generalized Woody method presented in [23] permits to determine the centers of gravity of the P wave. After a resynchronization of the P waves with regard to centers of gravity, the beat-to-beat normalized Euclidean distance is computed.

3. Results

ECG characteristics extracted from lead V1 are listed in Table 2. Means and standard deviations of each feature were computed for each group. Significant differences were observed between the AF and non-AF groups. The average P width and average P-R interval (defined as the distance between the P onset and the following R peak) were significantly longer in the AF group than in the non-

Measurement	non-AF group	AF group	p-value
Heart rate (bpm)	67.5 ± 12.6	53.2 ± 7.9	<0.005
P width (ms)	111.5 ± 15.8	156.2 ± 26.3	<0.005
P-R interval (ms)	210.8 ± 13.2	259.0 ± 28	<0.005
Variance of the beat-to-beat Euclidian distance	$2.42e^{-2}$	$1.35e^{-1}$	<0.1

Table 2. Characteristics of ECG extracted from lead V1

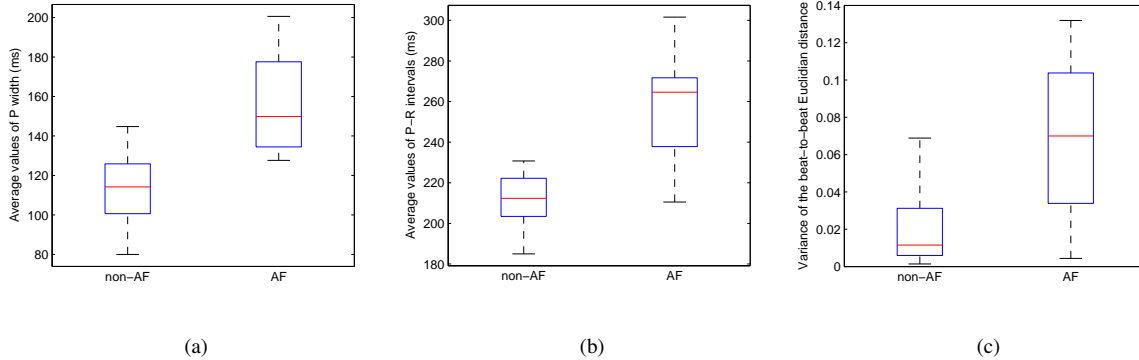


Figure 2. Box plot of the ECG characteristics extracted from lead V1 for non-AF and AF groups: P width (a), P-R interval (b) and variance of the beat-to-beat Euclidian distance between P waves (c).

AF group. Changes in P width are most related to the substrate of the AF. Moreover, P-R interval prolongation is primarily due to the extension of intra-atrial conduction, *i.e.* to the expansion of the P wave. Similarly, the variance of the beat-to-beat Euclidian distance between P waves, a measure of P wave time variability, was higher for the AF group than for the non-AF group. This may be indicative of disturbed conduction in atrial tissue in patients susceptible to AF.

Figure 2 displays differences between non-AF and AF groups for the following ECG characteristics: average P width in Fig. 2.a, average P-R interval in Fig. 2.b and average variance of the beat-to-beat Euclidian distance between P waves in Fig. 2.c. The relationship between the average P-R interval and the average P wave width for the non-AF and AF groups is displayed in Fig. 3(a). Using P width and P-R interval parameters, the correct classification rate was 90.4% using Fisher's linear discriminant.

Figure 3(b) shows the relationship between the average P-R interval and the heart rate for the non-AF and the AF groups (in which patients were under general anesthesia). Knowing that the heart rate decreases gradually with aging [24], and patients of AF group being older than those of the non-AF group, lower heart rates were expected for the AF group. However differences in P-R intervals between the two groups are observed for similar low heart rate. In accordance with our expectations, we observed that for a similarly low heart rate, the average P-R interval of the AF group was higher than for the non-AF group.

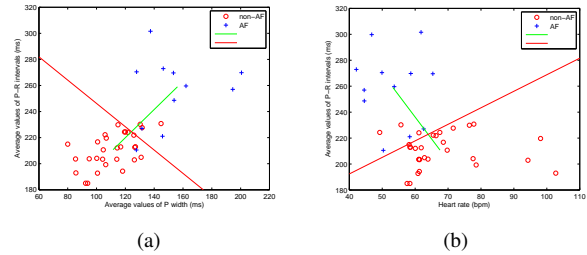


Figure 3. Relationship between the averages of the P-R interval and on (a) the P width, and on (b) the heart rate, for the non-AF (o) and AF groups (+). The two groups can be respectively well classified up to 90.4% and 92.8%.

4. Discussion and conclusions

Improving early detection of AF in order to prevent complications presents a significant clinical interest. Early recognition of patients at high risk for AF may guide upstream therapy, combine and thereby contribute to prevent AF from becoming chronic, minimize potential health risks, costs, and other complications.

Our hypothesis was that patients subject to AF may be detected by several P wave parameters. We have presented an analysis method for single lead data which makes this detection possible. Indeed, the analysis of ECG characteristics such as averages of P width, P-R interval and variance of the beat-to-beat Euclidian distance between P waves, revealed significant difference between the non-AF

and the AF groups. Moreover, by combining the P width and the P-R interval, a classification rate of 90.4% between the non-AF and the AF groups was achieved. The classification scheme could lead to an effective prevention tool for the management of this arrhythmia. It may help identify patients at high risk of developing AF, and trigger more frequent monitoring. However, subsequent larger studies are necessary to check if the anesthesia and the age in the AF group could not influence the results.

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References

- [1] Dilaveris P, Gialafos E, Sideris S, Theopistou A, Andrikopoulos G, Kyriakidis M, Gialafos J, Toutouzas P. Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. *Am Heart J* 1998; 135:733–738.
- [2] Aytemir K, Ozer N, Atalar E, Sade E, Aksoyek S, Ovunc K, Oto A, Ozmen F, Kes S. P Wave Dispersion on 12-Lead Electrocardiography in Patients with Paroxysmal Atrial Fibrillation. *Pacing Clin Electrophysiol* 2000;23:1109–1112.
- [3] Dilaveris P, Gialafos E. P-Wave Dispersion: A Novel Predictor of Paroxysmal Atrial Fibrillation. *ANE* 2001;6:159–165.
- [4] Carlson J, Havmøller R, Herreros A, Platonov P, Johansson R, Olsson B. Can orthogonal lead indicators of propensity to atrial fibrillation be accurately assessed from the 12-lead ECG? *Europace* 2005;7:S39–S48.
- [5] De Bacquer D, Willekens J, De Backer G. Long-Term Prognostic Value of P-Wave Characteristics for the Development of Atrial Fibrillation in Subjects Aged 55 to 74 Years at Baseline. *Am J Cardiol* 2007;100:850–854.
- [6] Perez M, Dewey F, Marcus R, Ashley E, Al-Ahmad A, Wang P, Froelicher V. Electrocardiographic predictors of atrial fibrillation. *Am Heart J* 2009;158:622–628.
- [7] Holmqvist F, Platonov P, Carlson J, Zareba W, Moss A. Altered interatrial conduction detected in MADIT II patients bound to develop atrial fibrillation. *ANE* 2009;14:268–275.
- [8] Havmøller R, Carlson J, Holmqvist F, Olsson B, Platonov P. Evolution of P-Wave Morphology in Healthy Individuals: A 3-Year Follow-Up Study. *ANE* 2009;14:226–233.
- [9] Herreros A, Baeyens E, Johansson R, Carlson J, Perán J, Olsson B. Analysis of changes in the beat-to-beat P-wave morphology using clustering techniques. *Biomed Signal Process Contr* 2009;4:309–316.
- [10] Holmqvist F, Platonov P, McNitt S, Polonsky S, Carlson J, Zareba W, Moss A. Abnormal P-wave morphology is a predictor of atrial fibrillation development and cardiac death in MADIT II patients. *ANE* 2010;15:63–72.
- [11] Ishida K, Hayashi H, Miyamoto A, Sugimoto Y, Ito M, Murakami Y, Horie M. P wave and the development of atrial fibrillation. *Heart Rhythm* 2010;7:289–294.
- [12] Ciaroni S, Cuenoud L, Bloch A. Clinical study to investigate the predictive parameters for the onset of atrial fibrillation in patients with essential hypertension. *American Heart Journal* 2000;139:814–819.
- [13] Magnani J, Mazzini M, Sullivan L, Williamson M, Ellinor P, Benjamin E. P-Wave Indices, Distribution and Quality Control Assessment (from the Framingham Heart Study). *ANE* 2010;15:77–84.
- [14] Chandy J, Nakai T, Lee R, Bellows W, Dzankic S, Leung J. Increases in P-Wave Dispersion Predict Postoperative Atrial Fibrillation After Coronary Artery Bypass Graft Surgery. *Anesth Analg* 2004;98:303–310.
- [15] Sovilj S, Van Oosterom A, Rajsman G, Magjarevic R. ECG-based prediction of atrial fibrillation development following coronary artery bypass grafting. *Physiol Meas* 2010; 31:663–677.
- [16] Steinberg J, Zelenkofske S, Wong S, Gelernt M, Sciacca R, Menchavez E. Value of the P-Wave Signal-Averaged ECG for Predicting Atrial Fibrillation After Cardiac Surgery. *Circulation* 1993;88:2618–2622.
- [17] Budeus M, Felix O, Hennersdorf M, Wieneke H, Erbel R, Sack S. Prediction of Conversion from Paroxysmal to Permanent Atrial Fibrillation. *Pacing Clin Electrophysiol* 2007;30:243–252.
- [18] Magnani J, Williamson M, Ellinor P, Monahan K, Benjamin E. P Wave Indices Current Status and Future Directions in Epidemiology, Clinical, and Research Applications. *Circ Arrhythm Electrophysiol* 2009;2:72–79.
- [19] Ihara Z, van Oosterom A, Hoekema R. Atrial repolarization as observable during the PQ interval. *Journal of Electrocardiology* 2006;39:290–297.
- [20] Lemay M, Vesin J, van Oosterom A, Jacquemet V, Kappenberger L. Cancellation of ventricular activity in the ECG: Evaluation of novel and existing methods. *IEEE Trans Biomed Eng* 2007;54:542–546.
- [21] Sörnmo L, Laguna P. *Bioelectrical Signal Processing in Cardiac and Neurological Applications*. Elsevier, 2005.
- [22] Meste O, Blain G, Berman S. Hysteresis Analysis of the PR-PP relation under Exercise Conditions. *Computers In Cardiology* 2004;31:461–464.
- [23] Cabasson A, Meste O, Blain G, Berman S. Quantifying the PR interval pattern during dynamic exercise and recovery. *IEEE Trans Biomed Eng* 2009;56:2675–83.
- [24] Umetani K, Singer D, McCraty R, Atkinson M. Twenty-four hour time domain heart rate variability and heart rate: relations to age and gender over nine decades. *Am J Coll Cardiol* 1998;31:593–601.

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