Post-stroke Atrial Fibrillation Predicted by P-wave Variability Analysis From a Single-Lead ECG

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Abstract

Recent evidences suggest that atrial cardiomyopathy is associated with an increased risk of stroke, regardless of the presence of atrial fibrillation (AF). Markers of atrial cardiomyopathy include ECG changes, particularly associated with the P-wave. P-wave analysis is therefore useful in characterizing atrial cardiomyopathy and thus in optimizing the therapeutic pathway of patients, even post-stroke. Today, technological advances allow high-resolution, beat-by-beat P-wave analysis from single-lead ECG. Patients with ischemic stroke were continuously monitored via ECG for 7 days post-stroke onset. On the second day, a 5-minute high-resolution single-lead ECG trace was recorded for each patient. P-wave parameters, including duration (Pdur), fragmentation (Pfrag), change of polarity (PCP), and beat-to-beat variability (Pvar), were extracted. Patients were divided into AF-detected and control groups, and statistical analysis was performed using the Mann-Whitney test.

AF was detected in 15 patients, and all P-wave parameters but Pvar were significantly higher in the AF group than in controls (Pdur: 104.5±23.3 ms vs 133.3±6.4 ms, Pfrag: 2.28±1.4 vs 3.8±1.7, PCP: 0.68±0.6 vs 1.3±0.5).

The study showed the potential link between single-lead ECG P-wave analysis and the electrophysiological changes of the atria in post-stroke patients.

1. Introduction

Atrial fibrillation (AF) is a cardiac arrhythmia characterized by disordered stimulation of the atrial chambers resulting in the absence of atrial contraction and irregular ventricular contraction. An episode of AF appears on the ECG as a pattern in which distinct repeating P-waves are absent and irregular RR intervals are present [1].

AF is the most widespread cardiac arrhythmia in clinical practice, it affects more than 30 million people worldwide today and its incidence is expected to grow in the coming years [2]. AF is not lethal but can have serious consequences increasing mortality and morbidity.

One of the worst consequences of AF is ischemic stroke, and for many years AF has been considered the main cause of cardioembolic stroke [3, 4]. In fact, during an episode of AF, blood clots can form in the left atrial appendage or left atrium as a result of local blood stasis, followed by dislodgment and embolization to the cerebral arteries (particularly upon the return of atrial contraction with sinus rhythm restoration) [5].

For this reason, stroke risk scores (e.g. CHA2DS2-VASc) are commonly used to decide on anticoagulation therapy when a clinical atrial fibrillation episode is documented [6].

However, this paradigm has recently been questioned by some studies [7, 8, 9], which have shown the lack of temporal relationships between subclinical AF events and strokes in patients under continuous rhythm monitoring via implanted devices.

Scientific evidence shows a new paradigm for the relationship between atrial fibrillation and stroke, according to which additional factors that are associated with substrate disease, such as atrial hypocontractility and impairment of atrial endothelial function, contribute significantly to the onset of the stroke even in the absence of AF [10, 11]. The new paradigm suggests that atrial cardiomyopathy, which is associated with an increased risk of AF, is also associated with a higher incidence of AF-related adverse outcomes such as stroke; hence, atrial cardiomyopathy is a distinct entity prognostically important.

If atrial cardiomyopathy leads to AF, structural and electrical remodeling of the atria occurs, further increasing the risk of thromboembolism: This creates a vicious cycle,

where atrial cardiomyopathy progressively worsens, and the risk of stroke continues to escalate [12].

The key challenge of this emerging paradigm is to identify a population of stroke patients who could benefit from secondary stroke prevention with anticoagulant therapy even in the absence of AF. For this purpose, atrial cardiomyopathy must be accurately characterized [13].

Among the markers of atrial cardiomyopathy, P-wave analysis has shown potential for evaluating the electrical alterations in the atrial substrate [14].

Therefore, it is essential to investigate P-wave predictors that can improve the stratification of the risk of post-stroke AF, ultimately optimizing treatment and management strategies for patients.

The aim of this paper is to evaluate the potential of P-wave analysis from a single-lead ECG in indicating atrial substrate modifications associated with post-stroke atrial fibrillation development.

2. Methods and materials

2.1 P-wave analysis

The analysis of the ECG P-wave can give significant information about the depolarization of the atria. The P-wave can have multiple measured parameters, in terms of duration, morphology, and variability, which can be altered even under various normal physiological conditions, but more so when atrial disease is present.

P-wave analysis has the potential to give information about the anatomical and electrical atrial substrate predisposing to different clinical events, principally AF and ischemic stroke.

Until recently, given the low signal-to-noise ratio (SNR) associated with the P-wave, the analysis of the P-wave has been mostly performed on a P-wave template obtained by the averaging technique. To date, the technological advancement makes it possible to obtain high-resolution ECG (< 0.1uV) allowing the analysis of the P-wave variability on a beat-by-beat basis, even from single-lead ECG.

In this paper, P-wave duration, morphology, and variability have been estimated to evaluate their potential in stratifying post-stroke patients in terms of AF occurrence. P-wave duration and morphology are estimated by analyzing a P-wave template obtained by the averaging technique. P-wave variability is estimated by performing a beat-by-beat analysis of the P-waves over time.

P-wave duration (Pdur) is estimated by an automatic identification of P-wave template onset and offset. These fiducial points are identified as the first and the last – respectively – over a threshold. The threshold is based on the estimation of the background noise obtained from the isoelectric line.

P-wave morphology is estimated by performing modelling of the P-wave template in terms of a sum of Gaussian waves. Two morphological parameters are then extracted from the P-wave Gaussian model: the number of maxima and minima (namely peaks and valleys) (Pfrag), and the number of zero crossings (change of polarity, PCP).

P-wave variability takes into account the variation over time of the morphology of the P-waves. An index has been extracted starting from the butterfly plot obtained by superimposing all the P-waves which contributes to the P-wave template. For each sample, the difference between the maximum and the minimum values among the P-waves is estimated, obtaining a vector of the amplitude dispersion over time. The P-wave variability index (Pvar) is defined as the mean value of this vector.

Details on the P-wave analysis algorithms can be found elsewhere [15, 16].

2.2 Experimental protocol

63 patients with ischemic stroke were recruited. To detect the onset of AF episodes, ECG continuous monitoring started soon after stroke onset and lasted 7 days. A 5-minute-long single ECG lead was recorded on the second day after stroke, for each patient, using a custom-made single-lead high-resolution ECG acquisition system. The single-lead ECG system was placed on the patient's chest.

All patients were in sinus rhythm at the time of the recording. ECG traces were processed to automatically extract and analyze the P-waves in terms of duration (Pdur), fragmentation (Pfrag), change of polarity (PCP), and beat-to-beat variability (Pvar). The study population was divided into two groups: those who developed AF and those who remained in sinus rhythm, during the 1-week monitoring time (control group). The non-parametric Mann-Whitney unpaired t-test was used to assess the statistical significance.

3. Results

15 out of 63 patients developed AF (about 25% of the population). All P-wave parameters resulted to be higher in patients who developed AF respect to the control group, except for Pvar.

Statistical significance (p-value < 0.05) was achieved by Pdur (104.6 ±23.4 ms vs 133.3 ± 6.4 ms), Pfrag (2.4 ±1.2 vs 3.8± 1.7), and PCP (0.7 ±0.6 vs 1.3 ± 0.5) but not for Pvar (0.3 ± 0.1 vs 0.3 ± 0.1).

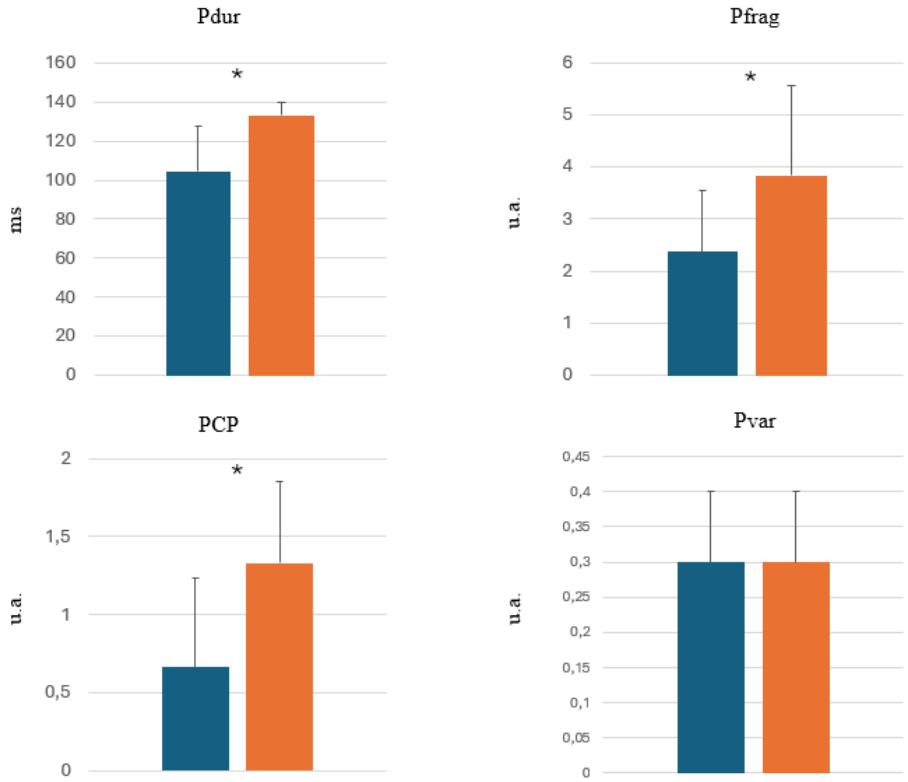

Figure 1. The control group is shown in blue-bar, while patients who had AF are shown in orange.

4. Discussion and conclusion

Recently a new paradigm has been proposed regarding the relationship between AF and stroke, suggesting that atrial cardiomyopathy plays a crucial role in stroke occurrences, even in the absence of AF.

The are several causes of atrial cardiomyopathy, ranging from aging to other concomitant factors, with markers such as atrial stretching, fibrosis, and mechanical dysfunction which are somehow related to electrical alterations measurable by the ECG [5].

Among these markers, atrial stretching is often a response to increased pressure or volume overload in the heart. This stretching can lead to remodeling of atrial tissue contributing to fibrosis, or the thickening and scarring of connective tissue, which disrupts the propagation of electrical impulses. This disruption may manifest as various ECG abnormalities, such as prolonged P-wave duration, abnormal P-wave morphology, and increased P-wave variability [13].

For this reason, it is important to investigate P-wave parameters as potential markers of atrial cardiomyopathy. These parameters provide detailed information about the electrical substrate of the atrium aiding in timely diagnosis and early intervention. almost importantly, these parameters can now be easily obtained directly from the ECG trace, thanks to advances in signal acquisition and processing techniques, which have become increasingly sophisticated.

This study showed that P-wave parameters from a single-lead ECG are significantly associated with an increased risk of post-stroke AF, being linked to the electrophysiological changes in the atria.

In particular, the parameters extracted include P-wave duration (Pdur), the number of peaks and valleys in the P-wave Gaussian model (Pfrag), the number of zero crossings (PCP), and P-wave variability (Pvar). There is strong evidence that AF occurs in the context of both electrical and anatomical abnormalities in the atria [14]. At the same time, atrial cardiomyopathy may lead to a thrombogenic substrate potentially identifiable through electrophysiological markers. Indeed, electro-anatomical abnormalities as extracted by the P-wave analysis may predict future AF or identify patients developing atrial cardiomyopathy.

Notably, the stroke risk indices proposed in the literature do not account for electrical markers of atrial cardiomyopathy, as they are primarily based on patient age and comorbidities. These findings suggest the opportunity to incorporate P-wave parameters into stroke risk indices, as these markers can provide valuable insights into atrial cardiomyopathy and its impact on stroke risk. This would

ultimately enhance the accuracy of risk assessment and the effectiveness of preventive strategies. The potentialities of the P-wave analysis as index of atrial cardiomyopathy should be further investigated in a control population who experience AF episodes without having stroke.

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