CorSalud. 2022 Jan-Mar;14(1):61-70

CorSalud

Cuban Society of Cardiology

Special Article

Cardiocentro ERNESTO CHE GUEVARA SANTA CLARA CUBA

Electrocardiographic predictors of atrial fibrillation

Maria Iovănescu[1], MD; Hussain Shah Sarfaraz[2], MD; Georgică Costinel Târtea[3], MD, PhD; Elibet Chávez-González[4], MD, PhD; and Ionuț Donoiu[5]✉, MD, PhD

[1] Doctoral school, University of Medicine and Pharmacy, Craiova, Romania.
[2] Cardiovascular Research and Innovation Division, Medorius Ltd. Birmingham, United Kingdom.
[3] Department of Physiology, University of Medicine and Pharmacy, Craiova, Romania.
[4] Division of Cardiac Stimulation and Electrophysiology, Cardiocentro Ernesto Che Guevara. Villa Clara, Cuba.
[5] Department of Cardiology, University of Medicine and Pharmacy, Craiova, Romania.

Este artículo también está disponible en español

ARTICLE INFORMATION

Received: 19 de marzo de 2021
Accepted: 26 de abril de 2021
Online first: 04 de junio de 2021

Competing interests
The authors declare no competing interests.

Abbreviations
AF: atrial fibrillation
ECG: electrocardiogram
IAB: interatrial block
LAFB: left anterior fascicular block
PWD: P-wave dispersion

✉ *I Donoiu*
Department of Cardiology
Craiova University of Medicine and Pharmacy. Petru Rareș 2, 200349
Craiova, Romania.
E-mail address:
ionut.donoiu@umfcv.ro

ABSTRACT

Atrial fibrillation is arguably the most common heart rhythm disorder with increasing incidence and prevalence recently. Atrial fibrillation significantly contributes to increased mortality especially through the onset/worsening of heart failure and the occurrence of cardioembolic stroke. Identifying markers that could indicate the installation of this arrhythmia in a specific patient would warrant closer monitoring, establishing a preventive antiarrhythmic treatment or even timely anticoagulant treatment. This article reviews the electrocardiographic indicators of atrial fibrillation installation presented in recent literature. The databases in which the search was made were PubMed, Scopus and Google Scholar. The search terms used were "atrial fibrillation", "supraventricular arrhythmias", "electrocardiographic predictors", "interatrial block", "atrial extrasystoles", "P wave dispersion", "left atrial enlargement". Most recent and relevant papers were included.
Keywords: Arrhythmia, Electrocardiogram, P wave, P wave dispersion, Atrial remodeling, Atrial fibrillation.

Predictores electrocardiográficos de fibrilación auricular

RESUMEN

La fibrilación auricular es posiblemente el trastorno del ritmo cardíaco más común y, recientemente, ha experimentado un aumento de su incidencia y prevalencia. Esta arritmia contribuye significativamente al aumento de la mortalidad, especialmente a través de la aparición o empeoramiento de la insuficiencia cardíaca y la ocurrencia de accidente cerebrovascular cardioembólico. Identificar marcadores que pudieran indicar la aparición de esta arritmia en un paciente específico, garantizaría un seguimiento más estrecho, la instauración del tratamiento antiarrítmico oportuno y el inicio de la anticoagulación. En este artículo se revisan los indicadores electrocardiográficos de aparición de fibrilación auricular que se encuentran en la literatura reciente. Las bases de datos donde se realizó la búsqueda fueron PubMed, Scopus y Google Scholar. Los términos de búsqueda utilizados fueron "fibrilación auricular", "arritmias supraventriculares", "predictores electrocardiográficos", "bloqueo interauricular", "extrasístole auricular", "dispersión de la onda P", and "dilatación de la aurícula izquierda". Se incluyeron las publicaciones relevantes más recientes.
Palabras clave: Arritmia, Electrocardiograma, Onda P, Dispersion de la onda P, Remodelado auricular, Fibrilación auricular

INTRODUCTION

Atrial fibrillation (AF) is one of the most frequent heart rhythm disorders, with an estimated prevalence of around 3%, which increases with age. Still, due to certain unknown factors, there are differences in its prevalence across different geographic areas. For example, South Asians, despite having a higher prevalence of cardiovascular risk factors, such as arterial hypertension or diabetes mellitus, have a lower incidence of atrial fibrillation compared to Europeans[1]. The mechanisms underlying this arrhythmia are complex and only partially understood. The initiation of atrial fibrillation requires the presence of a single, presumably automatic focus, while most cases of persistent atrial fibrillation fit the model of multiple reentrant wavelets coursing around islands of refractory tissue.

The importance of early diagnosis and moreover the need to find prediction factors, which would allow the identification of patients at risk comes mainly from the potentially fatal repercussions of this rhythm disorder such as cardioembolic stroke or the reduction of cardiac output due to loss of atrial contraction. If such markers were to be precisely established, selected patients could benefit from closer monitoring and different treatment strategies regarding antiarrhythmic or antithrombotic therapy. The electrocardiogram (ECG) is a routine examination, a quick and inexpensive diagnostic tool and could thus provide useful parameters with high prediction accuracy for the installation of atrial fibrillation. However, studies conducted so far had as areas of interest not only simple predictors of atrial fibrillation risk development but were extended to find associations with AF recurrence after therapeutic interventions or under certain pathological conditions, thus ensuring an even greater importance of these markers in determining new strategic approaches in the future.

This review describes the electrocardiographic features that are expressed in the literature as predictors of AF or associated with it. This paper strictly refers to standard ECG predictors, excluding other derived techniques such as ambulatory or signal-averaged ECG, which are valuable tools for assessing AF risk[2]. Also, it should not be forgotten that there are other biochemical, echocardiographic, or electrophysiological predictive markers of atrial fibrillation.

METHODS FOR REVIEW

The information in this review was obtained from specialized articles, both original and review type. The search terms used were “atrial fibrillation”, “supraventricular arrhythmias”, “electrocardiographic predictors”, “interatrial block”, “atrial extrasystoles”, “P-wave dispersion”, “left atrial enlargement.”

The databases in which the search was made were PubMed, Scopus and Google Scholar. The most recent articles were selected, most of them being published after 2010.

PATHOGENY OF ATRIAL FIBRILLATION

The mechanisms by which atrial fibrillation occurs and is perpetuated are complex, still insufficiently known and differ depending on its clinical form: paroxysmal or chronic (persistent/permanent). What is clear is that the occurrence of this rhythm disorder is closely related to atrial morphology. Just as heart failure is the final evolutionary stage of long-term heart damage, atrial fibrillation is the inevitable consequence of atrial damage, which can be of four kinds: structural, electrical, damage to the autonomic nervous system or ion channels[3]. These changes are called atrial remodeling that promotes the installation of atrial fibrillation, which, once installed, induces and perpetuates new remodeling elements, explaining the transition from paroxysmal atrial fibrillation to persistent atrial fibrillation.

Electrical remodeling has as a consequence the appearance of late post-depolarizations, and the alteration of the duration of repolarization periods and therefore the development of areas with different conduction velocities at the level of atrial cardiomyocytes.

Apparently, the main substrate of electrical changes is the diastolic calcium flow from the sarcoplasmic reticulum via ryanodine receptors, which leads to increased cytosolic calcium concentration that activates SERCA2a receptors that reintroduce calcium into the reticulum, but also the Ca^{2+}/Na^{+} pump, which through the flow of sodium increases the electrical gradient and favors the production of late post-depolarizations. The onset of these late potentials in several areas simultaneously creates the so-called “drivers” which, depending on their number, cause polymorphic atrial extrasystoles, multifocal atrial tachycardia or even atrial fibrilla-

tion, suppressing the activity of the sinoatrial node. Responsible for these electrical anomalies would be the mechanism of up-regulation of I_{K1} channels that reintroduce potassium into the cell in phase 3, prolonging the duration of the action potential and contributing to the spatial heterogeneity of the duration of resting potential and action potential. In addition, the existence of mutations in genes such as GJA5 encoding connexin 40 (intercellular gap junction present at the atrial level) predisposes to atrial fibrillation (cases of idiopathic atrial fibrillation)[4,5].

Structural remodeling usually includes global dilation and myocardial fibrosis at the atrial level. Both disrupt the continuity of the excito-conductor system fibers and thus generate local conduction disturbances and reentry circuits[6,7]. Adrenergic activation also affects the expression and permeability of L-type calcium channels, ryanodine receptors and promotes atrial ectopic activity[8,9].

In conclusion, the following major predisposing factors should be noted: atrial enlargement, atrial fibrosis, intra-atrial and interatrial conduction disorders, ectopic activity and the presence of late post-depolarizations. This brief description of the main pathogenic elements involved in the initiation and progression of atrial fibrillation explains and motivates the selection of electrocardiographic aspects that may indicate its onset. The causes and molecular mechanisms involved will no longer be emphasized because they are far too complex and are not the subject of this article.

STANDARD ELECTROCARDIOGRAPHIC INDICES OF ATRIAL FIBRILLATION RISK

P-wave duration

P-wave indices are useful in quantifying atrial electrical activity and function, derived from surface ECG and have been studied concerning their predictive ability of AF development.

P-wave duration is defined as the time measured from the onset to the end of P-wave deflection. P-wave represents atrial electrical activation, the first part corresponding mainly to right atrial depolarization, and the second part to left atrial depolarization.

With a normal duration ranging between 0,06-0,11 seconds, the process begins in the sinoatrial node and then spreads in a radial fashion to depolarize the right atrium, the interatrial septum, and then the left atrium. Three internodal tracts consisting of Purkinje myocardial fibers —anterior, middle (Wenckebach), and posterior (Thorel)—, ensure rapid delivery of stimuli to the atrioventricular node. From the anterior internodal tract, the Bachmann bundle emerges, allowing fast electrical communication between the right and left atrium. P-wave duration, as a quantifier of the time needed for atrial depolarization, is therefore linked to inter and intra-atrial conduction. Literature shows that aberrations (both an increase and a decrease) in P-wave duration are associated with higher risk of atrial fibrillation[10]. P-wave duration ≥120 ms was significantly associated with AF (hazard ratio 1.55).

An increase in P-wave duration has also been linked to AF recurrence after catheter ablation. In a study aiming to establish a positive connection between P-wave indices and their predictive capacity of AF recurrences after pulmonary vein isolation in patients with normal left atrial size, subjects with prolonged P-wave duration had higher rates of AF recurrence compared to those without prolongation of the P-wave[11]. From 201 analyzed patients, 49% of those with prolonged P-wave duration developed recurrent AF, compared to only 14% from the normal P-wave duration category. These findings were confirmed in another retrospective survey conducted on a selected cohort consisting of 100 patients that underwent successful pulmonary vein isolation for paroxysmal atrial fibrillation. Greater AF recurrence rates were found in 35 subjects, which had a prolonged P-wave duration (63 vs 38%), although, after multivariate analysis, this variable has not been proven to be an independent predictor of AF recurrence[12].

The study of P-wave duration has been extended to predict the risk of incidental ischemic stroke, even in the absence of AF. Since left atrial abnormalities can lead to mechanical and electric dysfunction and therefore to a higher thromboembolic risk, ECG abnormalities such as a prolonged P-wave duration have proved to be not only markers for AF development, but also useful predictors in ischemic stroke in the absence of AF. In a meta-analysis of P-wave indices in predicting stroke risk using various prospective or retrospective cohort studies, a significant relationship was observed between maximum P-wave duration and ischemic stroke, but only when P-wave duration was analyzed as a categorical variable (>110–120 ms; odds ratio, 1.86), and not as a continuous variable[13].

Interatrial block – Bayés syndrome

As mentioned earlier, the Bachmann tract is the

main structure that allows interatrial electrical connection. Both the conduction speed and the duration of the effective refractory period of the Bachmann bundle are higher than those of the working myocardium, and this functional difference may contribute to the creation of a reentry circuit. Interatrial block (IAB) signifies abnormal conduction through Bachmann bundle.

Bayés syndrome represents the association of advanced IAB with supraventricular arrhythmias and specifically atrial fibrillation[14]. Interatrial block can be of two types: partial and advanced (**Figure 1**). In the first case, there is only a delay in the transmission of the stimulus through the Bachmann bundle, while in the second case impulse transmission is blocked, so the activation of the left atrium is made in the caudocranial direction.

Partial block is diagnosed on the ECG by identifying a P-wave with duration of ≥ 120 ms (≥ 110 ms according to other authors) with normal P-wave morphology in the inferior leads. Alternatively, advanced interatrial block is defined by a P-wave duration ≥ 120 ms and biphasic P-wave with a negative terminal part in inferior leads. Apart from these entities which are considered to be typical IAB, other forms of advanced or otherwise known as complete IAB have been encompassed based on morphological and duration criteria and are called atypical advanced IAB[15].

Left atrium dilatation frequently coexists with interatrial conduction disturbances, especially since structural atrial remodeling is a potential cause of interatrial block. However, it was concluded that a P-wave duration ≥ 120 ms is not an indicator of left atrium dilatation, but of interatrial conduction disturbance. Studies demonstrate that interatrial block, particularly advanced forms, predisposes not only to future onset AF but also to recurrence of atrial fibrillation, thus decreasing the benefit of ablation procedures in certain patients. In a meta-analysis conducted by Tse *et al.*[16] on 18,204 patients, IAB significantly predicted new-onset AF, but with statistical importance only of the advanced forms, and not in partial IAB (HR 2.58 versus 1.42). Moreover, in a study regarding the relationship between IAB and new-onset AF in patients undergoing coronary angiography and carotid ultrasonography[17], the primary finding has been that IAB is a predictor of new-onset AF in a population of patients with carotid and coronary artery disease. Both carotid and coronary artery disease are associated with a higher prevalence of IAB. This retrospective study of 355 patients also found significant differences in the AF-free survival time between subjects with IAB and without IAB using a Cox proportional hazard analysis (52.9 months vs 62.6 months)[17].

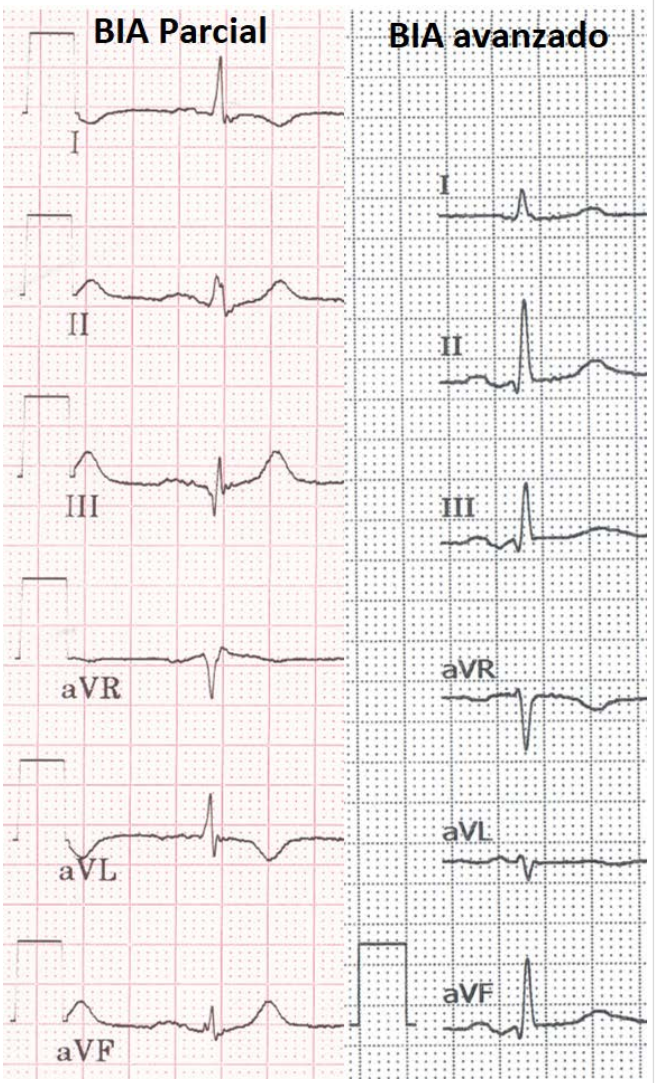

Figure 1. Examples of partial and advanced interatrial block (IAB).

P-wave dispersion (PWD)

Defined as the difference between the maximum and minimum P-wave duration in a 12-lead ECG (measures the degree of variability in P-wave duration) PWD can be calculated using manual or digital measurements[18]. This parameter has been adopted believing that electrical activity in the surface ECG closely correlates with the conduction in specific parts of the atria and could therefore be useful in assessing the heterogeneity of atrial conduction[19].

Although the evaluation of this parameter's usefulness has received controversial results, including the possibility that it is an artifact of an imprecise ECG tracing measurement[20], other studies[21,22] demonstrate its association not only with the development of new-onset AF but also with the risk of recurrence.

The connection between paroxysmal atrial fibrillation and cryptogenic stroke has been studied using P-wave dispersion as well as other P-wave indices. The results show that silent AF could play a key role in the development of cryptogenic stroke (in the absence of a direct causal relationship between certain diseases such as atherosclerosis, small vessel disease, cardiac embolism and ischemic stroke), and that there is a strong association between a high PWD, paroxysmal AF occurrence and cryptogenic stroke[21]. It has also been proven that PWD can predict later postoperative AF (POAF) in patients undergoing cardiac surgery. In a study by Lazzeroni *et al.*[22] in 200 patients in a setting of cardiac rehabilitation after cardiac surgery, there was a linear connection between PWD and POAF, with a 6% relative risk increase for each millisecond of PWD. The correlation was extremely strong over 60 ms of PWD, patients with PWD > 60 ms showed an 8.0-fold higher risk of POAF, with moderate accuracy in predicting POAF.

A role of PWD in the prediction of AF recurrence after cardioversion has also been demonstrated. The literature underlines higher PWD in patients with short-term AF recurrence (< 1 month), and no significant relationship regarding long-term recurrence[23]. Moreover, PWD was lower in patients pretreated with amiodarone, thus suggesting possible new future management strategies for patients at risk of developing AF or are likely to develop recurrence. Prolonged P-wave dispersion and duration as mentioned earlier were independently associated with increased recurrence frequency of AF after pulmonary vein isolation, and they could be useful in the future regarding the possibility of extensive ablation, or new anatomic approaches[11].

Coefficient of variation of P-wave duration

It is measured by dividing the standard deviation of P-wave duration by the mean value of P-wave duration. Among the P-wave parameters, the coefficient of variation of P-wave duration is considered to have a higher accuracy, partially because it is less prone to be affected by abnormal atrial morphology. In a study conducted to evaluate the predictive capacity of P-wave indices in AF recurrences after catheter ablation in paroxysmal AF, the coefficient of variation in P-wave duration has been significantly higher in the AF recurrence group of patients (0.090 ± 0.037 vs. 0.073 ± 0.024). Moreover, coefficient of variation of P-wave duration had the best diagnostic accuracy compared to other P-wave indices, and its predictive ability for AF recurrence was independent of other clinical parameters, with a hazard ratio of 3.180[24]. Thus, this parameter is useful in anticipating the risk of AF reappearance after interventional ablation procedures.

P-wave index

It is defined as the standard deviation of the P-wave duration across the 12 standard ECG leads. Representing a measure of disorganized atrial depolarization, P-wave index has proven its predictive power in several analyses. Moreover, it is considered one of the strongest ECG prediction factors. Even in patients not necessarily considered to be at risk for developing atrial fibrillation, certain indices, including an increased P-wave index but also premature atrial contractions, and an abnormal P-wave axis were more often encountered in the AF conversion group after 5.3 years mean follow-up in a retrospective cohort analysis of 42,751 patients[25]. The P-wave index had the strongest predictive capacity with a hazard ratio of 2.7. Furthermore, the extremes of age had a more pronounced risk, and the predictive power of P index > 35 was highest at both extremes of age.

P-wave axis

Represents the electrical wave propagation of the atria, with a mean value in the frontal plane of approximately 60° since the main vector of atrial depolarization is pointed downward and leftward. It is only recently that attention has been dedicated to this marker outside its well-known association with advanced pulmonary disease. This parameter is influenced by the positioning of the atria in the thoracic cavity and by atrial geometry, but changes in the P-wave axis may also translate an abnormal electrical propagation of the atrial depolarization wave front.

A P-wave axis greater than 55° on preoperative electrocardiograms has been independently linked to the development of postoperative atrial fibrillation in a retrospective study conducted on 526 patients, which underwent either coronary artery by-pass grafting, valve surgery, or a combination of valve

surgery and coronary artery by-pass grafting[26]. Studies show that P-wave axis outside 24–74 degrees in the frontal plane is a risk factor for new AF[27].

Maheswari *et al.*[28] tested in the ARIC study the hypothesis that an abnormal P-wave axis is associated with ischemic stroke independent of atrial fibrillation. An abnormal P-wave axis was defined as any value outside 0 to 75 degrees. Participants with abnormal P-wave axis had a higher incidence of definite ischemic stroke, after adjustment for sex, age, race and study center. This association remained significant after adjustment for stroke risk factors and AF.

P-wave morphology

This reflects the three-dimensional course of atrial depolarization propagation and can detect local conduction disturbances, which may occur in the absence of an increased total time of atrial depolarization represented by P-wave duration[29]. P-wave morphology depends on the right atrial depolarization, left atrial depolarization, and finally, on the size and shape of the atrial chambers.

Different P-wave morphologies were found in apparently healthy subjects, possibly due to variability of sinus rhythm origin and localization of the depolarization wave breakthrough site in the left atrium. A study of P-wave morphology in a high-risk population with a history of myocardial infarction and advanced congestive heart failure who participated in the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II) identified patients at risk of AF development in 20 months follow-up[30].

The orthogonal P-wave morphology was classified into one of three predefined classes (**Table**). P waves not classifiable according to these three types were denoted 'atypical'. Abnormal P-wave morphology (types 2, 3, atypical) was associated with an increased risk of AF development.

Table. Classification of the orthogonal P-wave morphology according to Holmqvist *et al.*[30].

Type	Features
Type 1	Positive leads X and Y, and negative lead Z
Type 2	Positive leads X and Y, and biphasic lead Z (−/+)
Type 3	Positive lead X and biphasic signals in leads Y (+/−) and Z (−/+)

Figure 2. Measurement of P wave terminal force in V1 lead (PTFV1) in a patient with severe left atrium dilatation due to mitral stenosis.

P-wave terminal force

Represents the product of the duration and amplitude of the negative P-wave deflection in V_1 and is considered suggestive of left atrial volume or pressure overload (**Figure 2**)[27]. However, its specificity for left atrial dilatation is low[28]. P-wave terminal force was evaluated for predicting paroxysmal AF in patients with acute ischemic stroke, without a history of paroxysmal or persistent AF[31]. The values of P-wave terminal force were significantly higher in subjects who subsequently developed paroxysmal AF after admission, with an optimal cut-off value of 40 ms×mm, which makes this parameter a strong predictor of paroxysmal AF prediction in acute ischemic stroke. In a systematic review comprising ten studies, a high P-wave terminal force (> 40 ms · mm) was associated with incident ischemic stroke even in the absence of AF, analyzed both as a continuous and a categorical variable[13].

However, in another research conducted on 78 patients with left atrial overload, there was no significant difference between the AF group and the non-AF groups regarding the P-wave terminal portion in lead V_1[32]. Moreover, the amplitude of the P-wave initial portion in V_1 was significantly higher in patients who developed atrial fibrillation. A meta-analysis conducted by Magnani *et al.*[10] regarding the P-wave terminal force from the FHS and ARIC study showed a strong association with AF in the ARIC

study, but not in the Framingham Heart Study.

P-wave area

This parameter has been studied as it is an index of left atrial geometry. Left atrial remodeling is associated with electrical conduction disturbances, providing a substrate for atrial arrhythmias, and atrial fibrillation. In a survey conducted on patients with coronary artery disease, which tested the predictive value of P-wave area for stratification of longitudinal clinical endpoints related to left atrial remodeling – AF, the total geometric area subtended within the waveform was measured. Results showed that P-wave area, among other indices, held the highest correlation with left atrial size, which was measured through cardiac magnetic resonance. Patients within the highest P-wave area quartile had a 2.4-fold increased risk of AF[33].

Magnani *et al.*[10] examined the contribution of P-wave area to risk enhancement using cross-cohort assessments from the Framingham Heart Study and ARIC study. In this meta-analysis, P-wave area was not significantly associated with AF (hazard ratio 1.31).

PR interval

Several studies linked AF development and a prolonged PR interval. In a survey conducted on 576 patients with previous AF that underwent catheter ablation, results showed that a prolonged PR interval reflected a greater left atrial size, reduced left atrial voltage, higher prevalence of persistent AF, and more importantly, it was found to be a significant predictor of recurrence after radiofrequency catheter ablation[34].

In a large study conducted on 288,181 individuals in Copenhagen, from the 11,087 that developed AF during a median follow-up period of 5.7 years, having a PR interval > 95th percentile (> 196 ms for women and > 204 ms for men) was associated with an increased risk of AF. Regarding the short PR interval (< 121 ms for women, < 129 ms for men), a higher risk of AF was found only in women[35]. However, variations in P-wave duration influence the length of the PR interval, and so its reliability in predicting AF risk.

Premature atrial contractions

Although it has been thought that these premature depolarizations are a benign electrophysiological condition with no possible serious consequences, this notion has been invalidated. Premature atrial contractions have a role in triggering atrial fibrillation and are thus independent predictors of ischemic stroke.

The frequency of atrial ectopy and the association with atrial fibrillation occurrence has been thoroughly evaluated and certified in a meta-analysis that included 12 studies[36]. Although various definitions of frequent premature atrial complexes were included, the results showed an up to 3-fold increased risk of new-onset atrial fibrillation. Alternatively, in a retrospective analysis aiming to improve the postoperative atrial fibrillation prediction model, data collected from preoperative electrocardiograms revealed that the presence of premature atrial contractions was independently associated with POAF[26]. Perez *et al.*[25] confirmed the predictive power of premature atrial beats in a retrospective analysis over 42,751 subjects, from which 1,050 developed atrial fibrillation. In the multivariate model, the presence of PACs was one of the strongest independent ECG predictors with an HR of 2.1.

Left anterior fascicular block (LAFB)

This represents an interruption or delay in conduction through the left anterior fascicle. ECG findings include left axis deviation (QRS axis from −45 to −90 degrees), qR aspect in D_I, aVL, rS in the inferior leads, and a normal or slightly prolonged QRS complex duration.

LAFB was formerly considered a simple and benign condition, but due to the fact that conduction disturbances may be caused by fibrosis of the conduction system, which is associated with myocardial fibrosis, studies regarding the connection between LAFB left heart fibrosis and atrial fibrillation, have been developed. In the Cardiovascular Healthy Study (CHS study), which was conducted on older subjects without overt cardiovascular disease, LAFB was significantly associated with atrial fibrillation after different adjustments such as age, race, sex, alcohol and tobacco consumption, body mass index, systolic blood pressure, with a hazard ratio (HR) of 1.89[37].

Moreover, LAFB was also associated with congestive heart failure and death. These observations were limited by the fact that only 39 patients with LAFB were eligible for inclusion. However, in the Copenhagen ECG study, which aimed to validate the previous findings, and replicated the analyses in their population, results showed that the link between LAFB and the risk of atrial fibrillation, heart failure and cardiovascular death were entirely con-

founded by age and sex[35]. These conflicting results might have several explanations, but further investigations regarding this topic are needed.

QT interval

It is measured from the beginning of the QRS complex to the end of the T wave on the surface electrocardiogram and represents ventricular depolarization and repolarization. This interval mainly reflects the time needed for ventricular repolarization.

A prolonged QT interval is a known risk factor for sudden cardiac death. A prolonged QTc interval (using the Framingham correction formula) was examined as a predictor of incident AF in the ARIC study. 14,538 participants were included, and results showed a 2-fold increased risk of AF in patients with a prolonged QTcFram, but no consistent data regarding a short QT interval[38].

Other studies sustain the possible link between the length of QTc interval and the onset of atrial fibrillation. The results from the Copenhagen ECG study revealed a J-shaped association between QTc interval duration and the risk of AF[39]. The risk was higher in subjects who had a QTc interval lower than the first percentile (< 372 ms), compared with the reference group; whereas with respect to longer QTc intervals, the risk increased in a dose-response manner, and there was a stronger association with lone AF.

CONCLUSIONS

The electrocardiogram is an endless source of information, education and learning, despite its use for more than a century. The fact that it is extremely accessible makes it an even more powerful clinical tool, from which new benefits should be constantly extracted. The presence of several easily obtainable electrocardiographic parameters for AF development and recurrence has certainly been proved. Numerous studies, including prospective or retrospective analyses, meta-analyses, found effective risk prediction models. Despite promising results, further research is needed to improve the existing data, or provide additional knowledge, and thus, strengthen their reliability. Nevertheless, it is certain that some of these parameters are representative of atrial electrophysiological disturbances, and undoubtedly will have a role in the discovery of both preventive and curative therapeutic interventions.

REFERENCES

1. O'Neill J, Bounford K, Anstey A, D'Silva J, Clark L, Plein S, *et al*. P wave indices, heart rate variability and anthropometry in a healthy South Asian population. PLoS One [Internet]. 2019 [citado 28 Feb 2021];14(8):e0220662. Disponible en: https://doi.org/10.1371/journal.pone.0220662
2. Militaru C, Donoiu I, Ionescu DD. P wave signal-averaged ECG in normal population and in patients with converted atrial fibrillation. Ann Noninvasive Electrocardiol. 2011;16:351-6. [DOI]
3. Nattel S, Harada M. Atrial remodeling and atrial fibrillation: recent advances and translational perspectives. J Am Coll Cardiol. 2014;63(22):2335-45. [DOI]
4. Igarashi T, Finet JE, Takeuchi A, Fujino Y, Strom M, Greener ID, *et al*. Connexin gene transfer preserves conduction velocity and prevents atrial fibrillation. Circulation. 2012;125(2):216-25. [DOI]
5. Gollob MH, Jones DL, Krahn AD, Danis L, Gong XQ, Shao Q, *et al*. Somatic mutations in the connexin 40 gene (GJA5) in atrial fibrillation. N Engl J Med. 2006;354(25):2677-88. [DOI]
6. Zou R, Kneller J, Leon LJ, Nattel S. Substrate size as a determinant of fibrillatory activity maintenance in a mathematical model of canine atrium. Am J Physiol Heart Circ Physiol. 2005;289(3):1002-12. [DOI]
7. Verheule S, Tuyls E, Gharaviri A, Hulsmans S, van Hunnik A, Kuiper M, *et al*. Loss of continuity in the thin epicardial layer because of endomysial fibrosis increases the complexity of atrial fibrillatory conduction. Circ Arrhythm Electrophysiol. 2013;6(1):202-11. [DOI]
8. Workman AJ. Cardiac adrenergic control and atrial fibrillation. Naunyn Schmiedebergs Arch Pharmacol. 2010;381(3):235-49. [DOI]
9. Bettoni M, Zimmermann M. Autonomic tone variations before the onset of paroxysmal atrial fibrillation. Circulation. 2002;105(23):2753-9. [DOI]
10. Magnani JW, Zhu L, Lopez F, Pencina MJ, Agarwal SK, Soliman EZ, *et al*. P-wave indices and atrial fibrillation: cross-cohort assessments from the Framingham Heart Study (FHS) and Atherosclerosis Risk in Communities (ARIC) study. Am Heart J. 2015;169(1):53-61. [DOI]
11. Mugnai G, Chierchia GB, de Asmundis C, Juliá J, Conte G, Sieira-Moret J, *et al*. P-wave indices as predictors of atrial fibrillation recurrence after pulmonary vein isolation in normal left atrial size. J Cardiovasc Med (Hagerstown). 2016;17(3):194-

200. [DOI]
12. Caldwell J, Koppikar S, Barake W, Redfearn D, Michael K, Simpson C, *et al.* Prolonged P-wave duration is associated with atrial fibrillation recurrence after successful pulmonary vein isolation for paroxysmal atrial fibrillation. J Interv Card Electrophysiol. 2014;39(2):131-8. [DOI]
13. He J, Tse G, Korantzopoulos P, Letsas KP, Ali-Hasan-Al-Saegh S, Kamel H, *et al.* P-Wave Indices and Risk of Ischemic Stroke: A Systematic Review and Meta-Analysis. Stroke. 2017;48(8):2066-72. [DOI]
14. Conde D, Baranchuk A. Bloqueo interauricular como sustrato anatómico-eléctrico de arritmias supraventriculares: síndrome de Bayés. Arch Cardiol Mex. 2014;84(1):32-40. [DOI]
15. Bayés de Luna A, Escobar-Robledo LA, Aristizabal D, Weir Restrepo D, Mendieta G, Massó van Roessel A, *et al.* Atypical advanced interatrial blocks: Definition and electrocardiographic recognition. J Electrocardiol. 2018;51(6):1091-3. [DOI]
16. Tse G, Wong CW, Gong M, Wong WT, Bazoukis G, Wong SH, *et al.* Predictive value of inter-atrial block for new onset or recurrent atrial fibrillation: A systematic review and meta-analysis. Int J Cardiol. 2018;250:152-6. [DOI]
17. Alexander B, Baranchuk A, Haseeb S, van Rooy H, Kuchtaruk A, Hopman W, *et al.* Interatrial block predicts atrial fibrillation in patients with carotid and coronary artery disease. J Thorac Dis. 2018;10(7):4328-34. [DOI]
18. Chávez-González E, Donoiu I. Utility of P-Wave Dispersion in the Prediction of Atrial Fibrillation. Curr Health Sci J. 2017;43(1):5-11. [DOI]
19. Michelucci A, Bagliani G, Colella A, Pieragnoli P, Porciani MC, Gensini G, *et al.* P wave assessment: state of the art update. Card Electrophysiol Rev. 2002;6(3):215-20. [DOI]
20. Zimmer K, Przywara W, Zyśko D, Sławuta A, Gajek J. The nature of P-wave dispersion - A clinically useful parameter that does not exist. Int J Cardiol. 2016;212:59-60. [DOI]
21. Acampa M, Guideri F, Tassi R, Dello Buono D, Celli L, di Toro Mammarella L, *et al.* P wave dispersion in cryptogenic stroke: A risk factor for cardioembolism? Int J Cardiol. 2015;190:202-4. [DOI]
22. Lazzeroni D, Parati G, Bini M, Piazza P, Ugolotti PT, Camaiora U, *et al.* P-wave dispersion predicts atrial fibrillation following cardiac surgery. Int J Cardiol. 2016;203:131-3. [DOI]
23. Boriani G, Diemberger I, Biffi M, Camanini C, Valzania C, Corazza I, *et al.* P wave dispersion and short-term vs. late atrial fibrillation recurrences after cardioversion. Int J Cardiol. 2005;101(3):355-61. [DOI]
24. Nakatani Y, Sakamoto T, Yamaguchi Y, Tsujino Y, Kataoka N, Kinugawa K. Coefficient of variation of P-wave duration measured using an automated measurement system predicts recurrence of atrial fibrillation. J Electrocardiol. 2019;53:79-84. [DOI]
25. Perez MV, Dewey FE, Marcus R, Ashley EA, Al-Ahmad AA, Wang PJ, *et al.* Electrocardiographic predictors of atrial fibrillation. Am Heart J. 2009; 158(4):622-8. [DOI]
26. Wong JK, Lobato RL, Pinesett A, Maxwell BG, Mora-Mangano CT, Perez MV. P-wave characteristics on routine preoperative electrocardiogram improve prediction of new-onset postoperative atrial fibrillation in cardiac surgery. J Cardiothorac Vasc Anesth. 2014;28(6):1497-504. [DOI]
27. Aizawa Y, Watanabe H, Okumura K. Electrocardiogram (ECG) for the Prediction of Incident Atrial Fibrillation: An Overview. J Atr Fibrillation [Internet]. 2017 [citado 14 Mar 2021];10(4):1724. Disponible en: https://doi.org/10.4022/jafib.1724
28. Maheshwari A, Norby FL, Soliman EZ, Koene RJ, Rooney MR, O'Neal WT, *et al.* Abnormal P-Wave Axis and Ischemic Stroke: The ARIC Study (Atherosclerosis Risk In Communities). Stroke. 2017; 48(8):2060-5. [DOI]
29. Platonov PG. P-wave morphology: underlying mechanisms and clinical implications. Ann Noninvasive Electrocardiol. 2012;17(3):161-9. [DOI]
30. Holmqvist F, Platonov PG, McNitt S, Polonsky S, Carlson J, Zareba W, *et al.* Abnormal P-wave morphology is a predictor of atrial fibrillation development and cardiac death in MADIT II patients. Ann Noninvasive Electrocardiol. 2010; 15(1):63-72. [DOI]
31. Goda T, Sugiyama Y, Ohara N, Ikegami T, Watanabe K, Kobayashi J, *et al.* P-Wave Terminal Force in Lead V1 Predicts Paroxysmal Atrial Fibrillation in Acute Ischemic Stroke. J Stroke Cerebrovasc Dis. 2017;26(9):1912-5. [DOI]
32. Ishida K, Hayashi H, Miyamoto A, Sugimoto Y, Ito M, Murakami Y, *et al.* P wave and the development of atrial fibrillation. Heart Rhythm. 2010; 7(3):289-94. [DOI]
33. Weinsaft JW, Kochav JD, Kim J, Gurevich S, Volo SC, Afroz A, *et al.* P wave area for quantitative electrocardiographic assessment of left atrial remodeling. PLoS One [Internet]. 2014 [citado 14 Mar 2021];9(6):e99178. Disponible en:

https://doi.org/10.1371/journal.pone.0099178
34. Park J, Kim TH, Lee JS, Park JK, Uhm JS, Joung B, *et al*. Prolonged PR interval predicts clinical recurrence of atrial fibrillation after catheter ablation. J Am Heart Assoc [Internet]. 2014 [citado 14 Mar 2021];3(5):e001277. Disponible en: https://doi.org/10.1161/jaha.114.001277
35. Nielsen JB, Kühl JT, Pietersen A, Graff C, Lind B, Struijk JJ, *et al*. P-wave duration and the risk of atrial fibrillation: Results from the Copenhagen ECG Study. Heart Rhythm. 2015;12(9):1887-95. [DOI]
36. Prasitlumkum N, Rattanawong P, Limpruttidham N, Kanitsoraphan C, Sirinvaravong N, Suppakitjanusant P, *et al*. Frequent premature atrial complexes as a predictor of atrial fibrillation: Systematic review and meta-analysis. J Electrocardiol. 2018;51(5):760-7. [DOI]
37. Mandyam MC, Soliman EZ, Heckbert SR, Vittinghoff E, Marcus GM. Long-term outcomes of left anterior fascicular block in the absence of overt cardiovascular disease. JAMA. 2013;309(15):1587-8. [DOI]
38. Mandyam MC, Soliman EZ, Alonso A, Dewland TA, Heckbert SR, Vittinghoff E, *et al*. The QT interval and risk of incident atrial fibrillation. Heart Rhythm. 2013;10(10):1562-8. [DOI]
39. Nielsen JB, Graff C, Pietersen A, Lind B, Struijk JJ, Olesen MS, *et al*. J-shaped association between QTc interval duration and the risk of atrial fibrillation: results from the Copenhagen ECG study. J Am Coll Cardiol. 2013;61(25):2557-64. [DOI]