Original Article

P-Wave Indices for Risk Assessment of Atrial Fibrillation in Chagas Disease

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Abstract

Background: Studies analyzing atrial activation on electrocardiograms (ECGs) have usually highlighted P-wave duration, P-wave dispersion, PR interval, P/PRi ratio, and atrial activation time (AAT). Although these indices can be predictors of atrial fibrillation (AF) in different clinical contexts, no study has analyzed them in the context of Chagas disease (CD).

Objectives: To evaluate the following electrocardiographic indices as predictors of AF in CD: P-wave duration, AAT, P-wave dispersion, PR Interval, and P/PRi ratio.

Methods: This retrospective study examined ECGs of CD patients who had been monitored for at least 10 years and analyzed the progression of five electrocardiographic indices over time in patients with and without AF.

Results: Of the 42 patients with CD included in the study, 13 experienced AF ("with AF" group) and 29 did not ("without AF"). The mean time elapsed between the first and the second ECGs analyzed was 20.55±7.54 years. While the P/PRi ratio was not different between the two groups at the time of the first ECG, it decreased from 0.68±0.11 to 0.57±0.11 in the "with AF" group and was significantly lower than the "without AF" group at the time of the second ECG (p=0.03). There were no statistically significant differences in the other parameters studied.

Conclusions: In our study, only the P/PRi ratio was shown to predict the onset of paroxysmal AF, with lower values predicting the occurrence of this arrhythmia.

Keywords: Chagas Disease; Atrial Fibrillation; Electrocardiography.

Introduction

Chagas disease (CD), described by Carlos Chagas[1,2] in 1909, is still a serious public health problem, not only in Latin America but also in several other regions due to immigration. Known and unknown parasite carriers have transmitted this disease in non-endemic countries, mainly through blood transfusion or organ donation. In Brazil, the prevailing transmission mode is the oral route, particularly in the country's northern region.

In the chronic phase, about 30 to 50% of those affected develop heart disease, including arrhythmia, thromboembolic phenomena, and heart failure. Sudden death can occur regardless of the presence of symptoms and is a cause of great concern.[2] To this day, there are no criteria to allow us to know which patients will develop heart disease and which will remain asymptomatic (that is, without clinical manifestations of the disease) throughout their lives.

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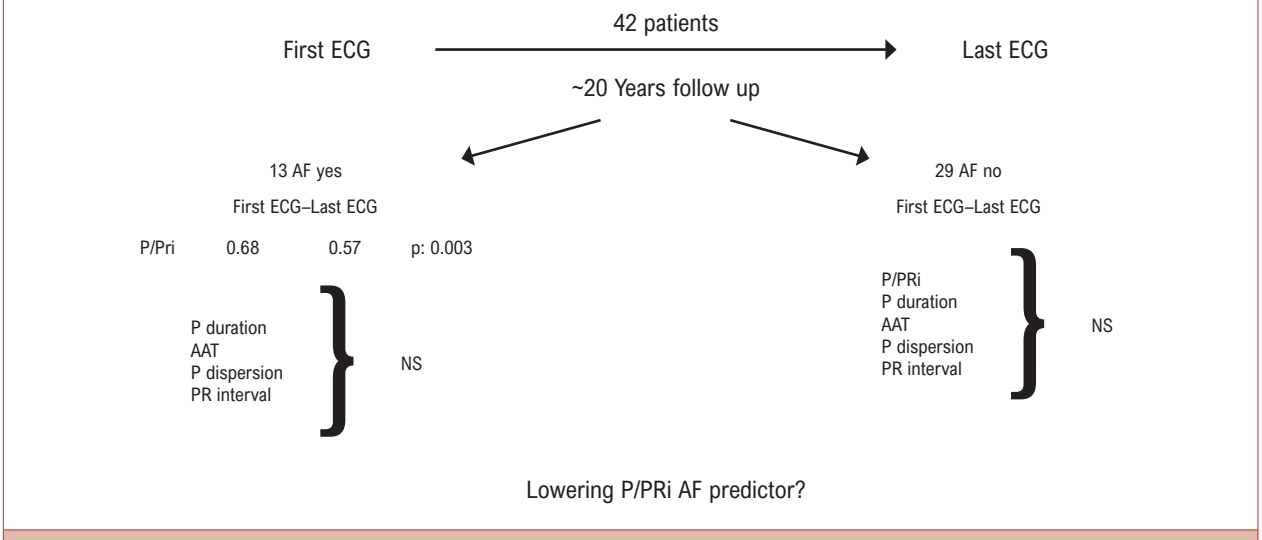
Based on what we know so far and on studies on the risk of cerebrovascular accident (CVA), atrial fibrillation (AF) seems to affect CD patients in a similar way to the general population[3-6] and is therefore an indicator of poor prognosis, usually occurring in conjunction with severe systolic dysfunction. However, information regarding its prevalence and prognosis is still required for paroxysmal or persistent AF in cases without dysfunction or with mild left ventricular ejection fraction impairment.[3-8]

There is a common-sense perception that AF may occur in more advanced stages of CD and that the prognosis of AF patients is poorer; however, specific studies are required to investigate this assumption and to provide definitive data on the incidence and prevalence of AF in CD.[3-8]

Benchimol-Barbosa et al.[9] retrospectively analyzed 50 patients with CD who were followed for approximately seven years; they found that AF occurred in nine patients (18%).[9]

Marcolino et al.[10] studied 262,685 patients treated in primary care units, with a mean age of 50.3 ± 19.3 years, 59.6% of whom were women. These authors observed that 2.8% (n=7,355) had CD. The prevalence of AF in that study was 1.8% (n=4,638). Of the AF patients, 51.8% had systemic arterial hypertension (2,402), and 8.8% (408) had CD. These two factors were independent risk factors for mortality. The low prevalence of diagnosed AF in patients with CD is noteworthy in general populations.[10]

Central Illustration: P-Wave Indices for Risk Assessment of Atrial Fibrillation in Chagas Disease



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AF: atrial fibrilation; P/PRi: P/PR ratio; AAT: atrial activation time; ECG: electrocardiogram ; NS: Not significant.

Ribeiro et al.[11] studied 499 blood donors who presented positive serology for CD, and they found evidence of AF or atrial flutter (0.4%) in two of them, and in all these patients, the ejection fraction was < 50%.

P-wave indices on the electrocardiogram and risk for AF

Publications investigating atrial activation on the electrocardiogram (ECG) have highlighted some indices that could predict AF occurrence, namely: duration of the P-wave, dispersion of the P-wave duration, atrial activation time (AAT) (interval between the beginning and the peak of the P-wave), PR interval; and the P/PRi ratio (relationship between the P-wave and PR interval).[12]

P-wave duration

For Luna,[13] the increase in the P-wave duration represents a delay in the conduction between the two atria in the Bachmann bundle.[13] This increase is related to arrhythmias. These anatomical and/or functional changes cause both structural and electrical disorganization of the atrial myocyte, resulting in atrial arrhythmias.[14,15]

Magnani et al.[16] observed that the presence of P-waves lasting > 120 ms was associated with a higher risk of AF in a study conducted in Framingham with 1,557 individuals aged over 60 years who were followed up for 15 years. However, the dispersion of P-wave duration was not associated with a higher risk of arrhythmia.[16]

In a retrospective study, Bacquer et al.[17] analyzed the morphology and P-wave measurements of 40 patients (aged 55 -74) with AF on ECG, obtained 10 years prior to the appearance of AF, and compared them with the values of 120 healthy controls matched for sex and age. An increase in P-wave duration and a bifid morphology were significantly associated with the development of arrhythmia over 10 years.[17]

Nielsen et al.[18] analyzed data of 287,933 individuals during a median follow-up period of 6.7 years. They observed that in those with a wave duration P > 130 ms, AF was more prevalent than in those with shorter P-waves. Similarly, individuals with prolonged P-waves had a 30% higher risk of cardiovascular death than those with P-waves of normal duration. With these data, the authors stated that increased P-wave duration identifies patients at higher risk for AF and cardiac death.

Analyzing ECGs performed five minutes after successful electrical cardioversion in AF patients, Censi et al.[19] observed AF recurred more often in patients with a higher P-wave duration, although this result was not statistically significant.

Kaykha et al.[20] analyzed ECGs from a cohort of 40,020 individuals, adjusted for age and heart rate, and they observed that P-waves > 120 ms corresponded to a 45% higher risk of cardiovascular death and that this was a stronger marker than QRS duration, ST segment depression, prolonged QT interval, pathological Q wave or electrocardiographic criteria of left ventricular overload. Annual mortality among individuals with P-wave duration > 120 ms was 1.2%, increasing progressively, with rates of 3.9% when P-wave duration > 140 ms.

P-wave dispersion

The P-wave dispersion is obtained by calculating average P-wave durations at each lead, and then calculating the difference between the highest and lowest of these values.

It is related to regional differences in AAT. Dilaveris and Gialafos carried out a literature review on the P-wave dispersion as a predictor of paroxysmal AF. They found that using a cutoff value of 40ms resulted in a sensitivity of 83% and a specificity of 85% for patients who would develop a recurrence of arrhythmia.[21]

Koide et al.[22] studied the P-wave dispersion to stratify the risk of progression from paroxysmal to permanent AF. Of 204 patients, 72 (35.3%) developed persistent AF in the 66 ± 8-month follow-up period. Multivariate analysis of this study showed that age (OR = 2.18; $p < 0.01$) and P-wave dispersion (OR = 1.91; $p < 0.01$) were independent predictors for the transition from paroxysmal AF to persistent AF, with P-wave dispersion having a sensitivity of 71%, a specificity of 77%, a positive predictive value of 63%, a negative predictive value of 83% and an accuracy of 75% for dispersion > 40 ms.[22]

Perez et al.[23] retrospectively analyzed the resting ECGs of 42,751 patients. After five years, 1,050 (2.4%) patients developed AF. P-wave dispersion, premature atrial beats, and changes in the P-wave axis proved to be good predictors for the emergence of this arrhythmia when the data were adjusted for sex, age, and risk factors.[23]

Başar et al.[24] evaluated the P-wave dispersion in successful maintenance of the sinus rhythm after electrical cardioversion in 26 patients with persistent AF of non-valvular etiology. Of these, 19 (73.1%) had a recurrence of the arrhythmia after 3±2.6 months. Logistic regression analysis showed that P-wave dispersion was the only independent predictor for arrhythmia recurrence. The ROC curve analysis showed that the best predictive value of P-wave dispersion for the maintenance of sinus rhythm was 58 ms, with a sensitivity of 86%, specificity of 95%, positive predictive value of 86%, and negative predictive value of 95%.[24]

To investigate potential predictors of AF recurrence, Salah et al.[25] studied 198 patients who underwent ablation along with pulmonary vein isolation, finding that a P-wave duration greater than or equal to 125 ms and P-wave dispersion greater than or equal to 40 ms were good clinical predictors of AF recurrence. However, these P-wave indices were not independent of factors such as left atrial size and age.[25]

Atrial activation time

The AAT, which is the time from the beginning of the P-wave until its peak, measured in the D2 derivation, was associated in some studies with coronary reperfusion. When coronary reperfusion is altered, it may lead to an increase in the left ventricular end-diastolic pressure and a subsequent increase in left atrial pressure, which manifests itself electrocardiographically as an extension of AAT.[13,14] This can lead to arrhythmias such as AF. In an analysis of 140 individuals, 70 of whom had a history of AF, Yildirim et al.[26] observed that an AAT above 49.5 ms was associated with AF occurrence with a sensitivity of 79.4% and specificity of 56.3%.

In a retrospective study of 90 patients admitted for ischemic CVA, Oz et al.[27] identified 34 patients (37.7%) with paroxysmal AF, and an AAT above 68.5 ms was a predictor of paroxysmal AF, with a sensitivity of 82.4% and specificity of 75%.[27]

PR interval duration

A longer PR interval has been associated with several cardiac comorbidities, such as coronary heart disease, heart failure, future need for pacemaker insertion, and death.[28] It has also been correlated with the appearance of AF and is used when calculating the Framingham risk score for AF.[29] In a large study involving 288,181 individuals followed for a period of approximately five years, Nielsen et al.[30] observed that 11,087 participants developed AF. Longer PR intervals were associated with a higher risk of AF in both men and women, and shorter PR intervals were correlated with AF in women.[30]

P/PRi Ratio

Few studies have analyzed the relationship between the P-wave and PR interval (P/PRi) and its relationship with AF. Soliman et al.[31] demonstrated that individuals with a P/PRi ratio above 0.70 had higher mortality than those in whom P/PRi was lower.[31] Analyzing Holter recordings, Moreira DAR observed that patients with episodes of AF had a P/PRi ratio above 0.69. This finding showed a positive correlation between P/PRi and the left atrial diameter determined by echocardiography. The P/PRi index appears to be a useful electrocardiographic marker for identifying patients at risk for AF.[32]

These values have been used as predictors of AF development in different clinical contexts. However, no specific studies have been performed in the context of CD.

Very little data currently exists on electrocardiographic predictors of AF in individuals with CD, and we therefore undertook to investigate this subject.

Objectives

To evaluate the following electrocardiographic P-wave indices as predictors of paroxysmal AF in patients with CD (following the order of appearance of the events on the ECG):

1. P-wave duration
2. mean P-wave dispersion
3. AAT
4. PR interval
5. P/PRi ratio

Methods

Inclusion criteria

Patients of both sexes, aged over 18 years, with a diagnosis of CD confirmed by two or more serology techniques, followed for at least ten years at Dante Pazzanese Institute of Cardiology (São Paulo, Brazil) were considered eligible for the study.

Exclusion criteria

Patients who, in addition to CD, had other relevant comorbidities – systemic arterial hypertension with target organ damage, symptomatic obstructive coronary disease, diabetes with systemic complications, renal failure, mitral valve disease, patients without a sinus rhythm on their electrocardiographic records, patients with implantable electronic cardiac devices

(ICED, which include pacemakers, cardiac resynchronizers, and cardiac defibrillators) and permanent AF were excluded.

Selection of cases

Medical records of patients with confirmed diagnosis of CD, treated at the Prof. Elias Boainain Chagas Disease Laboratory of the Dante Pazzanese Institute of Cardiology, who were followed up for at least 10 years, and whose first and last ECGs were in sinus rhythm were reviewed. AF was diagnosed by ECG or Holter recordings and clinical manifestations. If AF was not detected by these methods, the patient was classified as being "without AF". Patients were then divided into two groups: "with yes" and "without AF". The groups were then analyzed according to the following P-wave indices obtained from their ECG and Holter recordings: P-wave duration, AAT, P-wave dispersion, PR Interval, and P/PRi ratio.

Statistical analysis

As this is a retrospective study, sample calculations were not performed.

Continuous variables were described using mean and standard deviation. The comparison of ECG variables between individuals according to AF diagnosis ("with AF" or "without AF" at any time during the follow-up period) was performed using linear regression models adjusted by baseline values (first ECG) and the age at the time of the second evaluation. The results were presented as mean differences with 95% confidence intervals.

Evaluation of differences between the first and the second ECG was performed using linear regression models of AF diagnosis with the time between these ECGs as a cofactor.

Results

We retrospectively evaluated 513 medical records of patients with confirmed CD who attended the Prof. Elias Boainain Chagas Disease Laboratory of the Dante Pazzanese Institute of Cardiology (São Paulo, Brazil). Of these, 317 (61.8%) electrocardiographic traces were of sufficient quality to allow scanning and measurements to be performed. Forty-two patients (13.2%) met the inclusion criteria; 13 (31%) paroxysmal AF were identified, and in 29 (69%) patients, no electrocardiographic finding or symptoms that could be attributed to paroxysmal AF were found, and no patient had ICED. Thus, of the 317 patients initially evaluated, 13 had paroxysmal AF (4.1%). The data collected are shown in Table 1.

In the first evaluation, of the 42 patients, 24 (57.1%) had normal ECGs. The second test was normal in 16 (38.1%) patients. In both groups, most were female, 84.6% in the "with AF" group (11/13) and 62.1% in the "without AF" group (18/29). Table 2 and central illustration show the results by group in the first and second assessments.

The time elapsed between the two ECGs analyzed was, on average, 20.6 ± 7.5 years in the total sample, 19.4±7.3 years in the "with AF" group, and 21.1±7.7 years in the "without AF" group. There was no statistically significant difference between the two groups (p=0.503).

The mean age in the "with AF" group was 50.5±10.8 years, and in the "without AF" group, it was 42.7±7.5 years. There was a statistically significant difference between the groups (p=0.03), with patients who presented with AF in the ECG being significantly older in the first evaluation than those without AF. This age difference between the groups remained statistically significant in the second evaluation after at least 10 years of follow-up, with a mean age of 69.8 ± 8.1 years in the "with AF" group and 63.9 ± 9.1 years in the "without AF" group (p=0.046).

With regards to P-wave duration (Figure 1), the average duration in milliseconds (ms) in the "with AF" group was 99.5 ± 15.3 ms in the first ECG and 101.2 ± 21.5 ms in the second ECG, and in the "without AF" group it was 98.2±13.3 ms in the first ECG and 104.6±12.3 ms in the second ECG, with no statistically significant difference between the two groups (p=0.14).

For P-wave dispersion (Figure 2), the mean duration was 18.9 ± 13.9 ms in the first ECG and 19.5±9.2 ms in the second ECG in the "with AF" group, and 19.0 ±11.9 ms in the first ECG and 17.6±9.3 ms in the second ECG in the "without AF" group, with no statistically significant difference between the two groups (p=0.37).

Mean AAT in the "with AF" group was 48.9±7.2 ms in the first ECG and 50.1±10.7 ms in the second ECG, and in the "without AF" group, it was 48.2 ± 7.0 in the first ECG and 50.9 ± 6.9 ms in the second ECG. There was no statistically significant difference between the groups (p=0.21) (Figure 3).

The mean duration of the PR interval (Figure 4) in the "with AF" group was 149.5±32.0 ms in the first ECG and 184.0±54.6 ms in the second ECG. For the "without AF" group, it was 156.3±35.6 ms in the first ECG and 171.7±28.7 ms in the second ECG. There was no statistically significant difference between the groups (p=0.41).

Finally, with respect to the P/PRi ratio (Figure 5), the mean was 0.68±0.11 ms in the first ECG and 0.57±0.11 ms in the second ECG in the "with AF" group, and 0.65±0.15 ms in the first ECG and 0.62±0.12 ms in the second ECG in the "without AF", with a statistically significant difference between the two groups (p=0.03).

Discussion

It is difficult to state categorically that paroxysmal AF have not occurred in any condition, including CD, since it can only be detected by continuous monitoring using devices that can be interrogated.

The prevalence of AF in CD is still a controversial subject among the authors. Benchimol-Barbosa and Barbosa-Filho[3,9] found that it occurred in 18% of the studied patients, whereas Marcolino et al.[10] reported an 8.8% prevalence and Ribeiro et al.[11] a prevalence of 0.4%. These differences were related to the presence of heart disease in the populations. Most patients did not have chronic Chagas cardiomyopathy on the first ECG (4.1% of the 317 evaluated cases and 31% of the selected case). Patients with AF were significantly older, which is consistent with the fact that this arrhythmia is more prevalent in older individuals.

Table 1 – Data collected in the study

PATIENT	1st ECG	2nd ECG	SEX	AGE 1st ECG	AGE 2nd ECG	P WAVE 1	P WAVE 2	P1 DISPERSION	P2 DISPERSION	AAT1	AAT2	PR 1	PR 2	P/PRi 1	P/PRi 2	1st ECG	2nd ECG	AF (YES/ NO)
1	03/29/2011	03/03/2021	M	57	67	126	140	20	20	60	68	240	320	0.525	0.406	NTR	RBBB	YES
2	10/15/2004	01/01/2021	M	38	54	92	92	12	24	46	44	270	160	0.34	0.575	NDN	RBBB + LASDB	NO
3	09/04/2008	10/20/2020	F	50	63	108	84	8	32	52	40	136	160	0.79	0.525	NDN	NDN	YES
4	10/09/1991	08/31/2020	F	40	68	80	104	4	20	36	52	152	164	0.526	0.634	NDN	LBBB	YES
5	03/21/2003	08/20/2020	F	52	69	104	120	16	12	52	60	144	160	0.722	0.75	DAVR	DAVR	YES
6	05/02/1990	01/05/2015	F	42	66	116	96	4	4	54	48	148	172	0.783	0.558	RBBB + BDAS	RBBB + LASDB	YES
7	06/07/1989	10/22/2019	M	30	60	88	124	20	40	42	62	120	192	0.733	0.625	NDN	NDN	NO
8	10/25/2000	10/10/2016	F	47	63	112	88	30	8	56	42	168	136	0.666	0.647	NDN	NDN	NO
9	01/28/1988	10/21/2012	F	42	66	80	80	20	10	40	40	120	132	0.666	0.606	RBBB	RBBB	YES
10	07/17/2001	07/02/2019	F	60	78	108	104	20	20	54	52	120	132	0.9	0.787	NDN	NDN	YES
11	06/11/1974	07/16/2014	M	34	74	104	104	16	16	52	52	192	196	0.541	0.531	NDN	LASDB	NO
12	10/26/1982	05/18/2000	F	37	55	92	64	8	36	46	32	148	120	0.621	0.533	NDN	NDN	YES
13	07/17/1984	11/04/2019	M	34	69	96	96	30	8	48	46	132	196	0.727	0.489	RBBB + BDAS	RBBB + LASDB	YES
14	12/09/1985	09/18/2017	F	37	69	100	108	8	10	50	54	136	160	0.735	0.675	NDN	NDN	NO
15	12/02/2000	04/25/2019	M	52	71	88	104	26	8	44	50	144	192	0.611	0.541	NDN	NDN	NO
16	12/13/1983	04/30/2007	M	46	69	100	104	10	12	48	50	144	176	0.694	0.59	RBBB + BDAS	RBBB + LASDB	NO
17	02/03/1984	12/05/2016	F	43	76	88	92	24	6	42	46	132	148	0.666	0.621	NDN	RBBB	NO
18	01/17/1985	05/18/2020	F	44	79	64	80	12	8	32	40	168	156	0.333	0.512	RBBB	RBBB	NO
19	03/03/1983	02/02/2020	F	40	77	96	120	24	24	48	60	120	236	0.8	0.508	NDN	NDN	NO
20	12/07/1996	11/18/2019	F	50	73	100	108	0	14	50	54	196	228	0.51	0.473	NDN	NDN	NO
21	06/01/2004	02/18/2021	F	52	69	92	116	24	4	46	58	144	156	0.638	0.743	RBBB + BDAS	RBBB + LASDB	NO
22	04/13/2005	02/13/2020	M	40	55	120	116	16	18	60	58	156	152	0.769	0.763	RBBB + BDAS	RBBB + LASDB	NO
23	08/15/2005	01/30/2020	F	40	54	84	80	10	20	40	38	168	172	0.5	0.465	NDN	NDN	NO
24	08/30/1999	06/14/2020	F	36	57	104	96	12	20	52	48	128	188	0.812	0.51	RBBB + BDAS	RBBB + LASDB	NO
25	09/02/2005	03/02/2021	F	34	49	104	108	10	20	54	56	136	164	0.764	0.658	NDN	LBBB	NO
26	01/13/2004	03/16/2020	F	36	52	120	116	30	8	60	56	172	176	0.697	0.659	RBBB + BDAS	RBBB + LASDB	NO
27	02/08/2001	09/28/2020	F	60	80	88	100	12	20	44	50	132	188	0.666	0.531	RBBB	RBBB	YES
28	06/23/2005	05/05/2021	F	62	78	112	120	24	40	54	58	132	136	0.848	0.882	RBBB + BDAS	RBBB + LASDB	NO
29	04/11/2003	07/30/2019	F	54	70	88	96	16	20	44	48	220	200	0.4	0.48	NDN	NDN	NO
30	05/05/2000	05/12/2021	M	54	75	96	100	30	20	48	50	160	172	0.6	0.581	RBBB + BDAS	RBBB + LASDB	NO
31	11/X/1997	05/12/2021	M	33	57	100	112	16	32	50	56	144	180	0.694	0.622	BDAS	LASDB	NO
32	03/13/2003	05/23/2019	F	40	56	84	108	30	20	42	52	116	160	0.724	0.674	NDN	NDN	NO
33	03/10/1999	07/03/2017	M	37	56	112	128	24	24	52	60	192	212	0.583	0.603	BDAS	LASDB	NO
34	12/29/2005	05/25/2021	F	46	61	96	100	12	8	49	50	152	156	0.631	0.641	NDN	NDN	NO
35	03/15/2000	06/21/2017	M	44	61	116	108	10	16	58	54	168	192	0.69	0.565	NDN	NDN	NO
36	12/27/2005	10/08/2020	F	63	78	84	124	28	22	44	62	128	212	0.656	0.603	NDN	NDN	YES

37	04/28/2004	02/18/2021	F	43	60	116	108	64	8	58	54	128	124	0.906	0.87	NDN	NDN	NÃO
38	06/02/1996	07/02/2019	F	41	64	84	96	4	16	42	48	88	108	0.954	0.888	NDN	LASDB	NÃO
39	01/11/2001	01/16/2017	F	68	84	120	124	56	24	60	62	176	256	0.681	0.484	RBBB + BDAS	RBBB + LASDB	YES
40	11/05/2008	08/12/2020	F	52	64	92	80	20	26	46	40	168	180	0.547	0.444	NDN	LBBB	YES
41	09/25/2007	11/23/2020	F	37	51	108	112	18	24	42	36	168	172	0.643	0.651	RBBB + BDAS	RBBB + LASDB	NO
42	10/18/2006	05/31/2020	M	49	63	80	90	20	22	36	42	172	178	0.465	0.506	RBBB + BDAS	RBBB + LASDB	NO

AF: atrial fibrillation; AAT: atrial activation time ; ECG: electrocardiogram; RBBB: right bundle branch block; LBBB: left bundle branch block; LASDB: left anterior superior divisional block; NTR: nothing to report; DAVR: diffuse alterations of ventricular repolarization.

Table 2 – Analysis of electrocardiographic data

1st assessment	Presence of AF			p-value
	No (n=29)	Yes (n=13)	Total (n=42)	
Gender				
Female	18/29 (62.1%)	11/13 (84.6%)	29/42 (69.0%)	0.278
Male	11/29 (37.9%)	2/13 (15.4%)	13/42 (31.0%)	
Age at 1st ECG	42.72 ± 7.53	50.54 ± 10.80	45.14 ± 9.28	0.03
P1 Wave	98.21 ± 13.33	99.54 ± 15.32	98.62 ± 13.80	0.789
PR1	156.34 ± 35.59	149.54 ± 31.98	154.24 ± 34.27	0.544
P/PRi 1	0.65 ± 0.15	0.68 ± 0.11	0.66 ± 0.14	0.563
DISP P1	19.03 ± 11.88	18.92 ± 13.92	19.00 ± 12.37	0.98
AAT1	48.17 ± 6.99	48.92 ± 7.24	48.40 ± 6.99	0.756

2nd assessment	Presence of AF			Mean difference for the presence of AF			p-value
	No (n=29)	Yes (n=13)	Total (n=42)	Dif*	[95% CI]		
Age at 2nd ECG	63.90 ± 9.05	69.77 ± 8.06	65.71 ± 9.08				0.046
Time difference between ECGs, years	21.07 ± 7.71	19.38 ± 7.29	20.55 ± 7.54				0.503
P2 Wave	104.62 ± 12.32	101.23 ± 21.50	103.57 ± 15.54	-7.09	-16.5	2.32	0.14
PR2	171.66 ± 28.67	184.00 ± 54.65	175.48 ± 38.32	9.68	-13.61	32.97	0.41
P/PRi 2	0.62 ± 0.12	0.57 ± 0.11	0.60±0.12	-0.07	-0.13	-0.01	0.03
DISP P2	17.59 ± 9.28	19.54 ± 9.21	18.19 ± 9.19	2.95	-3.68	9.59	0.37
AAT2	50.90 ± 6.88	50.15 ± 10.66	50.67 ± 8.11	-3.02	-7.84	1.8	0.21

**Regression model adjusted by baseline assessment (1st ECG) and age (2nd ECG) (ANCOVA). AF: atrial fibrillation; P1 Wave: P-wave in the 1st electrocardiogram (ECG); P2 Wave: P-wave in the 2nd electrocardiogram; PR1: PR interval in the 1st electrocardiogram; PR2: PR interval in the 2nd electrocardiogram; P/PRi1: P/PRi ratio in the 1st electrocardiogram; P/PRi2: P/PRi ratio in the 2nd electrocardiogram; DISP P1: P-wave dispersion in the 1st electrocardiogram; DISP P2: P-wave dispersion in the 2nd electrocardiogram; AAT1: atrial activation time in the 1st electrocardiogram; AAT2: atrial activation time in the 2nd electrocardiogram.*

Studying the P-wave parameters in the 42 patients who met the inclusion criteria, we observed the following:

P-wave duration

Based on literature data on patients without CD, the increase in P-wave duration (above 125 ms) is associated with higher morbidity and mortality, in addition to a higher incidence of AF.[13,14,16-18,27] In our study, however, P-wave duration measurements were not statistically different between patients with AF and those without the arrhythmia (p = 0.503), both in the first and second ECGs. This agrees with the data by Censi et al.,[19] who observed that although P-wave duration increased in individuals with new arrhythmias after cardioversion, this increase was not statistically significant.

P-wave dispersion

Increased P-wave dispersion in non-chagasic patients has been shown to predict the onset and recurrence of AF, with borderline values ranging from 40 to 58 ms.[21-24] In our study, mean P-wave dispersion values were around 20ms, both in the first and second ECG, in patients with or without AF.

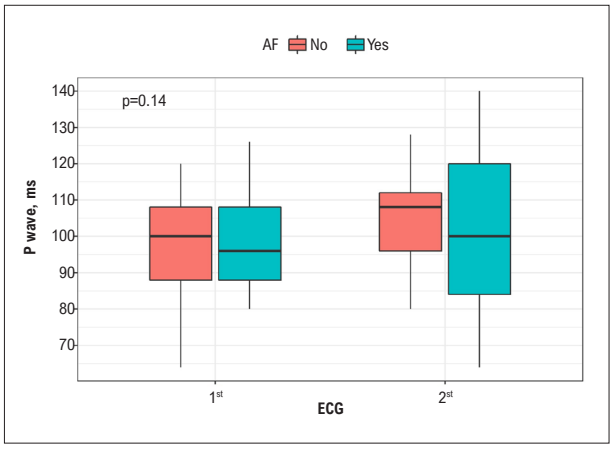

Figure 1 – *P-wave graph. AF: atrial fibrillation; ECG: electrocardiogram.*

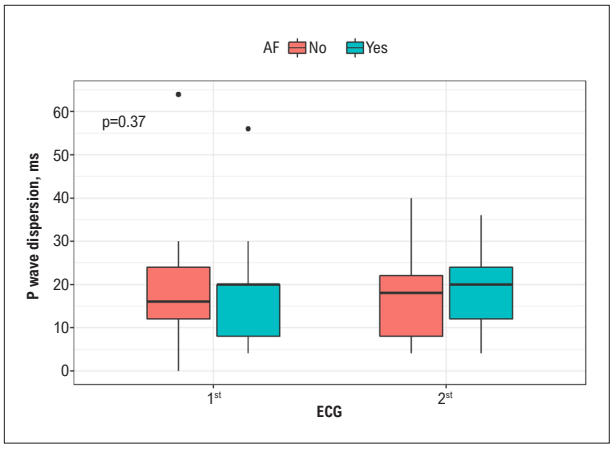

Figure 2 – *P-wave dispersion graph. AF: atrial fibrillation; ECG: electrocardiogram.*

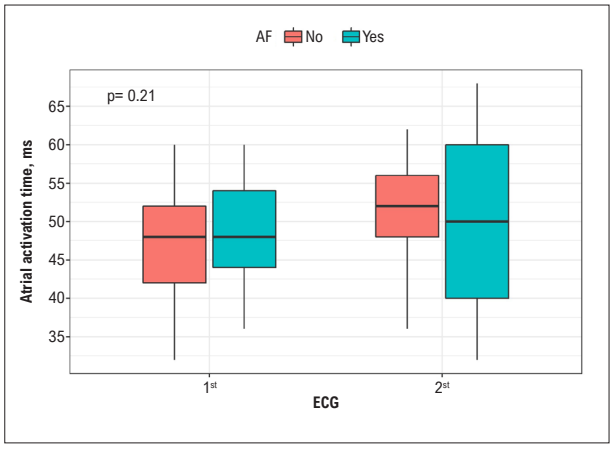

Figure 3 – *Atrial Activation Time (AAT) graph. AF: atrial fibrillation; ECG: electrocardiogram.*

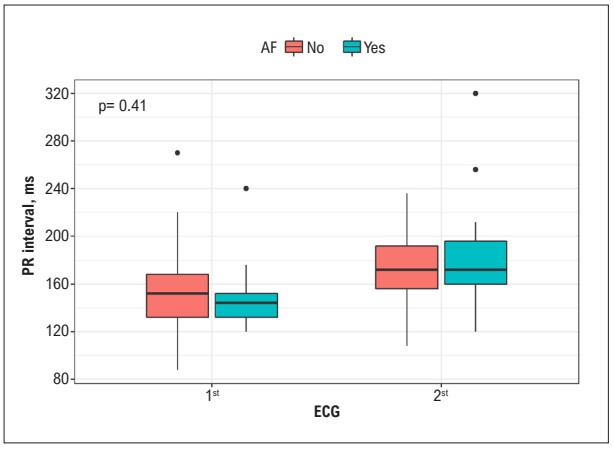

Figure 4 – *PR interval graph. AF: atrial fibrillation; ECG: electrocardiogram.*

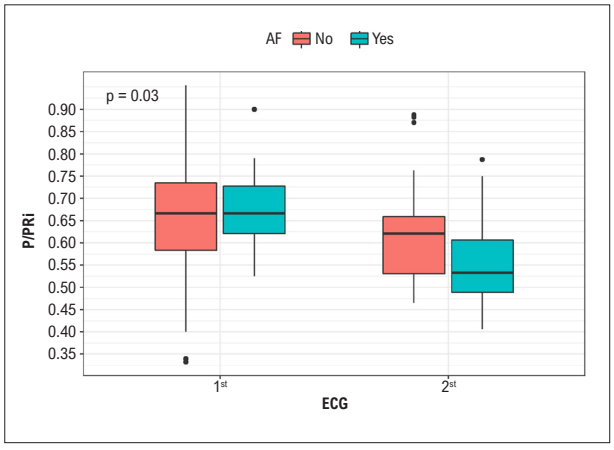

Figure 5 – *P/PRi graph. AF: atrial fibrillation; ECG: electrocardiogram.*

No significant difference was found between the groups. This was probably because P-wave duration was less than 110 ms, with no left atrial overload, which would not increase the dispersion.

Atrial activation time

Few data are available in the literature regarding the relationship between AAT and occurrence of AF. The level suggested by the literature ranges from 49.5 to 68.5 ms, above which the incidence of AF would be higher. In our study, these results were around 50 ms in both the first and second traces. However, they were not statistically different between the two groups, probably due to the absence of a significant increase in the P-wave in both ECGs.[13,14,26,27]

PR interval duration

An elevated duration of the PR interval is part of the Framingham score for predicting AF. The higher the PR, the greater the possibility of developing AF with no well-defined cutoff point. In our study, PR was maintained below 200 ms in all groups, with no difference between patients with or

without AF, and in the first and second ECG.[28-30] However, there was an increase in the PR interval between one ECG and another, even without atrioventricular block. However, this result did not reach statistical significance.

P/PRi Ratio

The relationship between the P-wave and PR interval (P/PRi) has been shown to be a predictor of AF occurrence, especially at levels above 0.69.[31,32] In our study, in the first ECG, P/PRi values were below 0.69, and there was no significant difference between patients with and without AF. In the second plot, mean P/PRi was significantly lower (p=0.03) among AF patients. Our data, therefore, differ from those in the literature. This was probably due to the lower P values in the group with arrhythmia, even though these were not significant. Another observation is that the PR interval increased between the first and second ECG in both groups, which may justify the discordant findings.

Additional comments

In our study, due to the small sample size and lower severity of our patients, we were able to demonstrate that P/PRi was just a possible predictor of AF, with an inverse relationship between P/PRi values and the occurrence of paroxysmal AF. However, the preliminary data suggest the importance of P-wave analysis in patients with CD, especially the P/PRi index, to predict possible AF, with the need for more frequent evaluations, aiming at early anticoagulation to prevent embolic events. Perhaps because our sample was composed of several patients without heart disease in the first evaluation, these measures, except for P/PRi, could not be predictors of paroxysmal AF.

The predominance of older patients in the group with AF may have been a confounding factor. However, this finding is in keeping with the literature on patients without CD, who present a higher incidence of AF with age.

Measurement techniques have not been standardized in the literature. The studies are limited due to their relatively small sample size, limited follow-up time, and several other confounding factors. No prospective study has been carried out to identify normal reference values in large populations. Population-based cohort studies are needed to evaluate the actual usefulness of electrocardiographic measurements of the P-wave and PR interval to predict not only AF but also other events such as CVA, heart failure, and even global mortality.

Prospective studies analyzing the long-term electrocardiographic evolution, together with the study of atrial function by echocardiography, could show us the importance of the behavior of the P-wave in the appearance of AF and also in CD, allowing better follow-up of these patients.

Limitations

This is a retrospective study with a small number of patients, mostly without heart disease on the first ECG. Notably, few conclusions can be drawn even after a long follow-up time (approximately 20 years), highlighting the need for long follow-up periods in CD. Due to the small number of patients, it was not possible to differentiate the behavior of the P-wave between the indeterminate and cardiac forms of CD. Prospective studies with a larger population are needed.

Conclusion

In our study on patients with CD, only the relationship between the P-wave and the PR interval (P/PRi) was shown to predict the onset of paroxysmal AF, with statistical significance, with lower values predicting the occurrence of this arrhythmia.

Author Contributions

Conception and design of the research, Analysis and interpretation of the data, Writing of the manuscript and Critical revision of the manuscript for important intellectual content h: Fragata CS, Fragata Filho AA; Acquisition of data: Fragata CS, França FF, Nogueira MF, Lourenço AM, Faccini CC; Statistical analysis: Fragata CS, Damiani LP; Obtaining financing: Fragata CS.

Potential conflict of interest

No potential conflict of interest relevant to this article was reported.

Sources of funding

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Study association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Instituto Dante Pazzanese de Cardiologia under the protocol number CAAE:2025924819.8.0000.5462. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

1. Chagas C. Nova tripanozomiaze Humana. Estudos sobre a Morfolojia e o Ciclo Evolutivo do *Schizotrypanum cruzi n. gen., sp.*, Ajente Etiolojico de Nova Entidade Morbida do Homem. Mem Inst Oswaldo Cruz. 1909;1(2):159-218. doi: 10.1590/S0074-02761909000200008.
2. Dias JC. Elimination of Chagas Disease Transmission: Perspectives. Mem Inst Oswaldo Cruz. 2009;104(Suppl 1):41-5. doi: 10.1590/s0074-02762009000900007.

3. Benchimol-Barbosa PR, Barbosa-Filho J. Mechanical Cardiac Remodeling and New-Onset Atrial Fibrillation in Long-Term Follow-Up of Subjects with Chronic Chagas' Disease. Braz J Med Biol Res. 2009;42(3):251-62. doi: 10.1590/s0100-879x2009000300006.

4. Matta JA, Aras R Jr, de Macedo CR, Cruz CG, Netto EM. Stroke Correlates in Chagasic and Non-Chagasic Cardiomyopathies. PLoS One. 2012;7(4):e35116. doi: 10.1371/journal.pone.0035116.

5. Paixão LC, Ribeiro ALP, Valacio RA, Teixeira AL. Chagas Disease: Independent Risk Factor for Stroke. Stroke. 2009;40(12):3691-4. doi: 10.1161/STROKEAHA.109.560854.

6. Maguire JH, Hoff R, Sherlock I, Guimarães AC, Sleigh AC, Ramos NB, et al. Cardiac Morbidity and Mortality Due to Chagas' Disease: Prospective Electrocardiographic Study of a Brazilian Community. Circulation. 1987;75(6):1140-5. doi: 10.1161/01.cir.75.6.1140.

7. Combellas I, Puigbo JJ, Acquatella H, Tortoledo F, Gomez JR. Echocardiographic Features of Impaired Left Ventricular Diastolic Function in Chagas's Heart Disease. Br Heart J. 1985;53(3):298-309. doi: 10.1136/hrt.53.3.298.

8. Acquatella H. Echocardiography in Chagas Heart Disease. Circulation. 2007;115(9):1124-31. doi: 10.1161/CIRCULATIONAHA.106.627323.

9. Benchimol-Barbosa PR, Barbosa-Filho J. Atrial Mechanical Remodeling and New Onset Atrial Fibrillation in Chronic Chagas' Heart Disease. Int J Cardiol. 2008;127(3):e113-5. doi: 10.1016/j.ijcard.2007.04.103.

10. Marcolino MS, Palhares DM, Benjamin EJ, Ribeiro ALP. Atrial Fibrillation: Prevalence in a Large Database of Primary Care Patients in Brazil. Europace. 2015;17(12):1787-90. doi: 10.1093/europace/euv185.

11. Ribeiro ALP, Sabino EC, Marcolino MS, Salemi VM, Ianni BM, Fernandes F, et al. Electrocardiographic Abnormalities in Trypanosoma Cruzi Seropositive and Seronegative Former Blood Donors. PLoS Negl Trop Dis. 2013;7(2):e2078. doi: 10.1371/journal.pntd.0002078.

12. 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: 10.1023/a:1016368723033.

13. Luna AB. Electrocardiographic Alterations Due to Atrial Pathology. In: Luna AB. Clinical Electrocardiography: A Textbook. 2nd ed. New York: Futura Company; 1998. p. 169-71.

14. Magnani JW, Williamson MA, Ellinor PT, Monahan KM, Benjamin EJ. P Wave Indices: Current Status and Future Directions in Epidemiology, Clinical, and Research Applications. Circ Arrhythm Electrophysiol. 2009;2(1):72-9. doi: 10.1161/CIRCEP.108.806828.

15. Ariyarajah V, Apiyasawat S, Spodick DH. Optimal P-Wave Duration for Bedside Diagnosis of Interatrial Block. Ann Noninvasive Electrocardiol. 2006;11(3):259-62. doi: 10.1111/j.1542-474X.2006.00113.x.

16. Magnani JW, Johnson VM, Sullivan LM, Gorodeski EZ, Schnabel RB, Lubitz SA, et al. P Wave Duration and Risk of Longitudinal Atrial Fibrillation in Persons ≥ 60 Years Old (from the Framingham Heart Study). Am J Cardiol. 2011;107(6):917-21.e1. doi: 10.1016/j.amjcard.2010.10.075.

17. 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(5):850-4. doi: 10.1016/j.amjcard.2007.04.017.

18. 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: 10.1016/j.hrthm.2015.04.026.

19. Censi F, Calcagnini G, Triventi M, Mattei E, Bartolini P, Corazza I, et al. P-Wave Characteristics After Electrical External Cardioversion: Predictive Indexes of Relapse. Annu Int Conf IEEE Eng Med Biol Soc. 2010;2010:3442-5. doi: 10.1109/IEMBS.2010.5627862.

20. Kaykha A, Myers J, Desser KB, Laufer N, Froelicher VF. The Prognostic Importance of Isolated P-Wave Abnormalities. Clin Cardiol. 2010;33(6):E87-93. doi: 10.1002/clc.20628.

21. Dilaveris PE, Gialafos JE. P-Wave Dispersion: A Novel Predictor of Paroxysmal Atrial Fibrillation. Ann Noninvasive Electrocardiol. 2001;6(2):159-65. doi: 10.1111/j.1542-474x.2001.tb00101.x.

22. Koide Y, Yotsukura M, Ando H, Aoki S, Suzuki T, Sakata K, et al. Usefulness of P-Wave Dispersion in Standard Twelve-Lead Electrocardiography to Predict Transition from Paroxysmal to Persistent Atrial Fibrillation. Am J Cardiol. 2008;102(5):573-7. doi: 10.1016/j.amjcard.2008.04.065.

23. 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: 10.1016/j.ahj.2009.08.002.

24. Başar N, Malçok Gürel O, Ozcan F, Ozlü MF, Biçer Yeşilay A, Cağlı K, et al. Diagnostic Accuracy of P-Wave Dispersion in Prediction of Maintenance of Sinus Rhythm After External Cardioversion of Atrial Fibrillation. Anadolu Kardiyol Derg. 2011;11(1):34-8. doi: 10.5152/akd.2011.006.

25. Salah A, Zhou S, Liu Q, Yan H. P Wave Indices to Predict Atrial Fibrillation Recurrences Post Pulmonary Vein Isolation. Arq Bras Cardiol. 2013;101(6):519-27. doi: 10.5935/abc.20130214.

26. Yıldırım E, Günay N, Bayam E, Keskin M, Ozturkeri B, Selcuk M. Relationship Between Paroxysmal Atrial Fibrillation and a Novel Electrocardiographic Parameter P Wave Peak Time. J Electrocardiol. 2019;57:81-6. doi: 10.1016/j.jelectrocard.2019.09.006.

27. Öz A, Cinar T, Kızılto Güler C, Efe SÇ, Emre U, Karabağ T, et al. Novel Electrocardiography Parameter for Paroxysmal Atrial Fibrillation in Acute Ischaemic Stroke Patients: P Wave Peak Time. Postgrad Med J. 2020;96(1140):584-8. doi: 10.1136/postgradmedj-2020-137540.

28. Crisel RK, Farzaneh-Far R, Na B, Whooley MA. First-Degree Atrioventricular Block is Associated with Heart Failure and Death in Persons with Stable Coronary Artery Disease: Data from the Heart and Soul Study. Eur Heart J. 2011;32(15):1875-80. doi: 10.1093/eurheartj/ehr139.

29. Schnabel RB, Sullivan LM, Levy D, Pencina MJ, Massaro JM, D'Agostino RB Sr, et al. Development of a Risk Score for Atrial Fibrillation (Framingham Heart Study): A Community-Based Cohort Study. Lancet. 2009;373(9665):739-45. doi: 10.1016/S0140-6736(09)60443-8.

30. Nielsen JB, Pietersen A, Graff C, Lind B, Struijk JJ, Olesen MS, et al. Risk of Atrial Fibrillation as a Function of the Electrocardiographic PR Interval: Results from the Copenhagen ECG Study. Heart Rhythm. 2013;10(9):1249-56. doi: 10.1016/j.hrthm.2013.04.012.

31. Soliman EZ, Cammarata M, Li Y. Explaining the Inconsistent Associations of PR Interval with Mortality: The Role of P-Duration Contribution to the Length of PR Interval. Heart Rhythm. 2014;11(1):93-8. doi: 10.1016/j.hrthm.2013.10.003.

32. Moreira DAR. Electrocardiographic Changes that Identify Patients at Risk for Atrial Fibrillation. J Card Arrhythm. 2018;31(2):45-51. doi: 10.24207/1983-5558v31.2-002.