











CHA₂DS₂-VASc score, P-wave indexes, and echocardiographic parameters in sinus rhythm patients without valvular heart disease

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SUMMARY

OBJECTIVE: The aim of this study was to evaluate the correlation between P-wave indexes, echocardiographic parameters, and CHA₂DS₂-VASc score in patients without atrial fibrillation and valvular disease.

METHODS: This retrospective cross-sectional study included patients of a tertiary hospital with no history of atrial fibrillation, atrial flutter, or valve disease and collected data from June 2021 to May 2022. The exclusion criteria were as follows: unavailable medical records, pacemaker carriers, absence of echocardiogram report, or uninterpretable ECG. Clinical, electrocardiographic [i.e., P-wave duration, amplitude, dispersion, variability, maximum, minimum, and P-wave voltage in lead I, Morris index, PR interval, P/PR ratio, and P-wave peak time], and echocardiographic data [i.e., left atrium and left ventricle size, left ventricle ejection fraction, left ventricle mass, and left ventricle indexed mass] from 272 patients were analyzed.

RESULTS: PR interval (RHO=0.13, p=0.032), left atrium (RHO=0.301, p<0.001) and left ventricle diameter (RHO=0.197, p=0.001), left ventricle mass (RHO=0.261, p<0.001), and left ventricle indexed mass (RHO=0.340, p<0.001) were positively associated with CHA₂DS₂-VASc score, whereas P-wave amplitude (RHO=-0.141, p=0.02), P-wave voltage in lead I (RHO=-0.191, p=0.002), and left ventricle ejection fraction (RHO=-0.344, p<0.001) were negatively associated with the same score. The presence of the Morris index was associated with high CHA₂DS₂-VASc (p=0.022).

CONCLUSION: Prolonged PR interval, Morris index, increased left atrium diameter, left ventricle diameter, left ventricle mass, and left ventricle indexed mass values as well as lower P-wave amplitude, P-wave voltage in lead I, and left ventricle ejection fraction values were correlated with higher CHA₂DS₂-VASc scores.

KEYWORDS: Heart function tests. Electrocardiography. Echocardiography. Risk factors.

INTRODUCTION

The CHA₂DS₂-VASc score is used to assess the risk of stroke in patients with atrial fibrillation (AF)^{1,2}. However, recent studies have shown validation of this score as a predictor of cardiovascular outcomes (including the development of AF), thromboembolic events, and death, even in the absence of AF³⁻⁷.

Electrocardiographic parameters such as P-wave duration (PWD), variability and dispersion, interatrial block, maximum P (Pmax), and P-wave voltage in lead I (PVL1) have been studied as risk stratifiers for AF⁸⁻¹¹. Echocardiographic parameters, including left atrial (LA) and left ventricular (LV) size, LV ejection fraction (LVEF), and LV mass, have also been associated with the risk of developing AF as well as all-cause mortality, myocardial infarction, and stroke or transient ischemic attack (TIA)¹²⁻¹⁴.

Despite the data presented, there are not enough data on the correlation between these parameters and the CHA₂DS₂-VASc score in the population without AF.

The aim of this study was to evaluate the correlation between P-wave indexes [i.e., Morris index, mean duration, standard deviation (SD) and variability of P-wave, Pmax, minimum P (Pmin), P-wave dispersion, PVL1, PR interval (PRi), P/PR ratio (PPRi), and P-wave peak time] and echocardiographic findings (i.e., LA and LV size, LVEF, LV mass, and LV indexed mass) and CHA₂DS₂-VASc score in patients without AF and without valvular disease.

METHODS

The research project that resulted in this article was sent to Plataforma Brasil, received the number CAAE

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46451521.2.0000.5462, and was approved on June 01, 2021 by the Research Ethics Committee of Dante Pazzanese Cardiology Institute. All patients included in the study signed an informed consent form.

This was a retrospective cross-sectional study that included patients with no history of AF, atrial flutter, or valve disease, who were followed up at Dante Pazzanese Cardiology Institute and underwent electrocardiogram (ECG) and echocardiogram at the same institution. Patients with unavailable medical records, pacemaker carriers, absence of echocardiogram report, or with uninterpretable ECG were excluded from the study. Overall, 321 patients were included in the study period and data collection was performed in the same period (06/01/2021 to 05/01/2022).

The insufficient data on the correlation of ECG parameters and CHA₂DS₂-VASc score made it impossible to calculate the sample size before carrying out this study, which, in turn, may serve as a basis for sample calculations for other future studies with similar objectives. Therefore, the sample size of this study was defined by convenience.

Calculation of the CHA₂DS₂-VASc score

The CHA₂DS₂-VASc score was calculated based on the data available on medical records. Information about heart failure (HF), hypertension (HTN), diabetes mellitus (DM), vascular disease, history of stroke or TIA, gender, and age at the time of ECG were obtained. A high CHA₂DS₂-VASc score was considered if ≥ 2 for males and ≥ 3 for females.

ECG analysis

All ECGs were analyzed by an investigator to determine the P-wave indexes using the CardioCalipers® program. A second investigator performed the same measurements on 20% of the sample in order to assess the interobserver agreement. Both investigators were unaware of the patients' clinical data.

PWD was measured in all 12 leads. The highest value was chosen to determine P_{max} and the lowest for P_{min}. P-wave dispersion was calculated by the difference between P_{max} and P_{min}. The mean PWD and SD were also calculated. P-wave variability was obtained by dividing the SD by the mean PWD.

The PRi was measured in lead II. The PPRi ratio was calculated by dividing the PWD by the PRi.

P-wave peak time was measured from the beginning to the peak of the P-wave in lead II. P-wave voltage (PVL1) was measured in lead I, while P-wave amplitude was measured in lead II.

The presence of the Morris index was considered when the product of the amplitude (mm) and time (ms) of a terminal negative P-wave in V1 was >40 .

Echocardiographic analysis

The following echocardiographic variables were collected: LA dimension, LV diastolic diameter, LVEF, LV mass, and LV indexed mass.

Statistical analysis

Continuous variables were presented by measures of central tendency (mean and median) and dispersion (variation and SD), and categorical variables were presented by frequency distribution (number of cases and relative percentage).

Categorical variables (high or low CHA₂DS₂-VASc score) were compared in relation to numerical variables (P-wave and echocardiographic measurements) with Student's t-test. Shapiro-Wilk's tests were used to test the normality of the data. If data normality was not verified, the Mann-Whitney U-test was adopted.

The chi-square test was used to verify the association between the categories. To verify the correlation between numerical variables, Spearman's rank correlation coefficient (RHO) was used. The kappa coefficient was applied to measure inter-rater reliability.

RESULTS

A total of 49 patients were excluded due to unavailable medical records (n=40) or the absence of available echocardiogram reports (n=9).

The mean age of the 272 individuals included in the final analysis was 62.4 (12.6) years, 56.6% (n=154) were females, 82% (n=223) of patients had HTN, 72.4% (n=197) had dyslipidemia, 35.3% (n=96) had atherosclerotic disease, 34.2% (n=93) had DM, and 21% (n=57) had HF. The mean CHA₂DS₂-VASc score was 3. The majority of patients [68% (n=185)] were on beta-blockers, and 18% (n=49) were on antiarrhythmics. Beta-blockers were indicated due to coronary disease, HF, and refractory HTN. Antiarrhythmics were indicated for the treatment of ventricular and supraventricular arrhythmias, excluding AF and atrial flutter (Table 1).

The mean LA and LV diameters were 40.1 (5.1) and 51.6 (6.9) mm, respectively. The mean LVEF was 57.9 (11)%. The mean LV mass and LV indexed mass were 209.5 (63.3) g and 117.2 (31.6) g/m², respectively. For P-wave indexes, the mean PWD was 110.3 (14.2) ms, PVL1 was 0.79 (0.27) mm, P amplitude was 1.1 (0.39) mm, and the PRi was 174.4 (39.9)

Table 1. Demographic characteristics, echocardiographic parameters, P-wave indexes, and CHA₂DS₂-VASc score.

Variable	Category/Measurements	Frequency (%) / Measurements
Age	Mean (SD)	62.4 (12.6)
Age range	18–64	140 (51.5)
	65–74	89 (32.7)
	≥75	43 (15.8)
Gender	Male	118 (43.4)
	Female	154 (56.6)
BMI (kg/m ²)	Mean (SD)	28.4 (5.5)
HF		57 (21.0)
HTN		223 (82.0)
DM		93 (34.2)
Stroke/TIA		16 (5.9)
Atherosclerotic disease		96 (35.3)
Dyslipidemia		197 (72.4)
Hypothyroidism		43 (15.8)
Smoking	Smoker	15 (5.5)
	Former smoker	69 (25.4)
	Never smoker	188 (69.1)
Beta-blocker		185 (68.0)
Antiarrhythmic		49 (18.0)
LA (mm)	Mean (SD)	40.1 (5.1)
LVEF (%)	Median (variation)	62.0 (22–79)
LV (mm)	Median (variation)	50 (36–88)
LV mass (g)	Median (variation)	198 (36–464)
LV indexed mass (g/m ²)	Median (variation)	113.1 (34–243)
Average PWD (ms)	Mean (SD)	110.3 (14.2)
P SD (ms)	Mean (SD)	14.4 (4.1)
P variability	Median (variation)	0.13 (0.03–0.24)
Maximum P (ms)	Mean (SD)	131.9 (15.2)
Minimum P (ms)	Mean (SD)	85.5 (16.1)
P dispersion (ms)	Median (variation)	44.0 (16–108)
PVL1 (mm)	Median (variation)	0.8 (0.3–2.2)
P amplitude (mm)	Median (variation)	1.1 (0.2–2.6)
PPRi	Median (variation)	0.69 (0.34–1.24)
P-wave peak time (ms)	Median (variation)	60 (28–100)
PRi (ms)	Median (variation)	172 (88–276)
Morris index		42 (15.4)
CHA ₂ DS ₂ -VASc	Median (variation)	3.0 (0–7)
CHA ₂ DS ₂ -VASc	0	5 (1.8)
	1	31 (11.4)
	2	67 (24.6)
	3	68 (25.0)
	4	59 (21.7)
	5	31 (11.4)
	6	10 (3.7)
7	1 (0.4)	
High CHA ₂ DS ₂ -VASc		193 (71.0)

BMI: body mass index; DM: diabetes mellitus; HF: heart failure; LA: left atrium; LV: left ventricle; LVEF: left ventricular ejection fraction; PPRi: P/PR ratio; PRi: PR interval; PVL1: P-wave voltage in lead I; PWD: P-wave duration; HTN: hypertension; SD: standard deviation; TIA: transient ischemic attack.

ms. The presence of the Morris index was observed in 15.4% of patients (Table 1).

The ECG analysis showed a slight correlation between the CHA₂DS₂-VASc score and PRi (RHO=0.13, p=0.032), P-wave amplitude (RHO=-0.141, p=0.02), and PVL1 (RHO=-0.191, p=0.002), when analyzed as continuous variables. The correlation was positive for PRi and negative for P-wave amplitude and PVL1. The other variables showed no correlation with the CHA₂DS₂-VASc score (Table 2).

All echocardiographic parameters analyzed were significantly correlated with the CHA₂DS₂-VASc score. The LA diameter (RHO=0.301, p<0.001), LV diameter (RHO=0.197, p=0.001), LV mass (RHO=0.261, p<0.001), and LV indexed mass (RHO=0.340, p<0.001) were positively correlated with the CHA₂DS₂-VASc score, whereas LVEF (RHO=-0.344, p<0.001) had a negative correlation (Table 2).

The CHA₂DS₂-VASc score was categorized into high (≥2 for males and ≥3 for females) and low (<2 for males and <3 for females). There was a statistically significant comparison between high CHA₂DS₂-VASc score and PRi (median of 176 ms in high CHA₂DS₂-VASc versus 164 ms in low CHA₂DS₂-VASc). A similar finding was observed with a high CHA₂DS₂-VASc score and all studied echocardiographic variables. The presence of the Morris index was also associated with high CHA₂DS₂-VASc. Morris index was observed in 18.6% of the individuals with high CHA₂DS₂-VASc (Table 3).

Interobserver variation analysis revealed CCC of 0.915 for PVL1 and 0.937 for P-wave amplitude and kappa coefficient of 1.0 for the presence of Morris index, 0.7047 for P-wave peak time, 0.9483 for PRi, and 0.9196 for PWD, indicating substantial to almost perfect agreement for all the examined variables.

DISCUSSION

In this study, we found a correlation between P-wave indexes, echocardiographic parameters, and the CHA₂DS₂-VASc score.

P-wave indexes and CHA₂DS₂-VASc score

The analysis of P-wave indexes should be stimulated by the wide availability and reproducibility of ECG in clinical practice, as it is a low-cost test.

The positive and significant correlation between PRi and the CHA₂DS₂-VASc score reflects that patients with cardiovascular comorbidities tend to have a higher occurrence of first-degree atrioventricular block. PRi prolongation alone is associated with an increased risk of AF, pacemaker implantation, and all-cause mortality¹⁵.

Table 2. Correlation between P-wave indexes, echocardiographic parameters, and CHA2DS2-VASc score.

Variable	Variation	Median	Mean (SD)	RHO	p-Value
Mean PWD (ms)	63–153.1	110.3	110.3 (14.2)	0.084	0.167
P dispersion (ms)	16–108	44	46.4 (13.5)	0.026	0.669
P amplitude (mm)	0.2–2.6	1.1	1.1 (0.4)	(-0.141)	0.020
PRi (ms)	88–276	172	174.4 (29.9)	0.130	0.032
PPRi	0.3–1.2	0.7	0.7 (0.1)	(-0.078)	0.200
P-wave peak time (ms)	28–100	60	59.0 (13.2)	(-0.027)	0.656
P SD (ms)	4.3–29.3	14.2	14.4 (4.1)	0.053	0.379
P Variability	0.03–0.24	0.13	0.13 (0.04)	0.027	0.662
PVL1 (mm)	0.3–2.2	0.8	0.8 (0.3)	(-0.191)	0.002
LA (mm)	25–57	40	40.1 (5.1)	0.301	<0.001
LVEF (%)	22–79	62	57.9 (11.0)	(-0.344)	<0.001
LV (mm)	36–88	50	51.6 (6.9)	0.197	0.001
LV mass (g)	36–464	198	209.5 (63.3)	0.261	<0.001
LV indexed mass (g/m ²)	34–243	113.1	117.2 (31.6)	0.340	<0.001

LA: left atrium; LV: left ventricle; LVEF: left ventricular ejection fraction; PPRi: P/PR ratio; PRi: PR interval; PVL1: p-wave voltage in lead I; PWD: P-wave duration; RHO: Spearman's rank correlation coefficient; SD: standard deviation. Statistically significant values are indicated in bold.

Table 3. P-wave indexes, echocardiographic parameters, and high or low CHA2DS2-VASc score.

Variable	Category/Measurements	CHA ₂ DS ₂ -VASc		p-Value
		Low	High	
PPRi	Mean (SD)	0.7 (0.1)	0.7 (0.1)	0.153*
Mean PWD (ms)	Mean (SD)	109.3 (13.3)	110.7 (14.6)	0.468*
P SD (ms)	Mean (SD)	13.9 (4.1)	14.6 (4.2)	0.224*
P variability	Median (variation)	0.13 (0.03–0.24)	0.13 (0.05–0.24)	0.292**
P-wave peak time (ms)	Median (variation)	60 (28–88)	60 (28–100)	0.946**
P dispersion (ms)	Median (variation)	44 (16–92)	48 (16–108)	0.339**
PVL1 (mm)	Median (variation)	0.8 (0.4–1.5)	0.7 (0.3–2.2)	0.220**
P amplitude (mm)	Median (variation)	1.1 (0.6–2.3)	1.1 (0.2–2.6)	0.183**
PRi (ms)	Median (variation)	164 (128–256)	176 (88–276)	0.020**
Morris index		6 (7.6)	36 (18.6)	0.022***
LA (mm)	Mean (SD)	36.7 (4.5)	41.5 (4.7)	<0.001*
LVEF (%)	Median (variation)	64 (32–75)	60 (22–79)	<0.001**
LV (mm)	Median (variation)	49 (36–61)	51 (38–88)	<0.001**
LV mass (g)	Median (variation)	172 (53.8–341)	213 (36–464)	<0.001**
LV indexed mass (g/m ²)	Median (variation)	99 (34–179.6)	118.7 (56.6–243)	<0.001**

*p-value obtained by Student's t-test. **p-value obtained by the Mann-Whitney U test. ***p-value obtained by the chi-square test. LA: left atrium; LV: left ventricle; LVEF: left ventricular ejection fraction; PPRi: P/PR ratio; PRi: PR interval; PVL1: P-wave voltage in lead I; PWD: P-wave duration; SD: standard deviation. Statistically significant values are indicated in bold.

PVL1, when reduced, is associated with recent-onset AF in the population with coronary artery disease¹⁰. This finding may be related to the propagation of the electrical stimulus of

the heart. By means of electrophysiological mapping, it was demonstrated that the electrical impulse of interatrial conduction is more displaced in the area of the Bachmann bundle in

individuals with low PVL1¹⁶. The negative correlation between PVL1 and CHA₂DS₂-VASc score in individuals without AF reinforces that this P-wave index should be valued in clinical practice.

P-wave amplitude in lead II was also negatively correlated with the CHA₂DS₂-VASc score. The P-wave amplitude, when reduced, is associated with greater rates of early AF recurrence after electrical cardioversion¹⁷.

Echocardiographic parameters and CHA₂DS₂-VASc score

In individuals with AF, echocardiographic abnormalities are commonly found such as changes in LA diameter, LA *strain*, left atrial appendage emptying velocity, presence of spontaneous contrast, and thrombus. Atrial abnormalities are also associated with thromboembolic risk and mortality¹⁸.

CHADS₂ and CHA₂DS₂-VASc scores are associated with echocardiographic risk factors for thromboembolism, such as decreased left atrial appendage emptying velocity, presence of spontaneous contrast, and thrombus¹⁹. Left atrial stasis, the presence of thrombi, and complex aortic plaque were associated with an increased risk of stroke, regardless of CHADS₂ and CHA₂DS₂-VASc scores in patients with AF²⁰. The addition of echocardiographic risk parameters can complement the clinical assessment to estimate stroke risk in patients with AF¹⁹.

Ventricular abnormalities also predict thromboembolic risk in patients with AF, such as increased LV mass, LV hypertrophy, and left ventricular dysfunction^{19,21}.

Even in the absence of AF, increased LV mass, abnormal LV geometry, and reduced LVEF are independent risk factors for death and cardiovascular diseases such as myocardial infarction and stroke^{13,14,22-24}.

In this study, a significant correlation between all echocardiographic parameters and the CHA₂DS₂-VASc score was demonstrated, being positive for LA diameter, LV, LV mass, and LV indexed mass and negative for LVEF.

ECG and echocardiographic parameters in clinical practice

The results of this study highlight the importance of the association of clinical, electrocardiographic, and echocardiographic variables in the stratification of systemic thromboembolism in patients with sinus rhythm.

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High-cost and less-available devices, such as implantable monitoring devices, have been gaining ground to identify individuals with silent AF as the identification can prevent stroke with early institution of anticoagulation. However, there is still no well-defined consensus on which patients such devices should be recommended considering health system costs²⁵.

There is still not enough evidence to establish anticoagulation as a preventive treatment for stroke in the absence of AF; however, the applicability of clinical, ECG, and echocardiographic parameters may be confirmed in the future with the development of randomized clinical trials.

Limitations

The unicentric, observational, and cross-sectional nature is the main limitation of this study. The sample size was not calculated before the start of the study because of insufficient data on the correlation of ECG parameters and CHA₂DS₂-VASc score. Moreover, information about AF and valve disease was based on medical records. Therefore, silent AF patients may be included in the study.

CONCLUSIONS

Prolonged PRi, Morris index, increased LA diameter, LV diameter, LV mass, and LV indexed mass values as well as lower P-wave amplitude, PVL1, and LVEF values were correlated with higher CHA₂DS₂-VASc scores.

AUTHORS' CONTRIBUTIONS

AVD: Conceptualization, Data curation, Formal Analysis, Methodology, Project administration, Writing – original draft. **LVA:** Conceptualization, Project administration, Supervision, Writing – review & editing. **DARM:** Conceptualization, Writing – review & editing. **MHS:** Formal Analysis, Investigation, Methodology. **KHV:** Formal Analysis, Investigation, Methodology. **PSG:** Formal Analysis, Investigation, Methodology. **RAMB:** Formal Analysis, Investigation, Methodology. **MAHV:** Formal Analysis, Investigation, Methodology. **MAD:** Formal Analysis, Investigation, Methodology. **GDC:** Formal Analysis, Methodology, Writing – review & editing.

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