ORIGINAL ARTICLE

Ratio Between Maximum and Minimum P Wave Duration (MaxPWD/MinPWD Ratio): a New Electrocardiographic Predictor for Atrial Fibrillation in Patients with ST-Elevation Acute Myocardial Infarction

Yaniel Castro-Torres[1], Raimundo Carmona-Puerta[2], Elibet Chávez-González[2]

Hospital Universitario Celestino Hernández Robau[1] and Cardiocentro Ernesto Che Guevara[2], Santa Clara – Cuba

Abstract

Background: There are electrocardiographic markers for prediction of atrial fibrillation (AF) in the clinical practice, but there is no consensus on their real utility. The development of new markers may be an alternative to improve AF prediction. This investigation has the aim to demonstrate the utility of MaxPWD/MinPWD ratio for AF prediction in patients with ST-elevation acute myocardial infarction (STEAMI).

Objective: The development of new markers may be an alternative to improve AF prediction. This investigation has the aim to demonstrate the utility of MaxPWD/MinPWD ratio for AF prediction in patients with ST-elevation acute myocardial infarction (STEAMI).

Methods: We retrospectively studied 108 patients with STEAMI admitted at Celestino Hernández Robau Hospital between January 2012 to July 2014. P wave dispersion and MaxPWD/MinPWD ratio in patients with AF were calculated. Sensibility and specificity of MaxPWD/MinPWD ratio for AF prediction was determined. Pearson linear correlation to determine the association between glycaemia values and MaxPWD/MinPWD ratio was explored.

Results: P wave dispersion and MaxPWD/MinPWD ratio were higher in patients with AF compared without AF (46.2 ms ± 8.9 ms vs. 38.7 ms ± 9.8 ms; p = 0.019) and (1.89 ± 0.37 vs. 1.65 ± 0.24, p = 0.003). The area under the ROC curve for the MaxPWD/MinPWD ratio was 0.755; 95% CI: 0.633 to 0.876; p = 0.006. There is a direct correlation between glycaemia values and MaxPWD/MinPWD ratio in patients with AF (r = 0.765; p = 0.016), but not in patients without AF (r = 0.076; p = 0.474).

Conclusion: MaxPWD/MinPWD ratio is useful to identify patients at risk for AF during STEAMI. There is association between the glycemic values and MaxPWD/MinPWD ratio. (Int J Cardiovasc Sci. 2016;29(5):370-377)

Keywords: Atrial Fibrillation/physiopathology; Electrocardiography; Myocardial Infarction; Glycemic Index; p Wave.

Introduction

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice, and is associated with an increased risk of cerebral and peripheral embolisms and heart failure.[1,2] The incidence of AF is around 1 to 2% in the general population; although it may occur in healthy hearts, its incidence is higher in several clinical settings. AF is common in patients with acute myocardial infarction, and is associated with adverse clinical outcomes.[3]

Recently, some researchers have proposed electrocardiographic markers for prediction of AF. These markers have been explored in many clinical conditions, in the improvement of patients' risk stratification and management. Some of them are the maximum p wave duration (MaxPWD),[4] the minimum p wave duration (MinPWD),[5] the p wave dispersion (PWD)[6] and p-wave terminal forces in lead V1.[7] Despite some progresses in this field, there is no international consensus on the usefulness of these predictors.

Mailing Address: Dr. Yaniel Castro-Torres
Luz Caballero #161 entre Hospital y Alejandro Oms, Parroquia, Santa Clara. Postal Code: 50200, Villa Clara – Cuba
E-mail: yanielct@infomed.sld.cu; castrotorresy@gmail.com

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Sensitivity and specificity values are very variable and in some cases have a low predictive value for AF. The discovery of new markers may represent an improvement in the prediction of this condition in different clinical settings. This study aims to demonstrate the usefulness of MaxPWD/MinPWD ratio as a new electrocardiographic marker for AF prediction in patients with ST-elevation acute myocardial infarction (STEAMI).

Methods

This was an observational cross-sectional study in patients with STEMI admitted at the intensive care unit of Celestino Hernández Robau Hospital in Santa Clara, Cuba between January 2012 to July 2014. The diagnosis of STEMI was made by clinical, electrocardiographic and biomarker criteria.

A total of 143 patients were considered eligible, and 108 patients were included in the study who were divided into two groups. We excluded patients with history of AF, febrile syndromes, infectious diseases, in use of corticosteroids or patients without complete clinical history. The first group was represented by patients that during hospitalization developed one or more episodes of AF. AF was documented by conventional electrocardiogram (ECG) or continuous monitoring (n = 11). The second group was represented by patients who did not develop AF during hospitalization (n = 97).

Clinical, electrocardiographic and laboratory variables were obtained from each patient. Clinical variables were collected by direct interview with patients, and laboratory data, including glucose levels, by conventional tests performed within the first 24 hours of admission, after an overnight fast (8 hours).

Electrocardiographic variables were obtained by the analysis and interpretation of the first ECG performed during patient's hospital stay. The ECGs were obtained in supine position by a specialized technician, using the CARDIOCID BB, a portable electrocardiogram machine made in Cuba. The tests were recorded at a paper speed of 25 mm/s and calibration of 1mV = 10 mm. All ECGs were digitized for further analysis. Measures were made with an electronic caliper by one observer in order to avoid inter-observer variability. P wave onset was defined as the junction between isoelectric line and the beginning of this wave. The offset was determined as the end of P wave and the junction with isoelectric line. P wave was measured in all leads, and only ECGs with ten or more measured P waves were included. The MaxPWD was defined as the longest P wave, MinPWD as the shortest P wave, and PWD was obtained as the difference between MaxPWD and MinPWD. MaxPWD/MinPWD ratio was calculated as the ratio between MaxPWD and MinPWD. All electrocardiographic measures were expressed in milliseconds (ms).

The qualitative variables were expressed in percentages, while quantitative variables as mean ± standard deviation. Chi-square test was applied to determine the differences in qualitative variables and the t-Student test for difference in quantitative variables between the two study groups. The normal distribution of quantitative variables was tested by the Kolmogorov-Smirnov test. The ROC curve was performed to determine the predictive capacity of MaxPWD/MinPWD ratio and to make a comparative analysis between this parameter and PWD. The Youden index, i.e., maximum (sensitivity + specificity-1) was used to identify the cutoff point for the highest sensitivity and specificity of MaxPWD/MinPWD ratio for AF prediction. Pearson linear correlation, adjusted for prior history of diabetes mellitus to determine the association between blood glucose levels at admission and MaxPWD/MinPWD ratio was applied. A p value < 0.05 was considered significant. Statistical analyses were performed using SPSS 21.0 for Windows.

Results

Table 1 shows the main clinical variables of the study population. The incidence of AF was 10.2%. Male sex was more prevalent in patients without AF compared to those with the arrhythmia (36.4% *vs.* 73.2%; p = 0.012).

In table 2 are presented the electrocardiographic markers. PWD and MaxPWD/MinPWD ratio were significantly higher in patients with AF than without AF (46.2 ms ± 8.9 ms *vs.* 38.7 ms ± 9.8 ms; p = 0.019 and 1.89 ± 0.37 *vs.* 1.65 ± 0.24; p = 0.003, respectively). MinPWD was significantly lower in patients with AF compared with those without AF (54.8 ms ± 10.2 ms *vs.* 61.4 ms ± 8.7 ms; p = 0.021).

Graph 1 shows the area under the ROC curve of MaxPWD/MinPWD ratio and PWD. The area of MaxPWD/MinPWD ratio was greater than that of the PWD for AF prediction (0.755; 95% CI: 0.633 to 0.876; p = 0.006 *vs.* 0.718; 95% CI: 0.597 to 0.838; p = 0.018, respectively). A cutoff point of 1.65 for MaxPWD/MinPWD ratio was established, which showed a sensitivity of 90.9% and a specificity of 53.6% for the diagnosis of AF.

Table 1
Clinical and laboratory variables in the studied population

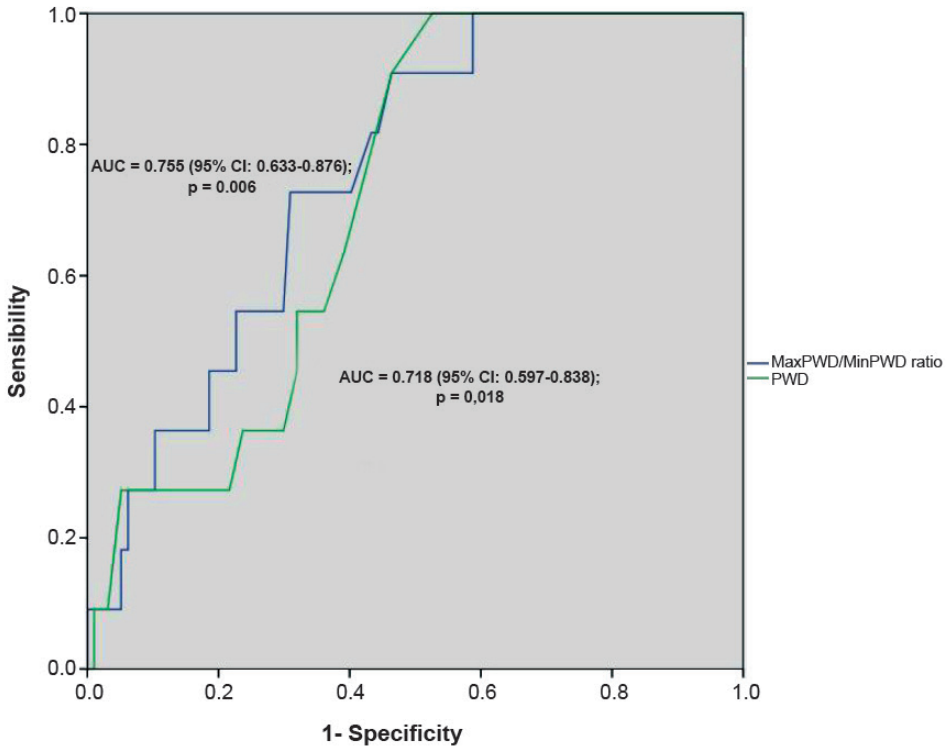
Variables	AF (n = 11)	Non AF (n = 97)	p value
Age (years)	63 ± 12	63 ± 13	0.989
Male (n; %)	4 (36.4)	71 (73.2)	0.012
Whites (n; %)	9 (81.8)	86 (88.7)	0.967
Weight (kg)	70.3 ± 10.9	71.6 ± 12.2	0.772
Height (m)	1.65 ± 0.09	1.68 ± 0.09	0.563
BMI (kg/m^2)	23.4 ± 2.0	25.9 ± 4.0	0.378
SBP (mmHg)	129 ± 21	131 ± 25	0.819
DBP (mmHg)	85 ± 20	81 ± 15	0.392
MBP (mmHg)	101 ± 22	97 ± 18	0.566
PP (mmHg)	43 ± 7	50 ± 15	0.226
Heart rate (b/m)	72 ± 14	72 ± 14	0.989
Hypertension (n; %)	6 (54.5)	59 (60.8)	0.687
IHD (n; %)	5 (45.4)	29 (29.8)	0.292
Diabetes mellitus (n; %)	1 (9.0)	10 (10.3)	0.899
Smokers (n; %)	2 (18.2)	42 (43.3)	0.108
ACEI (n; %)	3 (27.3)	32 (32.9)	0.701
Thiazide-type diuretics (n; %)	2 (18.2)	24 (24.7)	0.630
Beta-blockers (n; %)	4 (36.4)	13 (13.4)	0.048
CCB (n; %)	2 (18.2)	7 (7.2)	0.212
ASA (n; %)	4 (36.4)	16 (16.5)	0.108
Glycaemia (mmol/L)	7.6 ± 3.5	6.8 ± 2.7	0.387
Creatinine (mmol/L)	95.3 ± 35.0	85.1 ± 29.9	0.340
Uric acid (mmol/L)	346.3 ± 102.9	346.1 ± 146.7	0.997
Cholesterol-T (mmol/L)	4.7 ± 1.7	4.8 ± 1.1	0.822
TG (mmol/L)	1.4 ± 0.6	1.8 ± 0.9	0.253
Successful thrombolysis (n; %)	5/8 (62%)	39/59 (66%)	0.840

ASA: acetylsalicylic acid, ACEI: angiotensin converter enzyme inhibitor, BMI: body mass index, CCB: calcium channel blockers, DBP: diastolic blood pressure, IHD: ischemic heart disease, MBP: mean blood pressure, PP: pulse pressure, SBP: systolic blood pressure, TG: triglycerides.

Table 2
P wave parameters in patients with and without atrial fibrillation (AF)

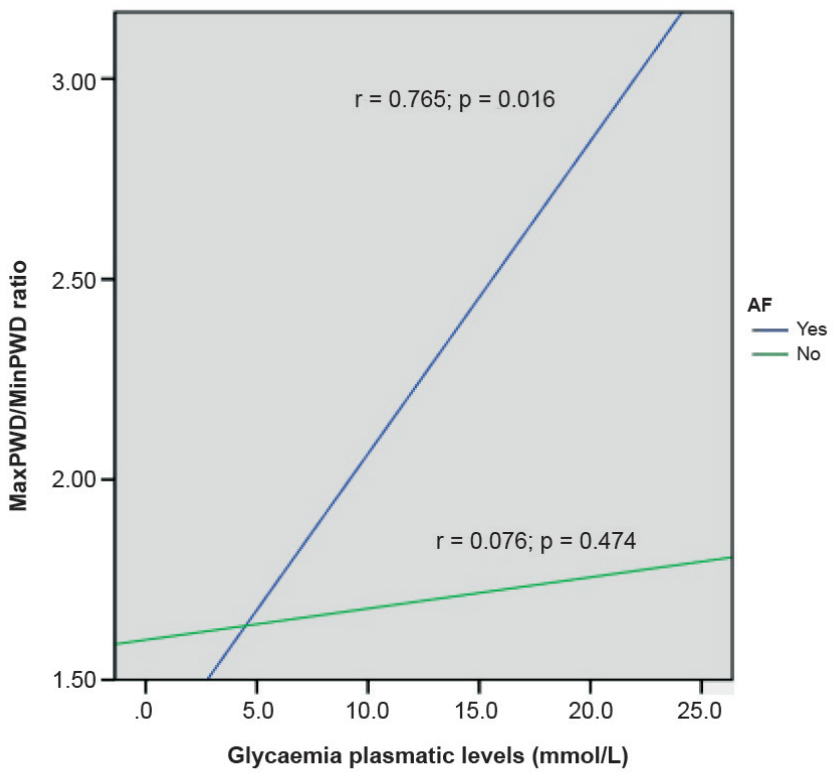
P wave parameters	AF (n = 11)	Non AF (n = 97)	p value
MaxPWD (ms)	100.9 ± 9.3	100.1 ± 11.3	0.816
MinPWD (ms)	54.8 ± 10.2	61.4 ± 8.7	0.021
PWD (ms)	46.2 ± 8.9	38.7 ± 9.8	0.019
MaxPWD/MinPWD ratio	1.89 ± 0.37	1.65 ± 0.24	0.003

MaxPWD: maximum P wave duration, MinPWD: minimum P wave duration, PWD: P wave dispersion, MaxPWD/MinPWD ratio: maximum P wave duration/minimum P wave duration ratio.



Graph 1
ROC curves of maximum p wave duration / minimum p wave duration (MaxPWD/MinPWD) ratio and P wave dispersion (PWD) for atrial fibrillation prediction.
AUC: area under the ROC curve.

Graph 2 shows that after correction by prior history of diabetes mellitus, there is a direct and significant correlation between blood glucose levels at admission and MaxPWD/MinPWD ratio in patients with AF, but not in patients who did not develop AF (r = 0.765; p = 0.016 *vs.* r = 0.076; p = 0.474, respectively).



Graph 2
Pearson linear correlation between glycaemia plasmatic values and maximum p wave duration / minimum p wave duration (MaxPWD/MinPWD) ratio, adjusted for prior history of diabetes mellitus.
AF: atrial fibrillation; PWD: P wave dispersion.

Discussion

The occurrence of AF is higher in the setting of acute myocardial ischemia. It has proven to be a risk factor for adverse clinical outcomes.[8,9] The incidence of AF in our study reached 10.2%. In a systematic review, Schmitt et al.[10] found an incidence of 2.3 to 21% of AF in hospitalized patients with acute myocardial infarction. Several factors may explain the heterogeneity of these results, as the sample size, patient comorbidities, genetic predisposition and prior drugs used to acute myocardial ischemia. Among the mechanisms involved in the development of AF in these patients are myocardial ischemia, hypokalemia, increased atrial pressure and activity of the sympathetic nervous system.[11,12]

In our study, the PWD was higher in patients who developed AF compared with those who did not suffer the arrhythmia. PWD and MaxPWD have shown to be increased during acute myocardial ischemia and to be useful in predicting AF in these patients.[13,14] However, in our study the increase in PWD depended on MinPWD, but there was not a clear influence of MaxPWD. Our results showed that MinPWD was significantly lower in patients with AF, whereas there were no significant differences in MaxPWD values between both groups. Several previous studies have shown the relationship between MinPWD and the risk for develop AF. The MinPWD has demonstrated to be a predictor for paroxysmal lone AF,[15] and Hashemi Jazi et al.[16] found an association between MinPWD and the development of AF in patients undergoing coronary artery bypass surgery. Increased activity of the sympathetic nervous system has been associated with higher cardiac conduction velocity in healthy individuals.[17] Short values of MinPWD may be observed in patients with acute myocardial infarction where there is an increased myocardial adrenergic stimulation. These findings reflect an increase in atrial electrical heterogeneity, favoring the development of AF.[18] However, in this investigation, MinPWD did not show to be useful for AF prediction.

Based on these arguments, our group proposed the creation of the MaxPWD/MinPWD ratio, which determines the ratio between the maximum and the minimum duration of the p wave on 12 leads ECG. This study showed that the MaxPWD/MinPWD ratio is significantly higher in AF patients compared without AF. Also, its area under the ROC curve was greater than that of PWD, which gives a greater ability to identify patients at risk for AF during the acute phase of acute myocardial infarction.

Variations in these parameters reflect conduction disturbances and changes in pressure and size of the atria. Differences in the electrophysiological properties between the tissues affected by ischemia and healthy tissues predispose to an inhomogeneous propagation of atrial impulse which, in turn, predisposes to AF. Another mechanism involved in the onset of AF is inflammation,[19,20] which helps to explain the higher incidence of this arrhythmia during acute myocardial infarction. Previous studies have shown increased levels of C-reactive protein,[21] interleukin 6,[22] and tumor necrosis factor[23] in patients with AF. Inflammation induces structural changes in cells, stimulating myocardial necrosis and fibrosis. Indeed, it has been observed that this process produces changes in cardiac connexins in atrial tissue, causing changes in cardiac impulse conduction.[24] During the acute phase of acute myocardial infarction, there is an increase in blood levels of inflammatory substances in response to damage to cardiomyocytes by acute ischemia. This inflammatory response is higher in patients with myocardial ischemia compared to healthy patients. Inflammation during myocardial infarction, associated with other pathophysiological mechanisms, determines an increase in electrocardiographic markers such as PWD and MaxPWD/MinPWD ratio in patients with AF.

This research showed that there is a direct and significant correlation between blood glucose levels at admission and MaxPWD/MinPWD ratio in AF patients, but not in those who did not develop the arrhythmia. Analysis of diabetes mellitus history was adjusted, avoiding the influence of this variable in the results. These findings allow us to infer that there is an association between the metabolic status of patients on admission and the risk of AF, regardless of previous condition. It has been shown that in diabetic patients, the risk of developing AF exceeds nondiabetic patients.[25] Also, during acute myocardial ischemia, elevated blood glucose levels are a predictor of poor prognosis regardless of prior diagnosis of diabetes mellitus.[26] High levels of glucose in patients with acute myocardial infarction may reflect an increase in the activity of the sympathetic nervous system, which is a well-known pathophysiological mechanism in the development of AF. In patients with acute myocardial infarction and high blood glucose levels, it has been shown an increase in platelet activation and thrombin levels and decreased fibrinolysis.[27] Acute hyperglycemia is also associated with endothelial dysfunction, increased oxidative stress and deterioration of ischemic preconditioning[28]. These mechanisms can perpetuate and/or extend myocardial ischemia and the tissue damage, which promotes the development of areas with atrial conduction disorders. Thus, the presence of elevated plasma levels of glucose in patients with AF may indirectly reflect changes in the conduction of atrial impulse, which partly explain the relationship of plasma glycaemia and values of the MaxPWD/MinPWD ratio in these patients.

This is the first study that evaluates the usefulness of MaxPWD/MinPWD ratio to identify individuals at risk for AF in the context of STEMI. The MaxPWD/MinPWD ratio is a novel marker which should be explored in future studies in order to determine its usefulness in predicting AF. In this research, this marker was associated directly with the blood glucose levels of patients at admission. However, further studies are needed to confirm such association to contribute for a better risk stratification of our patients.

Limitations

This study has several limitations. First, this is not a prospective analysis, and the sample size was relatively small. Second, the predictive capacity of MaxPWD/MinPWD ratio was limited. Third, we could not obtain echocardiographic variables including left atrial size and left ventricular ejection fraction, which would improve the interpretation of results. Also, we did not evaluate other variables associated with a high inflammatory state such as C-reactive protein. The association between acute inflammation and the MaxPWD/MinPWD ratio, and its effect on the risk for AF deserves further investigation.

Conclusions

The MaxPWD/MinPWD ratio may identify patients at risk of developing AF with greater precision than PWD in patients with STEMI. There is an association between plasma glucose levels at admission and the MaxPWD/MinPWD ratio.

Author contributions

Conception and design of the research: Castro-Torres Y. Acquisition of data: Castro-Torres Y, Carmona-Puerta R, Chávez-González E. Analysis and interpretation of the data: Castro-Torres Y, Carmona-Puerta R, Chávez-González E. Statistical analysis: Castro-Torres Y, Carmona-Puerta R, Chávez-González E. Obtaining financing: Castro-Torres Y. Writing of the manuscript: Castro-Torres Y, Carmona-Puerta R, Chávez-González E. Critical revision of the manuscript for intellectual content: Castro-Torres Y, Carmona-Puerta R, Chávez-González E.

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.

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