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Increased maximum p wave duration in smoking patients with ST-elevation acute myocardial infarction and its relationship with inflammatory markers

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SOUHRN

Úvod: Elektrokardiografické markery fibrilace síní a jejich korelace se zánětlivými markery u kuřáků s akutním infarktem myokardu dosud nebyly hodnoceny.
Materiál a metody: V článku se popisují výsledky zkřížené studie, která byla provedena v období od ledna 2012 do července 2014 ve fakultní nemocnici Hospital Universitario Celestino Hernández Robau v kubánském městě Santa Clara. Do studie bylo zařazeno celkem 115 pacientů. Vzorek byl rozdělen do dvou skupin (kuřáci a nekuřáci). Shromažďovali jsme jejich klinické a laboratorní údaje a porovnávali elektrokardiografické markery fibrilace síní se zánětlivými markery.
Výsledky: Hodnota maximální délky vlny p byla u kuřáků významně vyšší než u nekuřáků (102 ± 12 vs. 97 ± 9 s; $p = 0{,}020$). U kuřáků jsou větší i minimální délka vlny p a její disperze, ne však významně (61 ± 10 vs. 60 ± 7; $p = 0{,}476$, resp. 41 ± 10 vs. 37 ± 9; $p = 0{,}050$). U kuřáků byla zjištěna pozitivní a významná lineární korelace mezi počtem neutrofilů a maximální délkou vlny p ($r = 0{,}45$; $p = 0{,}004$), to však neplatilo pro nekuřáky ($r = 0{,}09$; $p = 0{,}49$). U kuřáků existuje negativní korelace mezi počtem lymfocytů a maximální délkou vlny p ($r = –0{,}44$; $p = 0{,}004$) stejně jako u nekuřáků ($r = –0{,}07$; $p = 0{,}62$).
Závěr: Maximální délka vlny p je při akutním infarktu myokardu s elevacemi úseku ST u kuřáků větší než u nekuřáků. Počet neutrofilů u kuřáků koreluje s maximální délkou vlny p; zatímco počet lymfocytů vykazuje negativní korelaci s maximální délkou vlny p.
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ABSTRACT

Introduction: Electrocardiographic markers for atrial fibrillation and the relationship with inflammatory markers have not been evaluated in smoker patients with acute myocardial infarction.
Material and methods: This is a cross-sectional study developed between January 2012 and July 2014 at Hospital Universitario Celestino Hernández Robau from Santa Clara, Cuba. One hundred fifteen patients were included finally. The sample was divided into two groups (smokers and non-smokers). We obtained clinical and laboratory data and compared electrocardiographic markers for atrial fibrillation in both groups and with inflammatory markers.

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Keywords:
Acute myocardial infarction
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p wave duration
Smoking

Results: Maximum p wave duration was significantly higher in smoker than non-smoker patients (102 ± 12 vs. 97 ± 9; $p = 0.020$). Minimum p wave duration and p wave dispersion also are higher in smoker patients but not significantly (61 ± 10 vs. 60 ± 7; $p = 0.476$ and 41 ± 10 vs. 37 ± 9; $p = 0.050$). There is a positive and significant linear correlation between neutrophils count and maximum p wave duration in smokers (r = 0.45; $p = 0.004$), but not in non-smokers patients (r = 0.09; $p = 0.49$). There is a negative correlation between lymphocyte count and maximum p wave duration in smokers (r = –0.44; $p = 0.004$) and in non-smoker patients (r = –0.07; $p = 0.62$).

Conclusion: Maximum p wave duration is higher in smoker patients than non-smoker patients during ST-elevation acute myocardial infarction. Neutrophil count is positively associated with maximum p wave duration in smoker patients. Lymphocyte count has a negative association with maximum p wave duration.

Introduction

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice. Its prevalence is around 1–2% in general population [1]. It increases the risk of stroke and heart failure and it is an important cause of disability and mortality. Among the risk factors for developing this condition, age, gender, hypertension, diabetes mellitus and obesity may be found [1,2]. AF has been associated with inflammation. In the atria of patients with AF, oxidative changes have been found. Furthermore, in these patients, there is higher plasma concentration of inflammatory markers [3]. Smoking has been recently recognized as a risk factor for developing AF in several populations [4]. It has been demonstrated that tobacco smoking is related with myocardial changes secondary to inflammation and atrial fibrosis [5]. It leads to electrical heterogeneity, which supports the appearance of AF. These processes may be accentuated during acute myocardial ischemia where AF is more frequent than general population and it is associated with impairment in patients' prognosis [6,7].

The analysis and interpretation of 12 leads surface electrocardiogram is a tool for prediction of AF. Some markers such as maximum and minimum p wave duration, p wave dispersion and V1 terminal forces have been proposed [8–11]. They have been demonstrated to be useful to predict AF in several clinical settings.

However, so far, these AF markers in smoker patients with acute myocardial infarction and their relationship with some markers of inflammation have not been explored. Patients with acute myocardial infarction have higher prevalence of tobacco consumption and this condition may predispose to AF. In this case, inflammation may be one of the pathophysiologic mechanisms that could link both conditions.

This study aims to evaluate some markers of AF in smoker patients with acute myocardial infarction and the correlation of maximum p wave duration with neutrophils and lymphocyte counts as inflammatory markers.

Material and methods

This is a cross-sectional study developed between January 2012 and July 2014 at Hospital Universitario Celestino Hernández Robau from Santa Clara, Cuba. One hundred forty three consecutive patients with the diagnosis of ST-elevation acute myocardial infarction were retrospectively evaluated during that time and finally 115 patients were included in the study.

The sample was divided into two groups. The first group is represented by patients with a past history of tobacco consumption and who currently continue as smokers. The second group only has patients with no past and present history of tobacco consumption. Patients were excluded if they had a concomitant condition at hospital admission such as infection, febrile status, tumors or taking anti-inflammatory drugs. Also those with electrocardiogram recording with vigorous motion and crying were excluded.

Clinical data were collected from individual history of each patient during hospital admission. Laboratory data were obtained using standard biochemical methods in the first 48 h. 12 leads electrocardiograms were recorded periodically in each subject after admission. They were obtained in supine position by a specialized technician. All electrocardiograms were electronically scanned and measures were made with an electronic caliper by two experts. p wave onset was defined as the junction between isoelectric line and the beginning of this wave and the offset as the termination of p wave and the junction with isoelectric line. p wave was measured in all leads. Only electrocardiograms with ten or more measured p waves were included. Maximum p wave was defined as the longest p wave duration and minimum p wave as the shortest p wave duration. p wave dispersion was obtained as the difference between maximum p wave and minimum p wave duration.

Categorical variables are presented as number and percent and continuous as mean ± standard deviation. Differences between two groups were evaluated using χ^2 test in categorical variables, while continuous variables were explored by Student's t-test. Normal distribution of continuous variables was determined by Kolmogórov–Smirnov test. A linear correlation was done between maximum p wave and neutrophils and lymphocytes count. The tests were considered significant when $p < 0.05$. Statistical analyses were made using the SPSS 21.0 software for Windows version.

This investigation was approved by Ethic Committee of the Celestino Hernández Robau Hospital.

Results

Table 1 shows general characteristics of the study participants. Forty-seven smoker and sixty-eight non-smoker patients were studied. Non-smoker patients had a median

age of 67 ± 12 years compared with 58 ± 12 years in smoker patients (p = 0.000). Male gender is more prevalent among smokers than non-smokers (87.2% vs. 60.3%; p = 0.002).

Table 2 shows the values of p wave in both groups. Maximum p wave duration was significantly higher in smoker than non-smoker patients (102 ± 12 vs. 97 ± 9; p = 0.020), while minimum p wave duration and p wave dispersion were also higher in smoker patients but not significantly (61 ± 10 vs. 60 ± 7; p = 0.476 and 41 ± 10 vs. 37 ± 9; p = 0.050).

Fig. 1 shows the linear correlation between maximum p wave duration and neutrophils count in smokers and non-smoker patients corrected by personal history of hypertension, diabetes mellitus and ischemic heart disease (r = 0.45; p = 0.004 vs. r = 0.09; p = 0.49).

Fig. 2 shows the linear correlation between maximum p wave duration and lymphocytes count in smoker and non-smoker patients corrected by personal history of hypertension, diabetes mellitus and ischemic heart disease (r = –0.44; p = 0.004 vs. r = –0.07; p = 0.62).

Discussion

In this study, we demonstrated that maximum p wave duration is significantly higher in smoker patients with acute myocardial infarction than non-smokers. AF is the most common arrhythmia in clinical practice. It has a higher incidence in patients with acute myocardial infarction and it is associated with an increased risk of mortality [7].

Table 1 – General data about smokers and non-smokers.

Variable	Smokers (n = 47)	Non-smokers (n = 68)	*P* value
Age (yr), mean ± SD	58 ± 12	67 ± 12	0.000
Male gender, n (%)	41 (87.2)	41 (60.3)	0.002
Whites, n (%)	42 (89.4)	60 (88.2)	0.371
Weight (kg), mean ± SD	71.38 ± 12.35	70.85 ± 11.75	0.824
Height (m), mean ± SD	1.69 ± 0.09	1.67 ± 0.07	0.403
BMI (kg/m^2), mean ± SD	25.6 ± 4.2	26.4 ± 3.7	0.463
SBP (mmHg), mean ± SD	131 ± 26	128 ± 26	0.553
DBP (mmHg), mean ± SD	81 ± 14	79 ± 17	0.613
MBP (mmHg), mean ± SD	97 ± 17	95 ± 19	0.570
PP (mmHg), mean ± SD	49 ± 15	48 ± 14	0.632
HR (b/m), mean ± SD	70 ± 12	73 ± 14	0.136
HTN, n (%)	22 (46.8)	49 (72.1)	0.006
IHD, n (%)	10 (21.3)	27 (39.7)	0.038
DM, n (%)	4 (8.5)	8 (11.7)	0.575
ACEIs, n (%)	11 (23.4)	28 (41.2)	0.048
Diuretics, n (%)	8 (17.0)	20 (29.4)	0.128
Beta-blockers, n (%)	7 (14.9)	11 (16.2)	0.852
Hematocrit (%), mean ± SD	41 ± 5	39 ± 5	0.055
WBC (109/L), mean ± SD	10.6 ± 2.2	10.9 ± 2.7	0.619
Neutrophils (%), mean ± SD	75 ± 9	72 ± 10	0.095
Lymphocytes (%), mean ± SD	23 ± 9	27 ± 10	0.064
Platelet count (10^9/L), mean ± SD	182 ± 13	182 ± 13	0.852
Inferior topography, n (%)	30 (63.8)	28 (41.1)	0.032

ACEIs – angiotensin-converting enzyme inhibitors; BMI – body mass index; DBP – diastolic blood pressure; DM – diabetes mellitus; HR – heart rate; HTN – hypertension; MBP – mean blood pressure; PP – pulse pressure; SBP – systolic blood pressure; WBC – white blood count.

Table 2 – Comparison of p wave parameters in both groups.

p wave parameters	Smokers (n = 47)	Non-smokers (n = 68)	*P* value
Max PWD	102 ± 12	97 ± 9	0.020
Min PWD	61 ± 10	60 ± 7	0.476
PW disp	41 ± 10	37 ± 9	0.050

Max PWD – maximum p wave duration; min PWD – minimum PWD; PW disp – p wave dispersion.

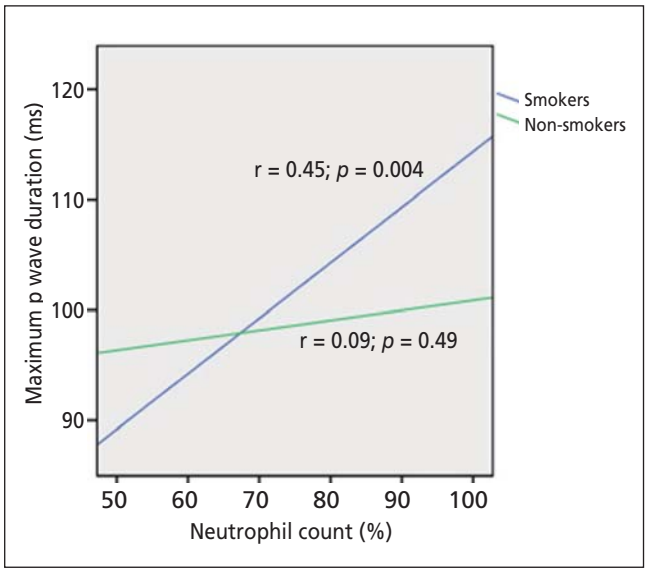

Fig. 1 – Pearson linear correlation between neutrophil count and maximum p wave duration in both groups.

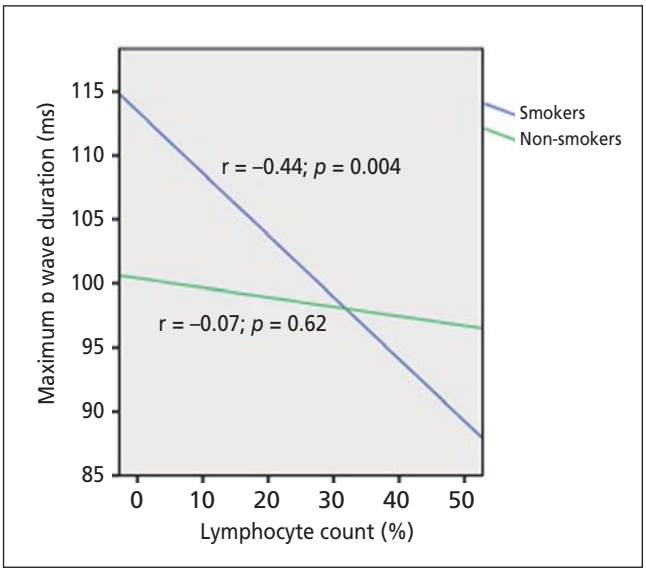

Fig. 2 – Pearson linear correlation between lymphocyte count and maximum p wave duration in both groups.

p wave duration has demonstrated to be a predictor of AF. In a cohort of patients from the Framingham Heart Study, p wave duration was related with an elevated risk for AF [8]. Recently, patients with intermediate (112–119 ms), long (120–129 ms) and very long p wave duration (≥ 130 ms) have an increased risk for incident AF compared to the reference group (100–105 ms) [12].

Tobacco consumption is one of the most important risk factors for developing cardiovascular diseases. Recently, it has been related with an increased risk for AF. Heeringa et al. [13] conducted an investigation in 5668 subjects without AF at baseline and found that, after a follow-up of 7.2 years, smoker patients had a greater risk for AF than non-smokers (RR 1.51, 95% CI 1.07–2.12; and RR 1.49, 95% CI 1.14–1.97, respectively). In another work, current smoking was associated with 2-fold risk for AF compared to non-smokers [14].

Tobacco consumption increases the oxidative stress, systemic inflammation and endothelial dysfunction, which are the mechanisms of many clinical conditions including AF [5]. Indeed, in patients with atrial fibrosis, elevated levels of nicotine associated with tobacco consumption that may stimulate the development of atrial structural and electrical abnormalities have been found [15,16]. The changes in cardiac tissue secondary to smoking increases p wave duration and hypothetically predispose to AF. These changes may be increased in patients with acute myocardial ischemia. That may explain why maximum p wave duration is significantly higher in smoker patients than non-smokers in our study.

In previous studies, AF has been associated with elevated inflammatory markers. Neutrophils might reflect systemic inflammation and they are commonly high in patients with acute myocardial ischemia [17] and AF [18]. Inflammation secondary to high neutrophils count has been associated with larger infarction size, poor short-term prognosis and further tissue damage in patients with acute myocardial infarction [19,20]. These conditions may predispose to AF. Moreover, low levels of lymphocytes have been linked to low ejection fraction and high degree of myocardial necrosis after acute myocardial infarction [21]. It appears there is a positive correlation between neutrophils counts and adverse clinical outcomes in patients with acute myocardial infarction, but a negative correlation between lymphocytes count. Both variables have been explored in this setting and are proposed as predictors of adverse outcomes. Higher levels of neutrophils to lymphocyte ratio have demonstrated to be a predictor of adverse clinical outcomes in patients with acute myocardial infarction [22,23], which support the above-mentioned relationship between these variables and clinical outcomes. These adverse outcomes may predispose to AF and prolong p wave duration on electrocardiogram.

In this study, we found that neutrophils count has significant linear correlation with maximum p wave dispersion in smoker patients but not in non-smokers. On the other hand, we also found a negative correlation between maximum p wave duration and lymphocytes count in both groups.

This allows to establish the theory that smokers have an inflammatory process more intensive during acute myocardial ischemia than non-smokers, which increase maximum p wave duration and secondarily predispose to AF.

This investigation reveals that maximum p wave duration could represent a choice for AF prediction in smoker patients with acute myocardial infarction. Additionally, the analysis of neutrophil and lymphocyte counts could help to identify those patients with elevated values of maximum p wave duration and take better preventive measures.

Both maximum p wave duration and neutrophil and lymphocyte counts are parameters that can be obtained easily in clinical practice. They do not need high cost equipment or specialized personnel. However, further studies are needed to validate these alternatives for AF prediction in smoker patients with acute myocardial infarction.

Conclusions

Maximum p wave duration is higher in smoker patients than non-smoker patients during ST-elevation acute myocardial infarction. Maximum p wave duration is positively associated with neutrophil count in smoker but not in non-smoker patients. Lymphocyte count is negatively associated with maximum p wave duration.

Conflict of interest
None declared.

Funding body
None.

Ethical statement
Authors state that the research was conducted according to ethical standards.

Informed consent
Informed consent for participation in this study was obtained from all patients.

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