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Correlation of P-wave Duration and Dispersion in Patients with Ischemia-Induced During Treadmill Exercise Testing with Duke Score

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Abstract: Prolonged P-wave duration and dispersion have been reported during transient coronary artery occlusions such as angioplasty, spontaneous angina episodes and exercise induced myocardial ischemia. The association of Duke score and P-Wave Dispersion (PWD) has been poor explored. To determine the correlation of Duke score with PWD during Treadmill Exercise Testing (TET) and this sensitivity. Study population included 78 patients with suspected coronary artery disease (64 men, mean age 53.3 years) who had underwent TET. The P-wave duration was calculated in at least eight derivations before exercise and at mean 4 min of recovery by two investigators independently. Duke score, exercise capacity and Cornell voltage were calculated. PWD were found to be significantly higher at recovery ($p = 0.008$) than at rest and in patients with ischemia-induced than those without ischemia-induced during exercise ($p = 0.003$) at recovery. There was no difference about measurements of P-wave at rest and use of beta-blocker, the Cornell voltage and exercise capacity. There was no influence of age and gender. Pearson's coefficient between Duke score and PWD at recovery was 0.005. At increase of 12 msec in this measurement, the analysis with receiver operator characteristic curve provides a sensitivity of 97% and a specificity of 96% for exercise positive response and 95 and 97%, respectively, for Duke scores ≤ 4. There was a significant increase in PWD at recovery in patients with exercise positive test. There was correlation between PWD and Duke score with increase of accuracy of TET.

Key words: P-wave dispersion, exercise testing, coronary artery disease, voltage, Duke score

INTRODUCTION

P-wave widening reflects inhomogeneous and discontinuous conduction of sinus impulses (Dilaveris *et al*., 1998). P-wave dispersion is defined as the difference between the maximum and the minimum P-wave duration on the 12-lead conventional Electrocardiogram (ECG). This recent ECG marker has been shown to be associated cardiovascular events such as atrial fibrillation, recurrent heart failure, myocardial ischemia and stroke (Dilaveris *et al*., 2000; Aytemir *et al*., 2000; Dogan *et al*., 2004; Boriani *et al*., 2005; Ozdemir *et al*., 2006; Ariyarajah *et al*., 2008; Dunbar *et al*., 2005; Altas *et al*., 2011). Prolonged P-wave duration and dispersion have been reported during transient coronary artery occlusions such as angioplasty, spontaneous angina episodes and exercise induced myocardial ischemia (Dunbar *et al*., 2005; Dilaveris *et al*., 1999; Ozmen *et al*., 2001; Batur *et al*., 2002; Ariyarajah *et al*., 2007).

However, several investigations have identified the significance of the P-wave in relation to ischemia during treadmill exercise testing, the literature is poor about association of Duke score and P-wave dispersion (Ariyarajah *et al*., 2006). Thus, the purpose of this study was to determine the correlation of Duke score with P-wave dispersion during exercise testing and this sensitivity.

MATERIALS AND METHODS

The study population consisted of 78 patients with suspected coronary artery disease. The patients with congestive heart disease, atrial fibrillation, ventricular pre-excitation, left bundle branch block and pacemakers rhythms were excluded from the study. The study was conducted after approval of local ethics committee and the patients gave their consent for inclusion in the study. All patients underwent clinical examination and exercise treadmill testing. The 12-lead ECG was recorded during

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exercise test at a paper speed of 25 mm sec^{-1} and 1 mV. The P-wave duration was calculated in all leads or at least eight leads of the ECG simultaneously recorded at rest before exercise and at mean 4 min of recovery after exercise. Measurement of P-wave duration was carried out manually using caliper. To improve accuracy, measurements were performed with magnifying lenses for defining ECG deflection. The onset of P-wave was defined as the point of the first visible upward departure of the trace from the bottom of the baseline for the positive waves and as the point of first downward departure from the top of baseline for negative waves. The return of the bottom of the trace to the baseline in positive waves was considered to be the end of the P-wave. The difference between the maximum P-wave duration and the minimum duration was defined as P-wave dispersion. These measurements were performed by two of the investigators without knowledge of patients' clinical status and independently. Inter-observer coefficients of variation (standard deviation of differences between two observations divided by the mean value) expressed in percent were determined in 44 randomly selected study participants and were found as 3.4 and 4.3% for P-wave maximum at rest and at recovery and 3.3 and 3.6% for P-wave dispersion, respectively.

Treadmill exercise testing had been considered positive in the presence of ≥1 mm horizontal or downsloping ST-segment depression (measured 80 msec after the J-point) in ≥3 consecutive beats of a single ECG lead during the exercise or recovery when compared with the ECG at rest (Gibbons *et al*., 2002). Duke treadmill score was calculated as exercise time (min) -5× (amount of ST-segment deviation in millimeters) -4× exercise angina index (which had a value of 0 if there was no exercise angina, 1 if exercise angina occurred and 2 if angina was the reason the patient stopped exercising). Exercise capacity was expressed as METs of work-load achieved (1 MET, a unit of oxygen uptake at rest was designated as oxygen 3.5 mL/kg/min). Chronotropic incompetence, characterized by an attenuated heart rate response to exercise was defined as the failure to achieve 85% of the maximum age-predicted heart rate (defined by 220 bpm minus the patient's age). The diagnostic criterion for left ventricular hypertrophy used was the Cornell voltage (Hancock *et al*., 2009). QT dispersion was calculated as the difference in ms between the longest and shortest measured QT intervals in all leads of the ECG simultaneously recorded at rest before exercise and at mean four minute of recovery after exercise. QT intervals were measured manually and were corrected for the effects of heart rate using a modified Bazett's original formula ($QTc = QT/RR^{1/2}$) (Bazett, 1920). Coronary angiography was performed in patients with ischemia-induced during exercise.

Statistical analysis: Statistical analyses were performed with SPSS for Windows Version 12.0 (SPSS Inc. Chicago, Illinois). Data are expressed as the mean value±SD for continuous variables and as frequencies for categorical variables. To compare continuous variables non-parametric methods (Mann-Whitney and Wilcoxon tests) were used and Chi-square statistics were used for categorical variables. Relation between variables was assessed using Pearson's and Spearman's correlation coefficients. Test performance for the discrimination of subjects with positive treadmill exercise testing and Duke score ≤4 (moderate and high risk) on the of their P-wave dispersion was tested with Receiver Operator Characteristic (ROC) curve (Cook, 2007). A $p<0.05$ was considered significant.

RESULTS AND DISCUSSION

The mean age of the patients enrolled is 53.34±10.64 years (range 23-70), 64 men. The characteristics at baseline and during exercise are shown in Table 1. There were significantly different in the mean maximum P-wave duration and P-wave dispersion at rest and at recovery with Wilcoxon test ($p = 0.042$ and 0.008, respectively). There was a significant increase in corrected QT dispersion at recovery ($p = 0.008$). About 25 patients were receiving beta-blocker agents and 23 were presented left hypertrophy ventricular. The measurements of QT intervals were similar with respect to these characteristics whereas P-wave dispersion was higher in patients with beta-blocker at rest (28.3×22.0 msec, $p = 0.026$) and at recovery (32.0×26.4 msec, $p = 0.026$). During treadmill exercise testing positive change ST-segment occurred in 34 patients. The comparisons between patients with and without ischemia-induced during exercise are shown in Table 2.

There was no difference about measurements of P-wave at rest and use of beta-blocker, the Cornell

Table 1: Characteristics baseline and during treadmill exercise testing of study patients

Variables	Values (mean±SD)
Age (years)	53.34
Gender (male/female)	64/14
Maximum P-wave duration at rest (msec)	107.69±12.12
Minimum P-wave duration at rest (msec)	83.69±11.51
P-wave dispersion at rest (msec)	24.05±11.08
Corrected QT dispersion at rest (msec)	42.72±16.32
ST-segment depression (mm)	0.86 (0-3.50)
Total exercise duration (min)	8.76
METs	9.78
Chronotropic incompetence (%)	14.05
VO2 (mL/kg/min)	34.20
Duke score	3.77 (-17.57 to 15.75)
Maximum P-wave duration at recovery (msec)	110.12±11.57
Minimum P-wave duration at recovery (msec)	81.63±7.06
P-wave dispersion at recovery (msec)	28.20±10.86
Corrected QT dispersion at recovery (msec)	48.90±19.52

VO2: maximal oxygen uptake; SD: Standard Deviation

Table 2: Comparison between patients with and without ischemia-induced during exercise

Variables	Patients with ischemia-induced during exercise (n = 34), mean	Patients without ischemia-induced during exercise (n = 44), mean	p-value
Age (years)	56.7	50.8	0.021
Patients with beta-blocker	7.0	18.0	0.086
P-wave dispersion at rest (msec)	21.6	25.9	0.139
Corrected QT dispersion at rest (msec)	41.8	43.3	0.813
Cornell voltaje (mm)	22.0	18.0	0.133
Exercise time (min)			
METs	9.6	9.8	0.175
P-wave dispersion at recovery (msec)	32.2	25.0	0.003
Corrected QT dispersion at recovery (msec)	52.3	46.0	0.375
Duke score	2.8	8.8	0.000

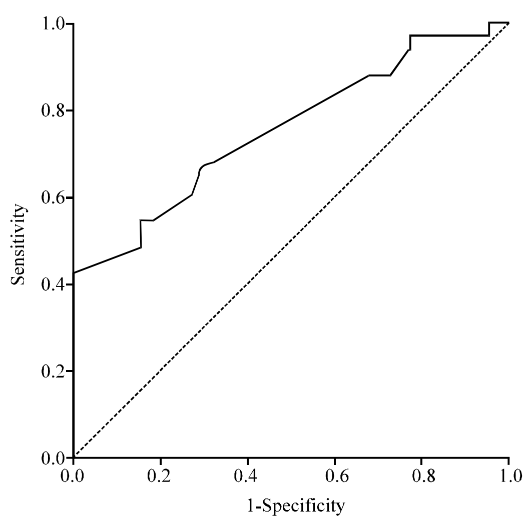

Fig. 1: ROC curve of the P-wave dispersion at recovery exercise for the diagnosis ischemia-induced exercise

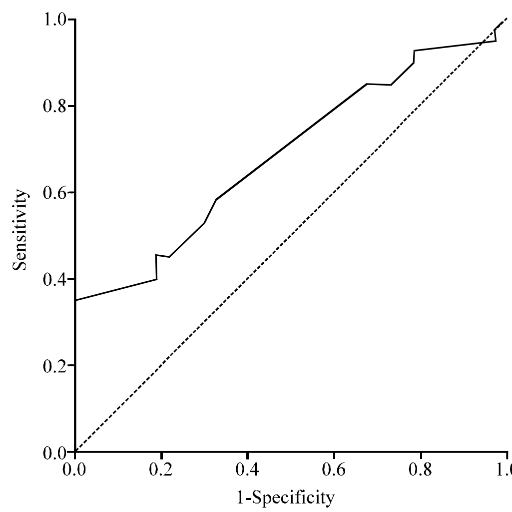

Fig. 2: ROC curve of the P-wave dispersion at recovery for the stratification Duke score

voltage and MET according to exercise response. There was no influence of age and gender about measurements of P-wave. Spearman's coefficient between positive exercise testing and use of beta-blocker was 0.06. Pearson's coefficient between Cornell voltage and P-wave dispersion at recovery was 0.10. The coronary artery lesion involved the left anterior descending coronary artery in 20 patients, the right coronary artery in four and the both coronary artery in eight patients. Coronary angiography was not performed in two patients.

Pearson's coefficient between Duke score and P-wave dispersion at rest was 0.43 and corrected QT dispersion was 0.69. These coefficients at recovery were 0.005 and 0.003, respectively. The Fig. 1 and 2 show the ROC curves for the P-wave dispersion at recovery in the diagnosis of exercise positive response and the stratification Duke score.

There are larges areas under the ROC curve (0.75 and 0.69) with 95% confidence interval. For all cut-off values, at increase of 12 msec in this measurement, the analysis provides a sensitivity of 97% and a specificity of 96% for exercise positive response and 95 and 97%, respectively, for Duke score ≤4. Previous studies indicated that there was an increase in left ventricular end-diastolic pressure during exercise-induced myocardial ischemia and a consequent increase in left atrial pressure and volume (Dilaveris *et al*., 1999; Ozmen *et al*., 2001; Ariyarajah *et al*., 2007). These induce inhomogeneous and discontinuous atrial conduction with prolongation of left atrial activation time that causes increase in P-wave dispersion. The results showed that P maximum and P- wave dispersion increased significantly immediately after treadmill exercise in patients with ST-segment depression. This study is in accordance with several investigations (Dunbar *et al*., 2005; Dilaveris *et al*., 1999; Ozmen *et al*., 2001; Batur *et al*., 2002; Ariyarajah *et al*., 2007). However, we studied the association P wave with Duke score and the effects of beta-blocker agents and left ventricular hypertrophy that have not been investigated for other studies.

The effects of beta-adrenergic blockade on P-wave were studied, demonstrating that these agents led to significant prolongation of P-wave duration in healthy volunteers (Cheema *et al*., 1995) but the early intravenous metoprolol injection acutely decreased maximum P-wave duration and P-wave dispersion in patients with acute coronary syndromes (Turgut *et al*., 2007). This is due to improve left ventricular filling with beta-blocker in patients with ischemic cardiomyopathy (Pousen *et al*., 1993). In this study despite the increase in P-wave dispersion in patients with beta-blocker at rest and at recovery, there is no influence of this drug in ischemia-induced during exercise. Then, the changes in P-wave were probably due increase atrial pressure with exercise in patients with ischemia and the use of beta-blocker can be increase P-wave duration only in patients without ischemia-induced exercise.

Left ventricular hypertrophy and diastolic dysfunction may cause hemodynamic and morphological changes in the left atrium, consequently instability and heterogeneity in atrial conduction. This is seen as an increase in maximum P-wave duration and P-wave dispersion on the electrocardiogram (Dagli *et al*., 2008). Besides, ST segment depression and/or myocardial perfusion abnormalities are frequently found with angiographically normal coronary arteries associated with left ventricular hypertrophy (Picano *et al*., 2001). The results indicated that there is no influence of Cornell voltage in measurements of P-wave. Then, the increase in P-wave dispersion at recovery is due ischemia-induced exercise.

Myrianthefs and Ozmen found a significant increase in P-wave duration and P-wave dispersion values during Left Anterior Descending (LAD) angioplasty (Ozmen *et al*., 2001; Myrianthefs *et al*., 1992). In this study, there was not possible this analysis because 20 patients presented lesion involved that artery and the right coronary artery lesion was in only four patients. Since that the left ventricle is mostly supplied from the territory of the LAD, there is an increase in left ventricular end-diastolic diameter and left atrial pressure and volume with temporary occlusion of the LAD during balloon inflation (Ozmen *et al*., 2001; Sigwart *et al*., 1990).

About the Duke treadmill score, it has been recommended by the American College of Cardiology/American Heart Association exercise testing guideline for risk stratification (Gibbons *et al*., 2002). There are very limited data related to the association of Duke prognostic treadmill scores with P-wave duration (Ariyarajah *et al*., 2006). These investigations have described that change in P-wave duration in patients with interatrial block and coronary heart disease was significantly associated with mean Duke score. The incremental change in P-wave duration was inversely associated with Duke score. The results showed that an increase of 12 msec in P-wave dispersion at recovery, analysis of the ROC curve provided a sensitivity of 97% and a specificity of 96% for exercise positive response and 95 and 97%, respectively, for Duke score ≤ 4.

Myrianthefs *et al*. (1991) demonstrated that including P-wave durations >120 msec during exercise testing in addition to conventional diagnostic criteria for myocardial ischemia could increase sensitivity from 57-75% and decrease specificity only from 85-77%. However, this study is the first that has investigated the effects of exercise-induced ST-segment depressed, Duke score, beta-blockers and of left ventricular hypertrophy on P- wave dispersion.

CONCLUSION

P maximum and P-wave dispersion were found to increase significantly immediately after treadmill exercise in patients with positive test. There was no influence of gender, age, use of beta-blocker agents, left ventricular hypertrophy, exercise time or capacity. There was correlation between P-wave dispersion and Duke score, with increase of accuracy of the treadmill exercise.

LIMITATIONS

The limitations of this study are the absence of left atrial and left ventricular measurements and the comparisons P-wave measurements among the three coronary artery groups. The fact that thallium-201 technique or SPECT evaluations were not performed for the ischemia screening may be another limitation of the study.

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