Severity of Coronary Artery Disease related to Prolonged P Wave Peak Time in Diabetic Patients

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ABSTRACT

***Background:** Coronary Artery Disease (CAD) is generally characterized by episodes of reversible myocardial demand/supply mismatch, related to ischemia or hypoxia. P wave peak time (PWPT) is a newly introduced electrocardiographic parameter that has been shown to be associated with no-reflow in patients with acute coronary syndrome (ACS). This study aimed to evaluate whether there is any association between prolonged PWPT in ECG and the severity of CAD in diabetic patients. **Patients and methods:** This study included 134 diabetic patients with history of coronary artery disease and were admitted to cardiology department Zagazig University. Patients were divided into group (I) of 40 patients with no evidence of obstructive CADs and group (II) of 94 patients with evidence of obstructive CADs. **Results:** The difference between both groups was statistically significant regarding the PWPT in lead II and V1. There was a significant difference between both groups concerning the R-wave peak time as the mean value in group I was 21.4 ± 3.7 while in group II was 29.2 ± 7.1. Regarding QRS duration, there was statistically significant increase in group II than in group I. Group II had statistically significant increase in PWD max, PW dispersion and PWTF in the lead V1 than group I. Regarding PWD min, there was no statistically significant difference between the two groups. The cut off value of PWPT in the lead II was 56.5msec with sensitivity (62.8 %) specificity was (80.0 %) and accuracy was 68.6 % .The PWPT in the lead V1, had a cut off value 54.5msec with sensitivity, specificity and accuracy were (66.0 %, 75.0 % and 67.9 %) respectively. the mean value of left ventricular ejection fraction in group I was 63.1 ± 8.3 while it was 53.5 ± 11.6 in group II. There was statistically significant increase in LVEF % among group I than group II. Group II had statistically significant increase in left atrial diameter than in group I (33.4 ± 4.1mm in group I vs 38.2 ± 11.6mm in group II). **Conclusion:** Prolonged P-wave peak time (PWPT) is a beneficial parameter for detecting high-risk patients with stable coronary artery disease. There was statistically significant older age among patients with obstructive coronary artery disease than those with non-obstructive coronary artery disease. Obstructive CAD group had statistically significant increase in left atrial diameter, left ventricular dilatation. Also, there was statistically significant increase in LVEF % among non-obstructive coronary artery than obstructive coronary artery disease one.*

***Keywords:** Electrocardiography, CAD, Diabetic Patients; PWPT*

INTRODUCTION

Coronary heart disease (CHD) is a major cause of mortality and this health problem is reaching pandemic in both developed, and developing countries. Every effort is done to risk stratify coronary artery disease patients and various risk stratification scores have been developed. Moreover, the assessment of severity of coronary artery lesion has gained major concern **(1)**. The signs of a heart attack are similar to angina except that they can occur during rest and tend to be more severe **(2)**.

The severity and duration of coronary artery obstruction, the volume of myocardium affected, and the level of demand and the ability of the rest of the heart to compensate are major determinants of a patients clinical presentation and outcome. A patient may present to the emergency department (ED) because of a change in pattern or severity of symptoms **(3)**. The SYNTAX scoring system is the most commonly used system to assess the severity of CAD. The number of lesions, localization, and functional effect are evaluated in order to provide guidance on the optimal treatment option. A high SYNTAX score is associated with increased mortality **(4)**.

Previous studies have assessed the change in P wave duration in ischemic heart disease, but there are limited data regarding their relationship with the severity of CAD **(5)**. P wave peak time (PWPT) has recently been introduced as an electrocardiographic parameter. A prolonged PWPT has been found to be related to the increased LV diastolic filling pressure and increased LA pressure because of the imperfect reperfusion in patients with anterior ST segment elevation myocardial infarction **(6)**.

Clinical models that incorporate information on risk factors for CVD, resting ECG changes, or coronary calcification have improved the identification of patients with obstructive CAD compared with age, sex, and symptoms alone **(7)**. Therefore, the presence of risk factors for CVD (such as family history of CVD, dyslipidemia, diabetes, hypertension, smoking, and other lifestyle factors) that increase the probability of obstructive CAD can be used as modifiers of the PTP estimate. If available, Q-wave, ST-segment, or T-wave changes on the ECG, LV dysfunction suggestive of ischemia, and findings on exercise ECG, as well as information on coronary calcium obtained by computed tomography (CT), can be used to improve estimations of the PTP of obstructive CAD **(8)**. The current study aimed to evaluate whether there is any association between prolonged PWPT in ECG and the severity of CAD in diabetic patients.

PATIENTS AND METHODS

This study included 134 diabetic patients with history of coronary artery disease and were admitted to cardiology department Zagazig University. Patients were divided into group (I) of 40 patients with no evidence of obstructive CADs and group (II) of 94 patients with evidence of obstructive CADs. Group II sub-classified according to severity of CAD by SYNTAX score into: Low SYNTAX score group (≤ 22), Intermediate SYNTAX score group (23-32), High SYNTAX score group (≥33) **(9).**

Inclusion and exclusion criteria:

Diabetic patients with clinical of stable coronary artery disease who undergoing coronary angiography (CAG), due to uncontrolled symptoms, low left ventricular ejection fraction and equivocal diagnosis to ascertain the cause. While, patients with STEMI, NSTEMI and unstable CAD, patients with known or newly diagnosed degenerative or rheumatic valvular disease, Patients with inappropriate ECG due to poor image quality (e.g. baseline drift or missing leads) were excluded.

All patients were given the necessary information about the study and a written informed consent was obtained. Our study was approved by Zagazig University institutional review board (IRB). All patients were subjected to clinical examination with emphasis on cardiac risk factors including smoking, diabetes mellitus, dyslipidemia and hypertension. Laboratory work up and 12 lead electrocardiography (ECG) analysis were performed.

A patient was assigned to be a current smoker (when he or she smoked any cigarettes on a regular basis within 3 weeks before the index event), ex-smoker (if they admit cessation for more than 3 weeks before the index event) or non-smoker **(10).** Diabetes mellitus was considered as fasting blood glucose ≥7.0 mmol/L (126 mg/dL), HbA1c ≥6.5% or post prandial ≥200 mg/dL **(11)**. Dyslipidemia was considered as total cholesterol >200 mg/dl, triglycerides >150 mg/dl**,** LDL >130 mg/dl**,** HDL <40 mg/dl or on statin therapy **(12)**. Thorough clinical examination: with special emphasis on heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) signs of heart failure and pulmonary edema. Hypertension was considered as blood pressure ≥140/90 mmHg or on antihypertensive medications **(13).**

Resting 12 lead electrocardiography (ECG) analysis for ST, T wave changes indicating ischemia, previous MI and ischemic LBBB. Heart rate was calculated from ECG strip. P-wave measurements were performed with calipers and a magnifying lens **(6)**.

Trans-thoracic echocardiography was done using GE, Vivid E9 machine equipped with a 4 MHz transducer. Images were taken while patient is in supine or in left lateral position. All measurements were taken according to the recommendations of the American society of echocardiography. The following measurements were obtained:

2D echocardiography: LV end-systolic (LVESD) and end-diastolic (LVEDD) dimensions and myocardial wall thickness were measured from the parasternal long-axis view using 2D guided M-mode recordings with the cursor positioned at the tips of the mitral valve leaflets and perpendicular to the posterior wall. LV volumes and ejection fraction were calculated from the apical four-chamber view using the modified Simpson's method **(14)**

SYNTAX Score corresponds to the lesion complexity measured by the coronary tree characteristics and the lesion locations and specifics **(15)**.

Statistical Analysis:

Data analyzed using Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. Qualitative data represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test (X^2). Differences between quantitative independent multiple by ANOVA, correlation by Pearson's correlation. P value was set at <0.05 for significant results & <0.001 for high significant result.

RESULTS

This comparative cross-sectional study included 134 participants for determining the association between prolonged p-wave peak time and the severity of coronary artery disease using SYNTAX score. The diabetic studied group was divided according to presence or absence of obstructive coronary artery disease by coronary angiography into two groups as shown in **(Table 1)**: Group I was diabetic patients without obstructive coronary artery disease who had zero SYNTAX score and consisted of 40 (29.9%) participants. Group II was diabetic patients with obstructive CAD who had low, intermediate and high SYNTAX Scores and consisted of 94 patients (70.1%) of the studied group. All the studied groups (100.0%) had Normal cardiac enzymes.

There was a statistically significant difference between both groups concerning age **(Figure 1)**. There was no significant difference between both groups concerning sex (X2=2.9, p= 0.08) **(Figure 2)**. Regarding hypertension, there was a significant difference between the two groups (X2= 5.6, p=0.01*), Also, dyslipidemia was statistically significant more among group II than group I **(Figure 3)**.

The difference between both groups was statistically significant regarding the PWPT in lead II and V1. There was a significant difference between both groups concerning the R-wave peak time as the mean value in group I was 21.4 ± 3.7 while in group II was 29.2 ± 7.1. Regarding QRS duration, there was statistically significant increase in group II than in group I. Group II had statistically significant increase in PWDmax, PW dispersion and PWTF in the lead V1 than group I. Regarding PWD min, there was no statistically significant difference between the two groups (**Figure 4).**

The cut off value of PWPT in the lead II was 56.5msec with sensitivity (62.8 %) specificity was (80.0 %) and accuracy was 68.6 % [area under curve (Auc); 0.74, 95 % (0.65 – 0.82), P-value <0.001]. that was highly significant. The PWPT in the lead V1, had a cut off value 54.5msec with sensitivity, specificity and accuracy were (66.0 %, 75.0 % and 67.9 %) respectively [area under curve (Auc); 0.66, 95% C.I (0.55 – 0.76), p_ Value = 0.003*] **(Table 2)**.

Regarding LVEF, the mean value of left ventricular ejection fraction in group I was 63.1 ± 8.3 while it was 53.5 ± 11.6 in group II. There was statistically significant increase in LVEF % among group I than group II (t= 4.7, p=0.001**). LA diameter: group II had statistically significant increase in left atrial diameter than in group I (33.4 ± 4.1mm in group I vs 38.2 ± 11.6mm in group II), (t= 4.8, p=0.001**). with regard to left ventricular size there was statistically significant higher percent of left ventricular dilatation among group II, as group I had only 1 (2.5 %) patient, while 28 (29.8 %) patients were in group II (X2= 12.3, p=0.001**) **(Table 3)**.

Table (1): classification of the main groups involved in our study:

variable	Group I	Group II
No (%)	40 (29.9%)	94 (70.1%)
SYNTAX score - Low (1 – 22) - Intermediate (23 – 32) - High (≥ 33)	 - - -	 52 (55.3 %) 23 (24.5 %) 19 (20.2 %)

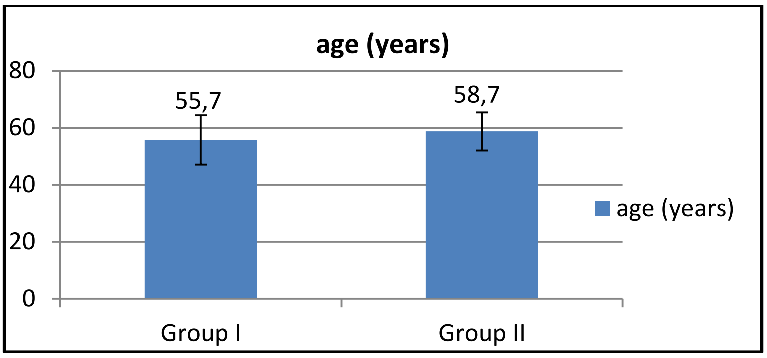

Figure (1): Bar chart demonstrates age distribution among the studied groups.

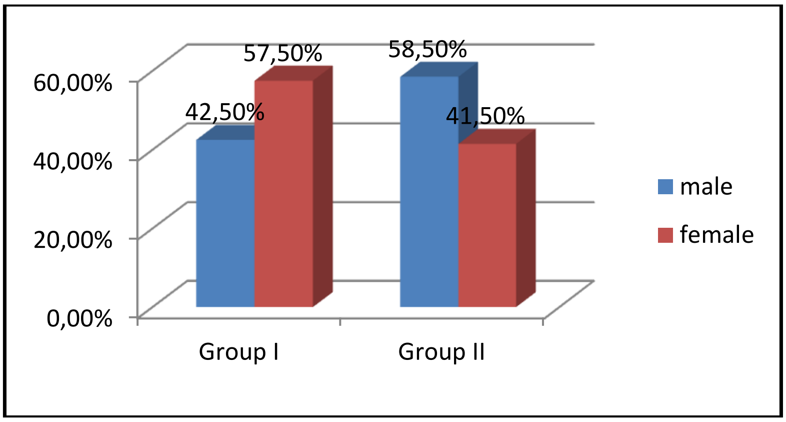

Figure (2): Bar chart demonstrates sex distribution among the studied groups.

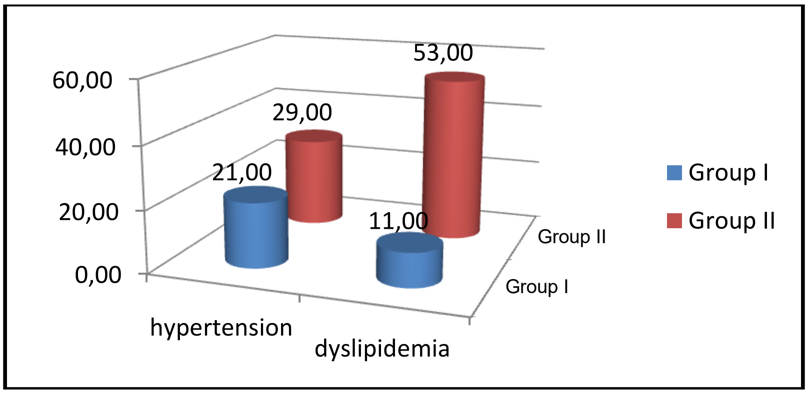

Figure (3): Bar chart demonstrates hypertension and dyslipidemia distribution among the studied groups.

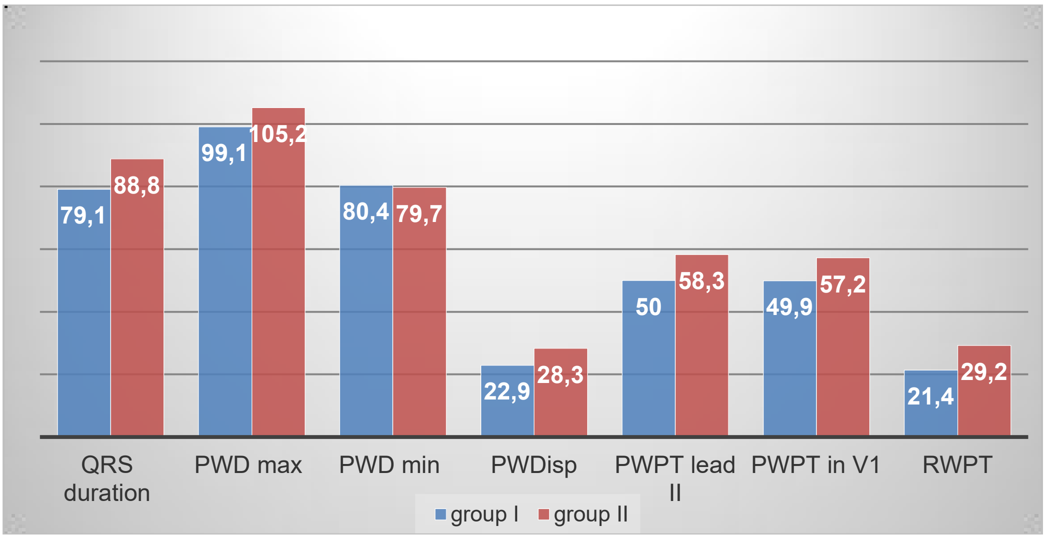

Figure (4): Bar chart demonstrates electrocardiographic characteristics (msec) between the two studied groups (PWDmax: p-wave duration maximum, PWDmin: p-wave duration minimum, PWDisp: p-wave dispersion, PWTF: p-wave terminal force, PWPT: p-wave peak time, RWPT: R-wave peak time)

Table (2): The predictive ability of PWPT in the lead II and PWPT in the lead V1 in detection of coronary artery disease severity:

Variables	**Cut off point**	**AUC**	**Sig**	**95 % CI**
PWPT in the lead II (ms)	> 56.5 ms	0.74	**0.001****	0.65 – 0.82
PWPT in the lead V1 (ms)	> 54.5 ms	0.66	**0.003***	0.55 – 0.76

Variables	**Sensitivity**	**Specificity**	**PVP**	**PVN**	**Accuracy**
PWPT in the lead II (ms)	62.8 %	80.0 %	88.1 %	47.8 %	68.6 %
PWPT in the lead V1 (ms)	66.0 %	75.0 %	86.1 %	48.4 %	67.9 %

Table (3): Echocardiographic data distribution between the two study groups:

Variables	**Group I** No: (40)	**Group II** No: (94)	**Test**	**P_Value**
LVEF % Mean ± SD	63.1 ± 8.3	53.5 ± 11.6	T 4.7	**0.001****
LA diameter Mean ± SD	33.4 ± 4.1	38.2 ± 11.6	T 4.8	**0.001****
Dilated LV Yes / No	1 (2.5 %) / 39 (97.5 %)	28 (29.8 %) / 66 (70.2 %)	X^2 12.3	**0.001****

LVEF: left ventricle ejection fraction, **LA:** left atrium, **LV:** left ventricle, T: t test, X^2: chi square * Statistically significant difference (P < 0.05), ** Statistically high significant (P < 0.001)

DISCUSSION:

Atherosclerosis is a major health problem affecting cardiovascular system, which makes coronary artery diseases the leading cause of death in developed countries and one of major health problems in developing countries. It is a degenerative disease affecting blood vessels and leads to catastrophic cardiovascular events. It is characterized by basement membrane disruption, inflammation, cell infiltration, lipid deposition and calcification **(16)**. The ECG is a simple, noninvasive, and readily available tool in daily routine practice. The relationship between CAD and electrocardiographic P wave parameters is mostly based on two basic pathophysiological mechanisms. The first is the atrial ischemia and/or scar due to CAD. The other is systolic and diastolic dysfunction due to left ventricular ischemia that gives rise to increased left ventricular end-diastolic pressure. Consequently, increased LA pressure and/or volume loading and the prolongation in atrial depolarization time may be seen **(17).**

In our study, there was statistically significant older age among group II than in group I. This is in agreement with the study of **Reeh et al. (18)** revealed the highest observed proportions were 52% in men age 70–79 with typical angina and 35% in women age 80+ with typical angina.

Regarding to the gender there was no statistically significant difference between the two groups, and this finding is not concordant with that of **Reeh et al. (18)** and **Patel et al. (19)** in which the highest observed proportions were men.

The current study showed hypertension and dyslipidemia were significantly more among group II than group I. Regarding smoking, there was no statistically significant difference between the two groups. **Ibrahim et al. (20)** reported that there was highly significant difference between non-obstructive and obstructive coronary artery disease groups regarding smoking (31 patients 91.2% versus 18 patients 56.2%, P = 0.0001), regarding dyslipidemia there was a significant difference between both groups (20 patients 58.8% versus 22 patients 62.5%, P = 0.02), regarding hypertension it was more in second group with no statistically significant difference (12 patients 35.3% versus 20 patients 62.5%, P = 0.08). **Bissinger et al. (21)** reported that hypertension there was no significant difference between both groups (56% versus 53%, P > 0.05).

The contemporary study revealed that group II had statistically significant increase in left atrial diameter, PWPT in the lead II, PWPT in the lead V1, QRS duration, PWD max, PW dispersion, PWTF in the lead V1, and RWPT than group I. Also, there was statistically significant higher percent of dilated left ventricle among obstructive coronary artery disease group. Oppositely, there was statistically significant increase on LVEF % among group I than in obstructive coronary artery disease group (group II). Regarding PWDmin, there was no statistically significant difference between the two groups. **Burak et al. (2)** reported that LVEF was significantly lower in the CAD group (54±9 vs. 57±9; p=0.037) and the left atrial diameter was increased significantly in CAD patients (39±4 vs. 37±5; p=0.017), the duration of QRS was longer in CAD patients significantly (104±9 vs. 99±12; p=0.022). The PWDmax was longer in the group with severe CAD (124±14 vs. 116±19; p=0.030), but there were no significant differences between the groups in terms of PWDmin, PWTF, and PWDISP. The PWPT in the leads II and V1 were significantly longer in the group with severe CAD (71±13 vs. 61±12; p<0.001, 63±24 vs. 53±18; p=0.024, respectively). **Bissinger et al. (21)** reported that P-wave duration was significantly longer in patients with CAD (137.4 ±12.0 ms vs. 126 ±23.0 ms in diabetics without CAD p < 0.001). Similarly, P-wave dispersion was longer in patients with CAD (53 ±19 ms vs. 36 ±18 ms and 34 ±20 ms, respectively; p < 0.001).

Abalı et al. (22) reported that there was no significant difference considering LV size, LVEF, LA size. **Burak et al. (2)** reported that duration of QRS was longer (104±9 vs. 99±12; p=0.022) and the percentage of patients was higher (11 patients (24.4%) vs. 12 patients (11.3%); p=0.040) in the group with CAD. Regarding to our present study the cut off value of PWPT in the lead II was found to be 56.5ms with sensitivity (62.8 %), specificity was (80.0 %) and accuracy was 68.6 % [area under curve (Auc); 0.74, 95 % (0.65 – 0.82), P_value <0.001]. whereas the PWPT in the lead V1, had a cut off value 54.5 ms with (66.0 %, 75.0 % and 67.9 %) sensitivity, specificity and accuracy respectively [area under curve (Auc); 0.66, 95% C.I (0.55 – 0.76), p- Value = 0.003*]. In predicting severe CAD, the ROC curve analysis was performed, and it revealed that the cut-off value of PWPT in lead II was 69.6 ms with sensitivity of 58.3% and specificity of 78.9% (area under curve (AUC): 0.708, 95% CI: 0.631-0.776, p < 0.001). The PWPT in lead V1 was 58.8 ms with sensitivity of 64.4% and specificity of 64.1% (AUC: 0.617, 95% CI: 0.533-0.695, p=0.03).

Bayam et al. (23) described that in ROC curve analysis, PWPT above a cut-off level of 45.5ms predicted a Gensini score ≥25 with a sensitivity of 62% and a specificity of 71%, (AUC: 0.663, 95%CI: 0.564–0.762; p< 0.001).

CONCLUSION:

Prolonged P-wave peak time (PWPT) is a beneficial parameter for detecting high-risk patients with stable coronary artery disease. There was statistically significant older age among patients with obstructive coronary artery disease than those with non-obstructive coronary artery disease. Obstructive CAD group had statistically significant increase in left atrial diameter, left ventricular dilatation. Also, there was statistically significant increase in LVEF % among non-obstructive coronary artery than obstructive coronary artery disease one.

No Conflict of interest.

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