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ASSOCIATION OF PROLONGED P WAVE PEAK TIME WITH THE SEVERITY OF CORONARY ARTERY DISEASE DETECTED BY SYNTAX-SCORE IN DIABETIC PATIENTS

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ABSTRACT

Background: Conventional risk factors for the development of CAD (Coronary Artery Disease) have an adverse influence on prognosis in those with established disease. P wave peak time (PWPT) as Electrocardiography (ECG) parameter, has been shown to be associated with imperfect reperfusion in patients with acute coronary syndrome (ACS).The aim of the present study was to investigate whether there is any association between prolonged PWPT in ECG and the severity of CAD detected by SYNTAX score in diabetic patients. **Patients and methods:** A cross sectional single center study was conducted on a total of 134 consecutive diabetic patients with history of stable coronary artery disease, in which coronary angiography was indicated, and were admitted to cardiology department Zagazig University. Patients were divided into group (I) included 40 patients with no evidence of obstructive CADs and group (II) included 94 patients with evidence of obstructive CADs. Invasive coronary angiography was performed via radial and femoral approaches according to Judkins technique. We select calculation of SYNTAX scores. **Results:** The mean SYNTAX Score among the obstructive coronary artery disease group was (20.97 ± 13.8) where about half of the group (55.3%) had low SYNTAX Score, (24.5%) had intermediate and (20.0%) had high SYNTAX Score. Left atrial diameter had statistically significant increase in high than intermediate than low syntax score groups (44.2 ± 4.4mm vs 37.9 ± 52mm vs 36.1 ± 4.7mm) respectively. Hypertension and dyslipidemia found to be statistically related to the severity of CAD (P= 0.01*, 0.002* respectively). There was significant statistical relation between QRS duration and the coronary artery disease severity (P=0.02*). **Conclusion:** Prolonged P-wave peak time (PWPT) which is a parameter easily obtainable from the ECG, is associated with the severity and complexity of coronary artery disease (CAD) detected by syntax score in diabetic patients with stable coronary artery disease. It might be useful for identifying high-risk patients with stable coronary artery disease. Therefore, it could be beneficial in risk stratification of patients with CAD.

Keywords: Coronary Artery Disease, **SYNTAX-Score**, **P Wave Peak Time**

INTRODUCTION

Coronary artery disease (CAD) is a major determinant of the long-term prognosis among patients with diabetes mellitus (DM). DM is associated with a 2 to 4-fold increased mortality risk from heart disease. Furthermore, in patients with DM there is an increased mortality after myocardial infarction (MI), and worse overall prognosis with CAD **(1).**

Near-normal glycemic control for a median of 3.5 to 5 years does not reduce cardiovascular events. Thus, the general goal of HbA1c <7% appears reasonable for the majority of patients. Iatrogenic hypoglycemia is the limiting factor in the glycemic management of diabetes, and is an independent cause of excess morbidity and mortality. Statins are effective in reducing major coronary events, stroke, and the need for coronary revascularization **(1).**

The SYNTAX (SYNergy between PCI with TAXUS and Cardiac Surgery) scoring system attempts to predict patients with severe CAD before performing coronary angiography (CAG) may contribute to improving the prognosis of these patients **(2).**

P wave peak time (PWPT) is a recently introduced ECG parameter, has been shown to be associated with imperfect reperfusion in patients with acute coronary syndrome (ACS) **(3)**. Changes in the P wave duration (PWD), indicating atrial depolarization, are known to demonstrate abnormal inter- and intra-atrial conduction times **(4)**. Also, prolonged PWPT which is a parameter easily obtainable from the ECG, is associated with severe CAD. Recognition of diabetic patients with severe CAD at the time of diagnosis before performing coronary angiography may be important for the planning of treatment **(2)**.

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Therefore, this study aimed to investigate whether there is any association between prolonged PWPT in ECG and the severity of CAD detected by SYNTAX score in diabetic patients.

PATIENTS AND METHODS

A cross sectional single center study was conducted on a total of 134 consecutive diabetic patients with history of stable coronary artery disease, in whom coronary angiography was indicated, and were admitted to cardiology department, Zagazig university in the period between November 2019 to July 2020. 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).

Our patients were divided according to invasive coronary angiography into: group (I): patients with no evidence of obstructive CADs and group (II): patients with evidence of obstructive CADs. Furthermore, 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) **(5).**

Inclusion criteria:

Patients with diabetes mellitus and clinical doubt of stable coronary artery disease undergoing coronary angiography (CAG), due to one or more of the following: uncontrolled symptoms, high risk stress testing, low left ventricular ejection fraction and equivocal diagnosis to ascertain the cause.

Exclusion criteria:

Patients with STEMI, NSTEMI and unstable CAD, patients with known or newly diagnosed degenerative or rheumatic valvular disease**,** patients with end-stage renal failure on dialysis and patients with atrial dysrhythmias including atrial fibrillation, flutter and tachycardia.

Methods:

All patients were subjected to Full clinical evaluation with emphasis on cardiac risk factors including smoking, diabetes mellitus, dyslipidemia and hypertension. Laboratory work up and 12 lead electrocardiography (ECG) analysis were performed.

P-wave measurements:

The P wave duration measured from the lead II (PWD_{II}) and PW_{DIS} was calculated by subtracting the minimum P wave duration (PWD_{MIN}) from the maximum P wave duration (PWD_{MAX}). The peak of the P wave was measured from lead II to define the PWPT from the lead II ($PWPT_{II}$) and the V1 lead ($PWPT_{V1}$) was measured.

Invasive coronary angiography (ICA):

Coronary angiography was performed via radial and femoral approaches according to Judkins technique. The coronary angiograms were interpreted by experienced interventional cardiologists who were blinded to the characteristics of the patients.

SYNTAX Score:

The SYNTAX score was designed to quantify the complexity of left main (LM) or three-vessel disease. Using the openly accessible web-based score calculator (http://www.syntaxscore.com) it is possible to calculate each patient's SYNTAX score by answering a series of questions. One of the most crucial features of the SYNTAX score is that it is a lesion-based score, which integrates all lesions to determine the degree of myocardium that is at risk and the technical success rate of treating each lesion. The syntax score consists of 11 questions: two questions are about the anatomy, 8 are about each lesion, and one about diffuse disease., which accumulates to form the overall SYNTAX score of the patient **(6)**.

Statistical Analysis:

Data analyzed using Microsoft Excel software. Data were then imported into 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

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(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

The present study showed the mean age in group I was 55.7 ± 8.6 years old while it was 58.7 ± 6.7 years old in group II. There was a statistically significant difference between both groups concerning age (t=2.1, p=0.03*). In group I; 17 (42.5 %) patients were males and 23 (57.5 %) were females while in group II; 55 (58.5 %) patients were males and 39 (41.5 %) were females. There was no significant difference between both groups concerning sex (X2=2.9, p= 0.08). Regarding to glycated hemoglobin the mean value was 7.48 ± 0.7 in group I and 8.38 ± 1.2 in group II. There was a highly statistically significant increase in group II than group I (t=4.1, p=0.001**). The mean value of creatinine in group I and II was (0.95 ± 0.17 and 1.12 ± 0.33) respectively. There was a statistically significant difference between both groups (t=2.9, p=0.004*). About 21 cases out of 40 (52.5 %) in group I and in 29 cases out of 94 (30.85 %) in group II. Statistical analysis showed that there was a significant difference between the two groups (X2= 5.6, p=0.01*). There were 11 patients out of 40 (27.5 %) with dyslipidemia in group I while there were 53 patients out of 94 (56.4 %) in group II. Statistical analysis found that dyslipidemia was statistically significant more among group II than group I (X2= 9.3, p=0.002*) **(Table 1).**

The mean SYNTAX Score among the obstructive coronary artery disease group was (20.97 ± 13.8) where about half of the group (55.3%) had low SYNTAX Score, (24.5%) had intermediate and (20.0%) had high SYNTAX Score **(Table 2).**

P-wave peak time (PWPT) in the lead II was 55.9 ± 7.4msec in low syntax and 59.7 ± 10.4msec in intermediate syntax, while it was 63.2 ± 10.9msec in high syntax grade (F=5.1, p=0.04*). Mean values of PWPT in the lead V1 in low, intermediate and high SYNTAX score groups were 54.6 ± 9.1, 56.5 ± 9.8 and 65.4 ± 11.3msec respectively (F=8.6, p=0.001**). The difference between SYNTAX Score grades was statistically significant regarding the PWPT in lead II and V1. Which means that prolonged PWPT is related to severity and complexity of CAD. Mean values of PWD isp in low, intermediate and high SYNTAX score groups were 22. 1 ± 10.4, 27.9 ± 5.4 and 31. 2 ± 16.8 respectively. Statistical analysis showed a significant increase of PWD is p in higher SYNTAX score group than intermediate than low SYNTAX score (K.W=3.4, p=0.03*). Regarding QRS duration the mean values in low syntax were 90. 1 ± 14.8msec and in intermediate syntax were 86.4 ± 11.4msec while in high syntax were 88. 5 ± 8.6 msec. there was no statistically significant association between SYNTAX Score groups (F=0.6, p=0.5). Regarding PWD max, PWD min and PWTF in the lead V1, there weren't statistically significant difference (p>0.05) **(Table 3)**.

Left atrial diameter had statistically significant increase in high than intermediate than low syntax score groups (44.2 ± 4.4mm vs 37.9 ± 52mm vs 36.1 ± 4.7mm) respectively (F=19.5, p=0.001**) **(Figure 1)**.

Syntax score was significantly positively correlated with the p wave duration maximum (r=0.2, p=0.004*). There was no significant correlation with the Syntax score in regard to p wave duration minimum (r=0.01, p=0.9), and p wave dispersion (r=0.01, p=0.8). Syntax score was significantly positively correlated with the PWTF in the lead V1 (r=0.2, p=0.02*). There was a highly significant positive correlation between Syntax score and PWPT in the lead II (r=0.4, p=0.001**).There was a statistically significant positive correlation between Syntax score and PWPT in the lead V1 (r=0.2, p=0.004*). There was a highly significant positive correlation between the Syntax score and the R wave peak time (r=0.4, p=0.001**) **(Figure 2)**.

In univariate analysis showed PWPT in the lead II and PWPT in the lead V1 were statistically related to severity of CAD (P=.0.001**). Regarding age and sex there were no statistical relation with the coronary artery disease severity (P>0.05). Hypertension and dyslipidemia found to be statistically related to the severity of CAD (P= 0.01*, 0.002* respectively). There was significant statistical relation between QRS duration and the coronary artery disease severity (P=0.02*). In multivariate regression analysis showed PWPT in the lead II and PWPT in the lead V1 were statistically significant predictor factors for severity of CAD (P=0.001**, 0.003* respectively) **(Table 4)**.

A case of female patient 65 years old have central obesity, hypertension, DM and no dyslipidemia. ECG: shows ischemic changes in V1 to V6, PWPT in lead II 50msec, PWPT in V1 40msec. Echocardiography: EF 55%, LA diameter 30mm. HGBA1C: 7.8% and Syntax score: 5 **(Figure 3)**.

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Table (1): Demographic and clinical data findings between studied groups:

variable	Group I No: 40	Group II No: 94	Test	P-Value
Age Mean ± SD	55.7 ± 8.6	58.7 ± 6.7	T 2.1	**0.03***
Sex Female Male	23 (57.5 %) 17 (42.5 %)	39 (41.5 %) 55 (58.5 %)	X^2 2.9	0.08
HbA1c Mean ± SD	7.48 ± 0.7	8.38 ± 1.2	T 4.1	0.001**
Creatinine Mean ± SD	0.95 ± 0.17	1.12 ± 0.33	T 2.9	0.004*
Hypertension Yes No	21 (52.5 %) 19 (47.5 %)	29 (30.85 %) 65 (69.15 %)	X^2 5.6	0.01*
Dyslipidemia Yes No	11 (27.5 %) 29 (72.5 %)	53 (56.4 %) 41 (43.6 %)	X^2 9.3	0.002*
Smoking Yes No	21 (52.5 %) 19 (47.5 %)	44 (46.8 %) 50 (53.2 %)	X^2 0.3	0.5

T: t test, $\mathbf{X^2}$: chi square, * Statistically significant difference (P < 0.05), ** Statistically highly significant difference (P < 0.001)

Table (2): SYNTAX score distribution among group II:

SYNTAX Score	Group II No = 94
Mean ± SD	20.97 ± 13.8
SYNTAX score	No (%)
- Low (1 – 22) - Intermediate (23 – 32) - High (≥ 33)	52 (55.3 %) 23 (24.5 %) 19 (20.2 %)

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Table (3): Relation between SYNTAX Score and electrocardiographic data in group II:

Variables	Low SYNTAX No: 52	intermediate SYNTAX No: 23	High SYNTAX No: 19	Test	P_Value
QRS duration (ms) Mean ± SD	90. 1 ± 14.8	86.4 ± 11.4	88. 5 ± 8.6	F=0.6	0.5
PWD max (ms) Mean ± SD	104.7 ± 12.1	102.2 ± 12.9	110 ± 7.4	F= 2.4	0.09
PWD Min (ms) Mean ± SD	79. 9 ± 10.1	78 ± 11.2	81 ± 7.3	F= 0.5	0.6
PWDisp (ms) Mean ± SD	22. 1 ± 10.4	27.9 ± 5.4	31. 2 ± 16.8	K.W= 3.4	**0.03***
PWTF lead V1 Mean ± SD	0.03 ± 0.01	0.028 ± 0.0	0.031± 0.01	F= 0.3	0.7
PWPT lead II Mean ± SD	55.9 ± 7.4	59.7 ± 10.4	63.2 ± 10.9	F= 5.1	**0.04***
PWPT lead V1 Mean ± SD	54.6 ± 9.1	56.5 ± 9.8	65.4 ± 11.3	F= 8.6	**0.001****
RWPT Mean ± SD	28.1 ± 6.7	29.5 ± 7.1	32.2 ± 7.4	F=2.5	0.08

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, **K. W**= Krusk all - Wallis test, **F**= ANOVA test, * Statistically significant difference (P < 0.05), ** Statistically highly significant difference (P < 0.001)

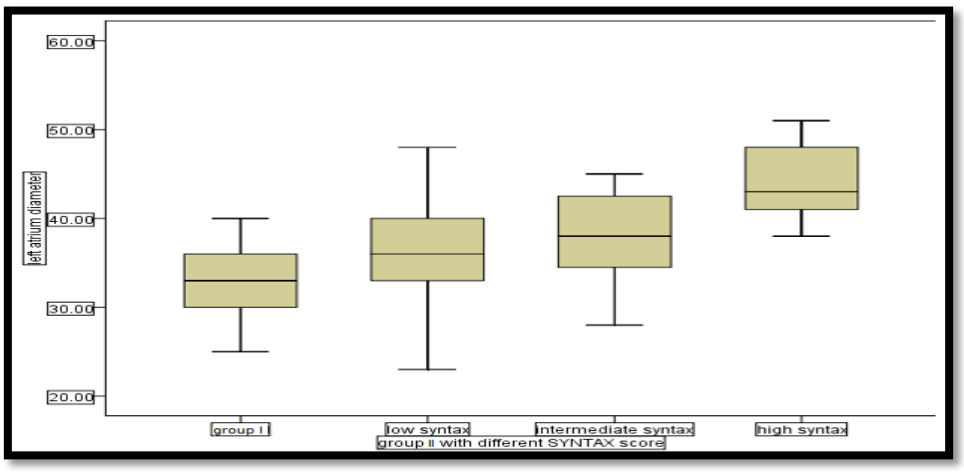

Figure (1): Box plot chart for the left atrium diameter among the studied groups.

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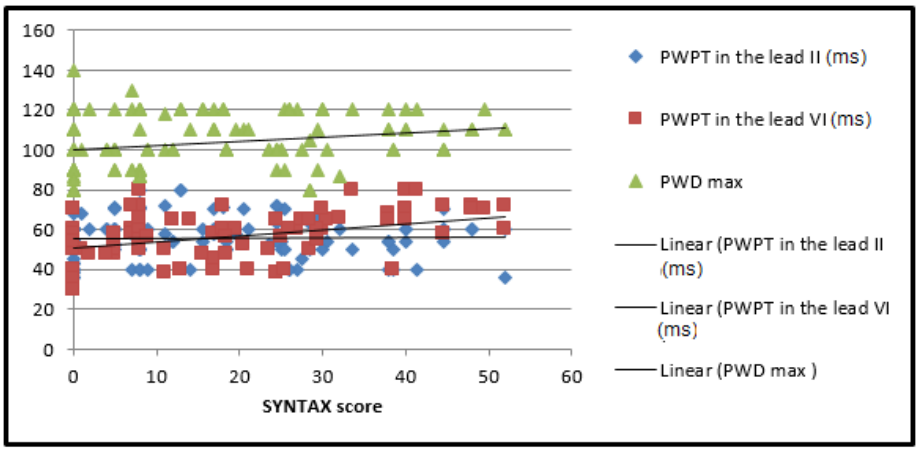

Figure (2): Scatter plot with line chart for the positive correlation between SYNTAX score, PWD max, PWPT in the lead II, PWPT in the lead V1 among the studied groups.

Table (4): Univariate and multivariate logistic analysis for the predictor factors of coronary artery disease severity:

Variables	Univariate analysis			Multi – variate analysis		
	regression co-efficient	p-value	OR (95 % CT)	regression co-efficient	p-value	OR (95 % CT)
Sex	2.8	0.09	1.9 (0.9 - 4.1)			
Smoking	0.05	0.8	0.9 (0.4 – 1.9)			
Hypertension	9.3	**0.01***	2.4 (1.15 – 5.25)	0.7	0.1	0.4(0.17-1.4)
dyslipidemia	0.9	**0.002***	3.4 (1.5 – 7.6)	0.6	0.18	0.5(0.19-1.3)
PWPT In the lead II	1.6	**0.001****	6.7 (2.79 - 16.26)	1.7	**0.001****	5.4(2.1-14.1)
PWPT in the lead V1	1.5	**0.001****	5.8 (2.5 – 13.37)	1.3	**0.003***	3.9(15-9.7)
QRS duration	0.8	**0.02***	1.03 (1.01 - 1.08)	1.4	0.2	0.2(0.02-2.1)

PWPT: p-wave peak time, * Statistically significant difference (P < 0.05), ** Statistically highly significant difference (P < 0.001)

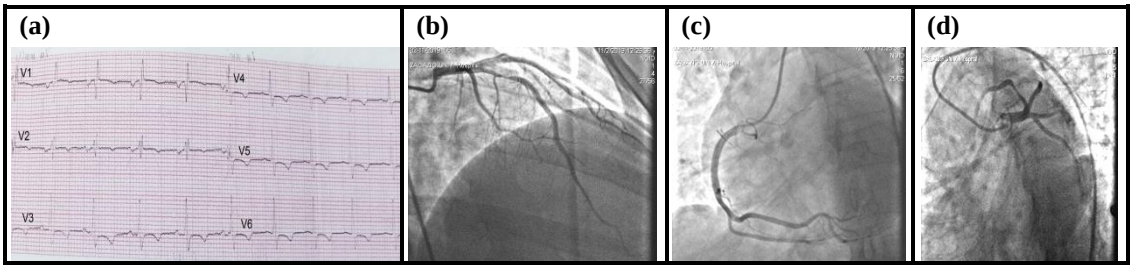

Figure (3): A female patient 65 years old, (a) ECG shows St depression and t wave inversion in V1 to V6, pwpt in lead II 50msec, pwpt in V1 40msec ; (b) RAO cranial view showing mid 90% LAD lesion ; (c) LAO caudal view of normal right system; (d) LAO caudal view of the left system showing mid LAD lesion.

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DISCUSSION:

The Emerging risk factor collaboration, a meta-analysis of 102 prospective studies, showed that diabetes mellitus involves a two-fold excess risk of vascular outcomes (coronary heart disease, ischemic stroke, and vascular deaths) independent of other risk factors. Both relative and absolute risk levels are higher in long-standing diabetes mellitus and microvascular complications, including renal disease or proteinuria **(8).**

This comparative cross-sectional study was conducted on 134 consecutive diabetic patients with history of stable coronary artery disease, in whom coronary angiography was indicated, and were admitted to cardiology department Zagazig university in the period between November 2019 to July 2020. This study aimed to determine the association between prolonged p-wave peak time and the severity of coronary artery disease using syntax score in Diabetic patients.

The current study showed that there was statistically significant older age among group II than in group I (58.7 ± 6.7 versus 55.7 ± 8.6) respectively. This goes with the fact that the incidence of cardiovascular disease in general, increases with advanced age. This is in agreement with the study of **Reeh et al. (8)** reported the proportion of patients diagnosed with obstructive CAD according to age. The highest observed proportions were 52% in men age 70–79 with typical angina and 35% in women age 80+ with typical angina. In patients with non-cardiac chest pain, the proportion with obstructive CAD did not exceed 10% in men and 2% in women in any group.

Patel et al. (9) also found that Patients with non-obstructive CAD were younger (mean age 59.8 vs 66.5 years, P b .001), more likely to be female (55.2% vs 35.8%, P b .001), compared with patients with obstructive CAD.

In regard to our study, PWPT in the lead II and PWPT in the lead V1 found to be significantly associated with the severity of syntax score, which means that prolonged PWPT is correlated with the complexity of coronary artery disease. This finding is in concordance with that of **Burak et al. (2)** in which P wave peak time was found to be correlated with severity of coronary artery disease.

Our current study revealed that there was statistically significant association between syntax score and Lt atrium diameter, PW Dispersion, as Lt atrium diameter, PWD were increased among high syntax than intermediate than low syntax score groups. Also, Regarding LVEF %, QRS duration, PWD max, PWD min, PWTF in the lead V1 and RWPT, there weren't statistically significant difference. **Rencüzoğulları et al. (10)** reported that patients in the high syntax score group had lower left ventricular ejection fraction (LVEF) than those in the low syntax score group. As expected, the prevalence of left main coronary artery disease, three vessel disease, longer RWPT and QRS duration were higher in the high than in the low syntax score group.

The univariate analysis of our study showed that hypertension, dyslipidemia, QRS duration, PWPT in the lead II and PWPT in the lead V1 were statistically related to severity of CAD. While in multivariate regression analysis, PWPT in the lead II and PWPT in the lead V1 were found to be statistically significant independent predictors for the severity of CAD. **Karakoyun et al. (11)** reported that multivariate logistic regression test was used for determining the independent predictors of high syntax score. Among those, HbA1c (OR: 1.683, 95% CI 1.228-2.307, P = .001), age (OR: 1.087, 95% CI 1.035-1.142, P = .001), and female sex (OR: 4.305, 95% CI 1.822-10.176, P = .001) were found to be the independent predictors.

Bayam et al. (12) found that among the demographic, laboratory, and electrocardiographic findings, those that were found to be associated with CAD in the univariate analyses were included in multiple logistic regression analysis. Presence of diabetes mellitus (OR: 3.33, 95% CI: 1.44–7.71; p= 0.004), left ventricular ejection fraction (OR: 0.94, 95% CI: 0.91–0.98; p= 0.011), PWPT (OR: 1.07, 95% CI: 1.02–1.13; p= 0.002), and RWPT (OR: 1.09, 95% CI: 1.02–1.17; p= 0.009) were found to be independent predictors of the severity and complexity of CAD.

Burak et al. (2) reported that in univariable analysis; sex, QRS duration, PWDmax, PWPT in lead II, were found to be related with CAD. In multivariate regression analysis, the PWPT was found to be an independent predictor of severe CAD (Odds ratio (OR): 1.066 per 1 ms increase, 95% Confidence Interval (CI): 1.030-1.102; p <0.001). The syntax score was positively correlated with PWPT in the leads II and V1, but not with PWTF and PWDISP. Further, PWDmax, PWDISP, and PWPT were positively correlated with LA diameter.

Rencüzoğulları et al. (10) a multivariate logistic regression analyses reported that, LVEF (OR: 0.933, 95% CI: 0.896-0.972; p=0.001), and RWPT (OR: 1.035, 95% CI: 1.003-1.067; p=0.030) were found to be independent predictors of high syntax score.

CONCLUSION:

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Prolonged P-wave peak time (PWPT) which is a parameter easily obtainable from the ECG, is associated with the severity and complexity of coronary artery disease (CAD) detected by syntax score in diabetic patients with stable coronary artery disease. It might be useful for identifying high-risk patients with stable coronary artery disease. Therefore, it could be beneficial in risk stratification of patients with CAD.

No Conflict of interest.

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