Original Article

Effect of No-Reflow/Reflow on P-Wave Time Indexes in Patients with Acute Myocardial Infarction Undergoing Percutaneous Coronary Intervention

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Abstract

Aim: The aim of this study was to investigate the relationship between no-reflow (no-RF), reflow (RF), and the P-wave time index in patients undergoing percutaneous coronary intervention (PCI) with a diagnosis of acute myocardial infarction (AMI) due to total occlusion. **Methods:** This study included a total of 272 AMI patients with no-RF (110 patients) and RF (162 patients). **Results:** The no-RF group had higher values of mean $maxPWT_{postPCI}$ (94.95 ± 15.61 vs. 117.86 ± 12.06, $P < 0.001$), $minPWT_{postPCI}$ (54.21 ± 12.13 vs. 67.31 ± 11.79, $P < 0.001$), and $PWD_{postPCI}$ (39.14 ± 12.55 vs. 50.91 ± 11.9, $P < 0.001$) during the post-PCI period. According to multivariate logistic regression analysis, $maxPWT_{postPCI}$ (odds ratio [OR]: 1.103, 95% confidence interval [CI]: 1.049–1.160, $P < 0.001$), $minPWT_{postPCI}$ (OR: 1.055, 95% CI: 1.011–1.101, $P = 0.0014$), and $PWD_{postPCI}$ (OR: 1.107, 95% CI: 1.037–1.181, $P = 0.002$) were the independent predictors of RF after PCI. ROC curve analyses demonstrated that the optimal cutoff values for $maxPWT_{postPCI}$, $minPWT_{postPCI}$, and $PWD_{postPCI}$ for predicting no-RF were 112.95 ms (area under the curve [AUC]: 0.852, 95% CI: 0.807–0.898, $P < 0.001$, sensitivity 70%, specificity 85.2%), 62.66 ms (AUC: 0.650, 95% CI: 0.585–0.716, $P < 0.001$, sensitivity 54.5%, specificity 72.8%), and 43.43 ms (AUC: 0.782, 95% CI: 0.727–0.837, $P < 0.001$, sensitivity 75.5%, specificity 60.5%), respectively. **Conclusions:** Prolonged $maxPWT_{postPCI}$, $maxPWT_{postPCI}$, and $PWD_{postPCI}$ are independent predictors that differentiate no-RF from RF in patients with AMI after PCI and can be used in the follow-up of no-RF patients during the post-PCI period.

Keywords: Acute myocardial infarction, no-reflow, P-wave dispersion, P-wave time, reflow

Introduction

Percutaneous coronary intervention (PCI) is the gold standard strategy that exhibits 95% efficacy in restoring blood flow in the infarct-related coronary artery (IRA); however, myocardial perfusion is still not well corrected in up to 60% of acute myocardial infarction (AMI) patients.[1-3] Insufficient correction of myocardial perfusion is known as the no-reflow (no-RF) phenomenon, and the etiopathogenesis of this phenomenon is related to persistent microvascular obstruction despite the opening of the IRA with PCI.[4] During no-RF, tissue necrosis continues with its hemodynamic and morphological disturbances in both atria and ventricles, resulting in an increased risk of arrhythmia.

Atrial arrhythmias, especially atrial fibrillation, occur during AMI in 5.8% of cases and are associated with increased mortality and morbidity.[5] Prolonged maximal P-wave time (PWT) and P-wave dispersion (PWD) have been shown as independent predictors of atrial fibrillation

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and its associated mortality and morbidity.[6-8] Although a few studies have highlighted the relationship between these parameters and AMI,[9-11] no study has investigated the relationship between PWT, PWD, and no-RF in addition to PWT, PWD, and reflow (RF) in patients with AMI before and after PCI.

Therefore, the present study aimed to investigate the effects of no-RF and RF on PWT and PWD in groups of AMI patients who underwent PCI with no-RF and RF.

Methods

Patient population

This was a retrospective, cross-sectional design and was based on patient files that were conducted between January 2014 and September 2018 at the University Hospital Cardiology Clinic. Between these dates, we scanned stored digital angiographic images of 4532 patients with AMI and reevaluated the angiographic images of patients with no-RF (no-RF group, *n*: 110). The RF patients were randomly selected from stored digital angiographic images of 4532 patients with reflow (RF group, *n*: 162). No-RF and RF were determined depending on their myocardial blush grade (MBG). The study started after obtaining written approval from the local ethics board, and the research protocol was as per the Declaration of Helsinki (ID: 80576354-050-99/108).

The inclusion criteria were as follows: total or subtotal occlusion of the IRA in AMI patients and postprocedural MBG 0–1 for no-RF patients and 3 for RF patients (Grade 0 = contrast density absent in the myocardium; Grade 1 = contrast density minimal in the myocardium; Grade 2 = contrast density moderate in the myocardium but less than that obtained from the ipsilateral non-IRA; and Grade 3 = normal contrast density in myocardium present during angiography).[12]

The excluded criteria were as follows: (1) patients with stable or unstable angina who had undergone PCI or had previous coronary artery bypass surgery history; (2) antiarrhythmic medicine usage; (3) valve disease; (4) constrictive/restrictive myocarditis, pericarditis, pericardial effusion, or cardiac tamponed; (5) electrolyte imbalance; (6) morbid obesity; (7) hypo-/hyperthyroidism; (8) chronic obstructive lung disease or secondary pulmonary hypertension (HT); (9) chronic renal or hepatic insufficiency; (10) pace rhythm or bundle branch block; and (11) an uncertain beginning or end of P-wave on a 12-lead electrocardiography (ECG).

Percutaneous coronary intervention variables

The PCI was performed through femoral access using conventional angiographic views. We stored all images obtained during the procedure were stored in a digital format. Stored images were reevaluated again, and we divided the study patients into the no-RF or the RF group depending on their MBG. Syntax scores (SS) (using an online calculator, http://www.syntaxscore.com/calculator/start.htm) and thrombolysis in acute myocardial infarction thrombus grade (TIMI-TG) (0 = no thrombus; 1 = hazy, possible thrombus present; 2 = thrombus present – small size [greatest dimensions ≤1/2 vessel diameter]; 3 = thrombus present – moderate size [linear dimension >1/2 but <2 vessel diameters]; 4 = thrombus present – large size [largest dimension ≥2 vessel diameters]; 5 = recent total occlusion; and 6 = chronic total occlusion) of the patients were calculated from the stored angiographic images.

Electrocardiography variables

ImageJ software (https://imagej.net/Downloads) was used for scanning and analyzing the electrocardiogram (ECG) of the patients. All of the ECGs were calibrated at 5 mm, which represented 200 ms maxPWT was measured in leads II and aVF, and the longest measurement was accepted as maxPWT. Likewise, minPWT was measured in leads aVL and V1, and the shortest measurement was accepted as minPWT. MaxPWT and minPWT were the longest and shortest measurements obtained in leads II or aVF, respectively. All measurements were made manually with a magnifying glass that had a magnifying power of 900–1200 times. We described atrial deflection from the isoelectric line as the beginning and the end of the P-wave. MaxPWT and minPWT were measured for all the patients. Preprocedural PWD ($PWD_{prePCI)}$ and postprocedural PWD ($PWD_{postPCI}$) were described as the difference between preprocedural maxPWT and minPWT and postprocedural maxPWT and minPWT, respectively. MaxPWD and minPWD wave measurements corrected for heart rate (i.e., the corrected P-wave parameters were equal to P-wave parameters/(RR) 1/2.[13] The maximum ST-elevation was measured from the lead, which exhibited the highest ST elevation, before and after PCI. The formula for the degree of ST-segment resolution (%STER) was: $[(maxSTE_{prePCI} - minSTE_{postPCI})/maxSTE_{prePCI} \times 100]$. Meanwhile, the number and percentage of the patients who showed 50% and 70% of ST-segment resolution were calculated. We evaluated all the atrial arrhythmias developed during the hospital stay from patients' follow-up ECG, monitor records, or cardiologist follow-up notes.

Statistical analysis

The statistical analyses were performed using SPSS 21.00 package software (SPSS, Inc., Chicago, Illinois, USA). The scale data were interpreted as parametric distribution data if the Skewness/Std. Error and Kurtosis/Std. Error ratio was within the range of ± 1.96. Nominal and ordinal data were evaluated with a Chi-square test, and all variables were presented as absolute values and percentages. Parametric data were compared between and within the groups using a Student's *t*-test and paired sample *t*-test, respectively. Nonparametric data were compared between and within the groups using a Mann–Whitney U-test and Wilcoxon signed-rank test, respectively. Scale parametric variables were reported as the mean value ± standard deviation, and scale nonparametric variables were reported as the median value (25^{th}–75^{th} percentile). $P < 0.05$ was considered significant. A receiver operating characteristic (ROC) curve analysis was used for determining the cutoff value, sensitivity, and specificity of PWT, and PWD, respectively.

Results

We expressed the clinical characteristics and biochemical parameters of the no-RF and RF groups in Table 1. Of 4532 patients with AMI undergoing PCI, 110 (2.43%) developed no-RF. The no-RF and RF groups consisted of 70.9/29.1% (78/32) males/females and 77.8/22.2% (126/36) males/females, respectively ($P = 0.199$). The mean age of no-RF and RF groups was 67.18 ± 11.81 and 63.57 ± 2.55 years, respectively ($P = 0.018$).

We found no significant differences in HT, hyperlipidemia, and family history between the two groups ($P = 0.117$, $P = 0.076$, $P = 0.366$, respectively); however, body mass index, diabetes mellitus, and smoking were significantly higher in the no-RF group ($P < 0.001$, $P < 0.001$, $P = 0.030$, respectively). The no-RF group also had a higher length of hospital and coronary care unit stay ($P < 0.001$ for both).

Preprocedural heart rate (HR_{prePCI}), systolic blood pressure, diastolic blood pressure, and pulse pressure showed no significant difference between the two groups ($P = 0.469$, $P = 0.416$, $P = 0.067$, $P = 0.146$, respectively). The postprocedural heart rate ($HR_{postPCI}$) of the no-RF patients was significantly higher than that of the RF patients ($P < 0.001$).

We detected 44 atrial arrhythmias (1.6%) in the study population during inhospital follow-up, 29 of which (29%) were in the no-RF group and 15 of which (9.3%) were in the RF group. Moreover, the rate of atrial arrhythmia observed in the no-RF group was higher than in the RF group ($P < 0.001$). Furthermore, we observed 15 atrial fibrillations (13.6%) in the no-RF group, and this rate was higher than the whole of the RF (5.6%) group ($P = 0.028$). Moreover, correlation analysis showed a significant correlation between atrial arrhythmia and $maxPWT_{postPCI}$ and PWD_{posPCI} [Table 2].

There was no significant difference between the two groups in terms of drug medication (β-blocker, Ca^{2+}-blockers, amiodarone, angiotensin-converting enzyme inhibitors, angiotensin receptor blocker, diuretics, nitrates, and H2-receptor blocker).

Nine patient deaths were recorded, and this rate was higher in the no-RF group (6.36%) than the RF group (1.24%) ($P = 0.033$).

Postprocedural left atrial posteroanterior diameter ($LAD_{postPCI}$), left ventricular diastolic diameter ($LVEDD_{postPCI}$), left ventricular systolic diameter ($LVESD_{postPCI}$), and left ventricular ejection fraction ($LVEF_{postPCI}$) showed a significant difference

Table 1: The demographic, clinical, biochemical, and echocardiographic characteristics of patients with no-reflow and reflow groups and with the *P* value

	Overall (*n*=272)	No-RF group (*n*=10)	RF group (*n*=162)	*P*
Age (years)	65.03±12.36	67.18±11.81	63.57±2.55	0.018
Male gender	40.4% (110)	70.9% (78)	77.8% (126)	0.199
BMI (kg/m^2)	29.8 (28.1-32.9)	30.5 (28.5-34.8)	29.1 (27.6-31.9)	<0.001*
Hypertension	48.2% (131)	52.7% (58)	45.1% (73)	0.117
Diabetes mellitus	30.5% (83)	44.6% (49)	20.7% (34)	<0.001
Smoker	33.8% (139)	58.2% (64)	46.3% (75)	0.030
Dyslipidemia	33.8% (92)	39.1% (43)	30.2% (49)	0.076
Family history	22.8% (62)	21% (34)	25.7% (28)	0.366
HR (bpm)				
Pre-PCI	72.5 (65-83)	72 (68-83)	74 (61-83)	0.469*
Post-PCI	74.1 (68-79)	76 (71-88)	73 (64-76)	<0.001*
Blood pressure (mmHg)				
SBP	137 (124-154)	138 (128.3-148.3)	123 (115-156)	0.416*
DBP	91 (78-99)	93 (81-99)	90.5 (73.3-102)	0.067*
Pulse pressure	49.89±10.96	48.72±10.76	50.7±11.6	0.146
Peak cardiac enzymes (ng/mL)				
CK-MB	195.6 (108.4-310.9)	261 (195.4-349.2)	140.5 (98-256.5)	<0.001*
Troponin-I	26.5 (25-67.75)	59 (46.5-80)	25 (18-26)	<0.001*
Echocardiography				
$LAD_{postPCI}$ (mm)	38.45±2.88	39.72±2.22	37.57±2.96	<0.001
$LVEDD_{postPCI}$ (mm)	47.69±2.73	48.11±3.28	47.4±2.25	0.044
$LVESD_{postPCI}$ (mm)	34.91±2.23	35.6±2.08	34.43±2.22	<0.001
$LVEF_{postPCI}$ (%)	47.21±7.43	44.24±8.35	49.26±5.93	<0.001
Hospital stay (days)				
Coronary care stay	2.7±1.58	3.23±1.65	2.29±1.45	<0.001
Cardiology clinic stay	6.312.7	7.14±2.92	5.77±2.41	<0.001

*Data are expressed as median (25th–75th percentiles). BMI: Body mass index, CK-MB: Creatine kinase-MB, DBP: Diastolic blood pressure, LVEF: Left ventricular ejection fraction, LAD: Left atrial posteroanterior diameter, LDL: Low-density lipoprotein, LVEDD: Left ventricular end-diastolic diameter, LVESD: Left ventricular end-systolic diameter, Post-PCI: Postpercutaneous coronary intervention, Pre-PCI: Prepercutaneous coronary intervention, SBP: Systolic blood pressure, HR: Heart rate, RF: Reflow

between the two groups ($P < 0.001$, $P = 0.044$, $P < 0.001$, and $P < 0.001$, respectively).

The preprocedural and postprocedural PWT indexes of the patients are shown in Table 3. $MaxPWT_{prePCI}$ and $maxPWD_{postPCI}$ of the no-RF and RF groups were 119.08 ± 16.85 ms versus 118.04 ± 20.09 ms ($P = 0.656$) and 117.86 ± 12.06 ms versus 94.95 ± 15.61 ($P < 0.001$), respectively. The $minPWT_{prePCI}$ and $minPWT_{postPCI}$ of the no-RF and RF groups were 67.54 ± 14.66 ms versus 70.02 ± 15.5 ms ($P = 0.187$) and 67.31 ± 11.79 ms versus 54.21 ± 12.13 ms ($P < 0.001$), respectively.

The no-RF group had higher values of PWD_{prePCI} and $PWD_{postPCI}$ when compared to the RF group (51.54 ± 17.11 ms vs. 48.02 ± 19.36, P=0.125, and 50.91 ± 11.9 ms vs. 39.14 ± 12.55 ms, $P < 0.001$, respectively). Although the preprocedural mean PWD did not exhibit a statistically significant difference, the postprocedural mean PWD was significantly higher in the no-RF group than the RF group.

Pairwise comparisons of 0, 1, 2, and 3 MBG subgroups with PWT indices are shown in Table 4. We did not observe significant differences regarding $maxPWT_{prePCI}$, $minPWT_{prePCI}$, and PWD_{prePCI} between MBG subgroups during pre-PCI period. However, we observed significant differences in some PWT indices during post-PCI period. The differences were as follows: (1) mean difference of $maxPWT_{postPCI}$ between MBG 0 and 2, 0 and 3, 1 and 2, 1 and 3, 2 and 3 (all $P < 0.01$); (2) mean difference of $minPWT_{postPCI}$ between MBG 0 and 3, 1 and 3 (all $P < 0.05$); and (3) mean difference of $PWD_{postPCI}$ between MBG 0 and 2, 0 and 3, 1 and 3 (all $P < 0.001$).

The mean of the preprocedural maximum ST-segment elevation ($maxSTE_{prePCI}$) was not statistically significantly different between the no-RF group and RF group (6.13 ± 3.2 vs. 6.5 ± 2.99, $P = 0.333$); however, the mean of the postprocedural maximum ST-segment elevation ($maxSTED_{postPCI}$) was significantly higher in the no-RF group than the RF group (4.16 ± 2.29 vs. 2.56 ± 1.55, $P < 0.001$). Similarly, the percentage of patients who exhibited 70% and 50% ST-segment resolutions (STSR) was lower in the no-RF group than the RF group (4.5% vs. 34.6%, $P < 0.001$, and 23.6% vs. 66%, $P < 0.001$, respectively). The no-RF group did not show any significant differences in maxPWT and minPWT ve PWD values before and after PCI, whereas these parameters decreased after PCI in the RF group.

The mean stent length, TIMI-TG, and SS of the no-RF patients were significantly higher than those of the RF group; however, stent diameter, $TIMI\text{-}MBG_{prePCI}$, and $TIMI\text{-}MBG_{postPCI}$ were significantly lower than those of the RF group.

The no-RF group showed a meaningful correlation with $HR_{postPCI}$, $maxPWT_{postPCI}$, $minPWT_{postPCI}$, and $PWD_{postPCI}$. Although there was no correlation between TIMI-TG and $minPWT_{postPCI}$, %STER, HR_{prePCI}, $maxPWT_{prePCI}$, $minPWT_{prePCI}$, and PWD_{prePCI}, TIMI-TG and %STER exhibited a meaningful correlation with $HR_{postPCI}$, $maxPWT_{postPCI}$, $minPWT_{postPCI}$, $minPWT_{postPCI,}$ and $PWD_{postPCI}$. Furthermore, the atrial arrhythmias showed a significant correlation with $maxPWT_{postPCI}$ and $PWD_{postPCI}$. Correlation analyses of the parameters are shown in Table 2, and correlation graphics of $maxPWT_{postPCI\ and}$ $PWD_{postPCI}$ are shown in Figure 1.

The univariate logistic regression analysis showed that $maxPWT_{postPCI}$ (odds ratio [OR] = 0.1.105, 95% confidence interval [CI]: 0.1.078–1.133, $P < 0.001$), $minPWT_{postPCI}$ (OR = 1.035, CI: 1.015–1.054, $P < 0.001$), and $PWD_{postPCI}$ (OR = 1.106, CI: 1.076–1.137, $P < 0.001$) were absolute predictors of the no-RF. This analysis displayed that $maxPWT_{postPCI}$, $minPWT_{postPCI}$, and $maxPWT_{postPCI}$ were the predictors of the no-RF [Table 5]. According to multivariate logistic regression analysis-entered models, including STER, peak troponin-I, TIMI-TG, $MBG_{postPCI}$, IRA, and three coronary disease, $maxPWT_{postPCI}$ (OR: 1.103, 95% CI: 1.049–1.16, $P < 0.001$), $minPWT_{postPCI}$ (OR: 1.055, 95% CI: 1.011–1.101, $P < 0.014$), and $PWD_{postPCI}$ (OR: 1.107, 95% CI: 1.037–1.181, $P = 0.002$) were the independent predictors of no-RF after PCI.

The ROC curve analyses demonstrated that the optimal

Table 2: Correlation analysis between P-wave time index and no-reflow, percentage ST-elevation resolution, thrombolysis in acute myocardial infarction-thrombus grade, and syntax score

	No-RF		Atrial arrhythmias		%STER		TIMI-TG		Syntax score	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
HR_{prePCI}	0.033	0.590	−0.019	759	−0.010	0.872	0.205	0.001	0.039	0.523
$HR_{postPCI}$	0.277	<0.001	116	0.060	−0.125	0.039	0.235	<0.001	0.207	<0.001
$MaxPWT_{prePCI}$	0.020	0.742	047	0.439	−0.027	0.652	0.259	<0.001	0.196	0.001
$MaxPWT_{postPCI}$	0.571	<0.001	0.223	<0.001	−0.329	<0.001	0.203	0.001	0.313	<0.001
$MinPWT_{prePCI}$	−0.016	0.793	−059	0.335	0.025	0.676	−0.202	0.001	0.055	0.363
$MinPWT_{postPCI}$	0.219	<0.001	−0.110	0.069	−0.181	<0.003	−0.049	0.422	0.103	0.090
PWD_{prePCI}	0.034	0.579	0.097	0.112	−0.049	0.419	0.433	<0.001	0.158	0.009
$PWD_{postPCI}$	0.545	<0.001	0.385	<0.001	−0.239	<0.001	0.300	<0.001	0.293	<0.001

HR: Heart rate, MaxPWT: Maximum P-wave time, minPWT: Minimum P-wave time, post-PCI: Postpercutaneous coronary intervention, pre-PCI: Prepercutaneous coronary intervention, PWD: P-wave dispersion, TIMI-TG: Thrombolysis in acute myocardial infarction thrombus grade, RF: Reflow, STER: ST-elevation resolution

Table 3: Comparison of maximal P-wave time, minimal P-wave time, P-wave dispersion values, and other parameters between no-reflow and reflow groups before and after percutaneous coronary intervention and with the *P* value

	Overall (*n*=272)	No-RF group (*n*=110)	RF group (*n*=162)	*P*
$MaxPWT_{prePCI}$ (ms)	118.56±19.08	119.08±16.85	118.04±20.09	0.656
$MaxPWT_{postPCI}$ (ms)	105.56±17.8	117.86±12.06	94.95±15.61	<0.001
$MinPWT_{prePCI}$ (ms)	67.92±15.06	67.54±14.66	70.02±15.5	0.187
$MinPWT_{postPCI}$ (ms)	60.46±13.64	67.31±11.79	54.21±12.13	<0.001
PWD_{prePCI} (ms)	50.63±18.46	51.54±17.11	48.02±19.36	0.125
$PWD_{postPCI}$ (ms)	45.11±14.25	50.91±11.9	39.14±12.55	<0.001
$MaxSTE_{prePCI}$ (mm)	6.35±3.07	6.13±3.2	6.5±2.99	0.333
$MaxSTE_{postPCI}$ (mm)	3.21±2.03	4.16±2.29	2.56±1.55	<0.001
MaxSTER (%)	45.52±26.7	27.9±22.95	58.14±21.66	<0.001
MaxSTER (≥70%)	22.4% (61)	4.5% (5)	34.6% (56)	<0.001
MaxSTER (≥50%)	48.9% (133)	23.6% (26)	66% (107)	<0.001
Atrial arrhythmias				
AF	8.8% (24)	13.6% (15)	5.6% (9)	0.028
All atrial arrhythmias	16.2% (44)	26.4% (29)	9.3% (15)	<0.001
Drug therapy				
β-blocker	53.7% (146)	60.9% (67)	48.8% (79)	0.063
Ca^{2+}-blockers	7.7% (20)	8.2% (9)	6.8% (11)	0.644
Amiodarone	2.9% (8)	1.8% (2)	3.7% (6)	0.480
ACE inhibitors	34.9% (95)	35.5% (39)	34.6% (56)	0.897
ARB	18.8% (51)	20.0% (22)	17.9% (29)	0.752
Diuretics	7.7% (21)	10.9% (12)	5.6% (9)	0.112
Nitrates	7.7% (21)	10.0% (11)	6.2% (10)	0.256
H2-receptor blocker	% (195)	66.4% (73)	75.3% (122)	0.131
IRA				
LAD	71.7% (104)	30.9% (50)	49.1% (54)	0.005
CX	7.4% (20)	11.7% (19)	10% (11)	0.591
RCA	45.6% (124)	54.9% (89)	31.8% (35)	0.001
HL	5.2% (14)	11.7% (4)	9.1% (10)	0.015
Coronary critical lesions				
One coronary	29.8% (81)	14.5% (16)	40.1% (65)	<0.001
Two coronary	53.3% (145)	58.2% (64)	50.0% (81)	0.184
Three coronary	16.5% (46)	9.9% (16)	27.3% (30)	<0.001
CTO present	5.5% (15)	10.9% (12)	1.9% (3)	0.002
Stent number				
One stent	84.2% (229)	81.8% (90)	85.7% (139)	0.377
Two stent	12.9% (35)	13.6% (15)	12.4% (20)	0.755
Three stent	2.9% (8)	4.5% (5)	1.9% (3)	0.197
Stent diameter (mm)	2.95±0.43	2.82±0.32	3.04±0.48	<0.001
Stent length (mm)	23.99±7.09	26.17±7.29	22.5±6.59	<0.001
TIMI-TG	3.08±1.07	3.43±0.87	2.85±1.12	<0.001
$TIMI\text{-}MBG_{prePCI}$	0.121±0.359	0.091±0.319	0.142±0.384	0.251
$TIMI\text{-}MBG_{postPCI}$	1.967±1.269	0.782±1.008	2.772±0.643	<0.001
Syntax score	19.66±7.84	22±8	16.24±7.41	<0.001
Mortality	3.3% (9)	6.36% (7)	1.24% (2)	0.033

ACE: Angiotensin-converting enzyme inhibitor, AF: Atrial fibrillation, APC: atrial premature contraction, ARB: Angiotensin receptor blocker, CTO: Chronic total occlusion, Cx: Circumflex, HL: High lateral, LAD: Left anterior descending, maxPWT: Maximal P-wave time, maxSTE: Maximal ST elevation, MBG: Myocardial blush great, minPWT: Minimal P-wave time, post-PCI: Postpercutaneous coronary interventions, pre-PCI: Prepercutaneous coronary intervention, PWD: P-wave dispersion, RCA: Right coronary artery, STER: ST-elevation resolution, TG: Thrombus grade, TIMI: Thrombolysis in acute myocardial infarction, RF: Reflow, IRA: Infarct related artery

cutoff values of $maxPWT_{postPCI}$, $minPWT_{postPCI}$, and $PWD_{postPCI}$ for predicting the no-RF were 112.95 ms (area under the curve [AUC]: 0.852, 95% CI: 0.807–0.898, $P < 0.001$, sensitivity 70%, specificity 85.2%), 62.66 ms (AUC: 0.650, 95% CI: 0.585–0.716, $P < 0.001$, sensitivity 54,5%, specificity 72,8%), and 43.43 ms (AUC: 782, 95% CI: 0.727–0.837, $P < 0.001$, sensitivity 75.5%, specificity 60.5%), respectively [Figure 2].

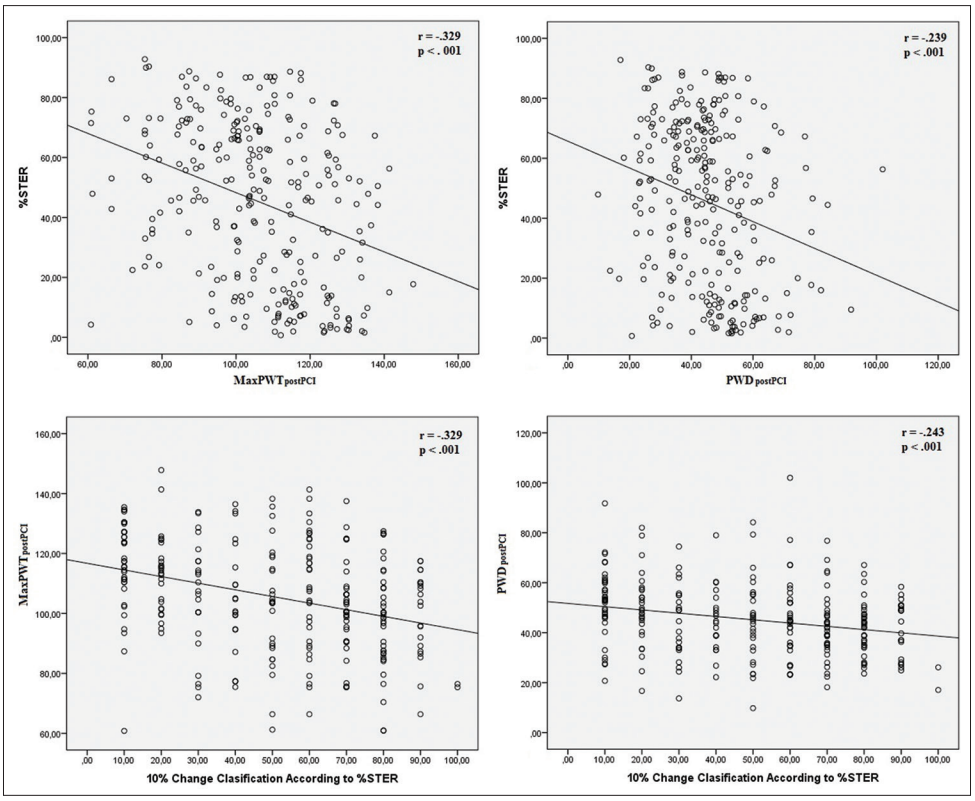

Figure 1: Correlation analysis between $maxPWT_{postPCI}$, $PWD_{postPCI}$, %STER, and the 10% change classification according to %STER (a-d). PWD: P-wave dispersion, PWT: P-wave time, STER: ST-elevation resolution

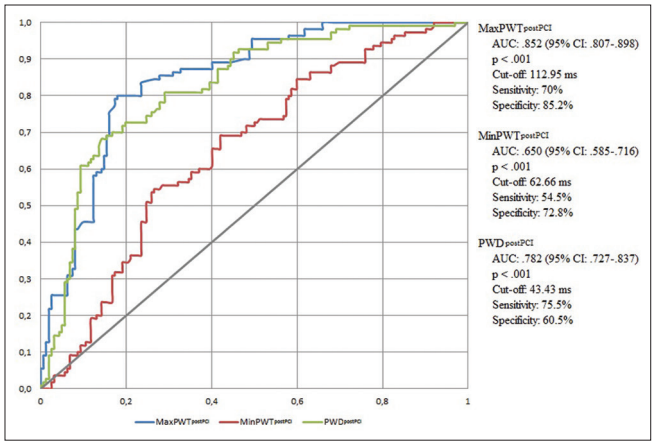

Figure 2: The receiver operating characteristics curves for the $maxPWT_{postPCI}$, $minPWT_{postPCI}$, and $PWD_{postPCI}$ values in the prediction of the no-reflow. PWD: P-wave dispersion, PWT: P-wave time, AUC: Area under the curve, CI: Confidence interval

Discussion

The present study revealed the impact of the no-RF/RF on PWT indexes. During the pre-PCI period, maxPWT, minPWT, and PWD were prolonged in both the no-RF and RF groups, whereas, during the post-PCI period, they were shorter in only the RF group. Moreover, maxPWT, minPWT, and PWD correlated with %STER, TIMI-TG, and coronary artery complexity. These findings suggest that no-RF and RF have favorable adverse effects on P-wave morphology.

No-RF can be defined as impaired tissue circulation and continuing necrosis despite the opening of the IRA with PCI.[4] Distal coronary embolization during PCI (within 0–40 min), which causes microvascular obstruction, an inflammatory response, ischemia (interventional no-RF), and microvascular obstruction caused by prolonged ischemia (after 90 min) along with ischemia-reperfusion injury, myocardial edema, endothelial swelling, changes in blood viscosity, capillary obstruction, vasospasm, inflammatory response, and thrombus formation (reperfusion no-RF) are mechanisms suggested as playing a role in the pathogenesis of the no-RF.[14]

Regardless of the pathophysiological mechanism, tissue necrosis continues and ischemic/necrotic tissue extends beyond the ischemic area during no-RF.[15] Production of reactive oxygen species (ROS), such as superoxide anion (O^{2-}), hydrogen peroxide (H_2O_2), and hydroxyl radical ($HO^{\bullet}$), may lead to some morphological, hemodynamic, and arrhythmogenic effects in the heart.[16-19]

Besides tissue degeneration, the presence of too much ROS directly or indirectly causes conduction disorders in atrial and ventricular myocytes, arrhythmias, and a reduction in conduction velocity.[17-19] Experimental studies have shown that ROS promotes arrhythmia formation by lengthening action potential duration, early inducting afterdepolarization, and retarding afterdepolarization.[20] Increased ROS may provide a basis for a re-entry mechanism by making differences in action potential duration in the ischemic myocardium.[21-23] The myocardial effects

Table 4: Pairwise comparisons of myocardial blush Grade 0, 1, 2, and 3 subgroups with P-wave time indices before and after percutaneous coronary intervention

	MBG N_0/N_1: 24/86			MBG N_0/N_2: 24/36			MBG N_0/N_3: 24/126			MBG N_1/N_2: 86/36			MBG N_1/N_3: 86/126			MBG N_2/N_3:36/126		
	0	1	*P*	0	2	*P*	0	3	*P*	1	2	*P*	1	3	*P*	2	3	*P*
HR_{prePCI}	83.5±24.6	73.2±9.1	0.057	83.5±24.6	72.5±21.6	0.088	83.5±24.6	74.7±19.3	0.117	73.2±9.1	72.5±21.6	0.998	73.2±9.1	74.7±19.3	0.923	72.5±21.6	74.7±19.3	0.914
$HR_{postPCI}$	81.4±17.5	78.2±11.4	0.645	81.4±17.5	72.5±13.3	0.020	81.4±17.5	72±9.8	0.002	78.2±11.4	72.5±13.3	0.061	78.2±11.4	72±9.8	0.001	72.5±13.3	72±9.8	0.998
$MaxPWT_{prePCI}$	124.9±22	117.4±15.1	0.317	124.9±22	123.4±23.6	0.990	124.9±22	116.8±19.2	0.221	117.4±15.1	123.4±23.6	0.388	117.4±15.1	116.8±19.2	0.996	123.4±23.6	116.8±19.2	0.259
$MaxPWT_{postPCI}$	123±15.6	116.5±10.6	0.194	123±15.6	104.9±16.7	<0.001	123±15.6	95±15.3	<0.001	116.5±10.6	104.9±16.7	<0.001	116.5±10.6	95±15.3	<0.001	104.9±16.7	95±15.3	0.002
$MinPWT_{prePCI}$	69.2±18.2	67.2±13.1	0.945	69.2±18.2	69.2±17.4	1	69.2±18.2	67.8±15.1	0.979	67.2±13.1	69.2±17.4	0.915	67.2±13.1	67.8±15.1	0.991	69.2±17.4	67.8±15.1	0.966
$MinPWT_{postPCI}$	64.9±15.6	63.9±10.4	0.987	64.9±15.6	61.8±16.7	0.813	64.9±15.6	56.9±13.5	0.038	63.9±10.4	61.8±16.7	0.859	63.9±10.4	56.9±13.5	0.001	61.8±16.7	56.9±13.5	0.218
PWD_{prePCI}	55.7±24.2	50.2±14.3	0.557	55.7±24.2	54.2±20.6	0.989	55.7±24.2	49±19	0.350	50.2±14.3	54.2±20.6	0.691	50.2±14.3	49±19	0.965	54.2±20.6	49±19	0.437
$PWD_{postPCI}$	58.1±16.9	52.6±10	0.203	58.1±16.9	43.1±15.2	<0.001	58.1±16.9	38.1±11.6	<0.001	52.6±10	43.1±15.2	0.001	52.6±10	38.1±11.6	<0.001	43.1±15.2	38.1±11.6	0.128

HR: Heart rate, MaxPWT: Maximum P-wave time, minPWT: Minimum P-wave time, post-PCI: Postpercutaneous coronary intervention, pre-PCI: Prepercutaneous coronary intervention, PWD: P-wave dispersion, MBG: Myocardial blush grade

Table 5: The univariate and multivariate logistic regression analysis of the P-wave time index for prediction of no-reflow

	B	SE	*P*	OR	95% CI for Exp (B)	
					Lower	Upper
Univariate logistic regression analysis						
$MaxPWT_{postPCI}$	0.100	0.013	<0.001	1.105	1.078	1.133
$MinPWT_{postPCI}$	0.030	0.010	<0.001	1.035	1.015	1.054
$PWD_{postPCI}$	0.101	0.014	<0.001	1.106	1.076	1.137
Multivariate logistic regression analysis for the MaxPWTpostPCI						
$MaxPWT_{postPCI}$	0.098	0.026	<0.001	1.103	1.049	1.160
STER	−0.053	0.016	0.001	0.949	0.920	0.978
Peak troponin-I	0.047	0.016	0.003	1.048	1.016	1.082
TIMI-TG	−0.871	0.400	0.030	0.419	0.191	0.917
$MBG_{postPCI}$	−2.340	0.456	<0.001	0.096	0.039	0.236
IRA	−0.741	0.342	0.030	0.477	0.244	0.932
Three coronary disease	3.882	1.076	<0.001	48.534	5.895	399.592
Multivariate logistic regression analysis for the MinPWTpostPCI						
$MinPWT_{postPCI}$	0.053	0.022	0.014	1.055	1.011	1.101
STER	−0.065	0.015	<0.001	0.937	0.911	0.965
Peak troponin-I	0.052	0.014	<0.001	1.053	1.025	1.083
TIMI-TG	−0.784	0.358	0.029	0.457	0.226	0.922
$MBG_{postPCI}$	−2.230	0.388	<0.001	0.108	0.050	0.230
IRA	−858	0.319	0.007	0.427	0.227	0.792
Three coronary disease	3.913	1.001	<0.001	50.062	7.042	355.918
Multivariate logistic regression analysis for the PWD						
$PWD_{postPCI}$	0.101	0.033	0.002	1.107	1.037	1.181
STER	−0.062	0.015	<0.001	0.939	0.912	0.968
Peak troponin-I	0.040	0.014	0.004	1.041	1.013	1.069
TIMI-TG	−1.202	0.425	0.005	0.300	0.131	0.691
$MBG_{postPCI}$	−2.345	0.431	<0.001	0.096	0.041	0.223
IRA	−0.795	0.325	0.014	0.452	0.239	0.854
Three coronary disease	2.745	0.929	0.003	15.557	2.519	96.083

SE: Standard error, *P*: Significance (two-tailed), OR: Odds ratio, CI: Confident interval, MaxPWT: Maximum P-wave time, minPWT: Minimum P-wave time, post-PCI: Postpercutaneous coronary intervention, pre-PCI: Prepercutaneous coronary intervention, PWD: P-wave dispersion, MBG: Myocardial blush grade, TIMI-TG: Thrombolysis in acute myocardial infarction thrombus grade, STER: ST-elevation resolution, IRA: Infarct related artery

of ROS are as follows: (1) reducing conduction velocity through the activation of fibrotic processes by the assembly of connexin-43 into gap junctions and the inhibition of the Na current through protein kinase C and c-Src kinase pathways; (2) causing repolarization abnormalities through K_{ATP}, I_{to}, I_{Kr}, and I_{Ks} channel inhibition; (3) increasing intracellular Ca^{2+} through Na^{+}/Ca^{2+} exchanger activation; (4) activation of a delayed Na^{+} current; (5) impairment of sarco- or endoplasmic reticulum Ca^{2+}-ATPase activity; and (6) facilitation of afterdepolarizations through ryanodine receptor effects (through CaMKII activation).[17-19]

PWD is characterized by a difference between the maximum and minimum P-wave durations on a surface ECG.[24]

Increased PWD reflects intra- and interatrial heterogeneity, which is associated with atrial arrhythmias, most notably atrial fibrillation, increased mortality, and morbidity.[15,25-30] Andrikopoulos *et al*.[25] found that PWD >40 ms predicted idiopathic atrial fibrillation with an 83% sensitivity and 85% specificity. Aytemir *et al*.[26] observed that a value of PWD greater than 36 ms was a good predictor of separating idiopathic paroxysmal atrial fibrillation and a healthy subject. Rosiak *et al*.[27] led a study on patients with AMI using a signal-averaged electrocardiogram. The sensitivity and specificity of PWD > 25 ms and PWT > 125 ms for predicting high-risk patient atrial fibrillation were 74%, 77% and 81%, 82%, respectively.

In literature, although we encountered some studies that found PWD and PWT as the predictors of atrial fibrillation, we did not find any study investigating the effects of the no-RF and RF on PWT and PWD. Since we found three studies assessing the effects of reperfusion therapy (PCI or thrombolytic therapy) on PWT and PWD, we compared the present results with them.

Akdemir *et al*.[9] investigated the effects of PCI and thrombolytic therapy on PWD in two groups of patients who showed similar clinical characteristics, such as age, gender, left ventricular ejection fraction, cardiac risk factors, left atrial anteroposterior diameter and volume, and average symptom duration. The PWD_{prePCI} value was higher in both PCI and thrombolytic groups and did not show any statistical difference between them (46 ± 12 ms versus 57 ± 8 ms, $P > 0.05$). Patients who experienced RF after PCI had normal values for PWD, whereas the thrombolytic group continued to have higher values (31 ± 13 ms vs. 55 ± 5 ms, $P = 0.001$). Likewise, $maxPWT_{prePCI}$ and $minPWT_{prePCI}$ were higher in both the patient groups (113 ± 11 ms vs. 116 ± 13 ms, $P = 0.371$, and 66 ± 10 ms vs. 60 ± 12 ms, $P = 0.189$, respectively). After reperfusion therapy, $maxPWT_{postPCI}$ remained elevated in the thrombolytic group. The $minPWT_{postPCI}$ did not exhibit any significant differences between the groups (68 ± 12 ms vs. 61 ± 9 ms, $P = 0.336$).

Khan *et al*.[11] studied PWD after 120 min of thrombolysis in two groups of patients who had more and <70% of ST-segment resolution on their ECGs. PWD values for Group 1 (≥70% ST-segment resolution) and Group 2 (<70% ST-segment resolution) decreased postthrombolytic therapy when compared to prethrombolytic values (40.86 ± 7.25 vs. 48.97 ± 10.72 ms and 47.91 ± 6.14 ms vs. 51.59 ± 8.34 ms, respectively). Although the prethrombolytic PWD values did not exhibit any statistically significant differences between the two groups ($P = 0.45$), the postthrombolytic values did ($P = 0.001$).

Karabag *et al*.[10] investigated the relationship between the patency of IRA, STER, and PWD at 0, 30, 90, and 120 min of fibrinolysis. The PWD values at 0, 30, 90, and 120 min were higher in patients without STER than those of patients with STER (51.5 ± 13.8 ms, 47.0 ± 12.3 ms, 47.9 ± 9.6 ms, 48.3 ± 11.2 ms, 52.9 ± 10.3 ms, and 46.2 ± 15.2 ms, 47.2 ± 12.8 ms, 46.5 ± 14.5 ms, 43.9 ± 13.3 ms, and 44.8 ± 11.5 ms, respectively). Among these values, only the PWD value at 120 min exhibited statistical significance ($P < 0.001$). They additionally found almost similar results concerning the patency of the IRA. Patients with occluded IRA exhibited higher PWD values than patients with patent IRA (49.1 ± 1 4.7 ms, 47.3 ± 12.7 ms, 48.6 ± 11.4 ms, 47.8 ± 11.4 ms, 53.5 ± 10.7 ms and 47.9 ± 14.9 ms, 46.9 ± 12.4 ms, 45.3 ± 14.0 ms, 43.5 ± 13.1 ms, 42.3 ± 9.7 ms, respectively), and only the PWD value at 120 min was statistically significant ($P = 0.001$).

The present results were compatible with the previous research. Pre-PCI values of maxPWT and PWD were elevated in both the groups without any statistical differences. After PCI, the RF group had statistically significantly lower values of maxPWT, minPWT, and PWD, suggesting a positive impact of RF on these values. Moreover, PWD and PWT had a negative correlation with %STER and a positive correlation with SS, which is an indicator of coronary artery complexity.

Conclusion

In light of the literature data, thrombolytic or PCI therapy reduces the incidence of atrial arrhythmia in patients with AMI and the no-RF. Increases in PWT indices can cause an increased incidence of atrial arrhythmia. The results of this study showed that PCI has a more favorable effect on the decrease in PWT indices. Furthermore, our results suggest that P-wave indices are simple electrocardiographic predictors that can differentiate between the no-RF and RF in AMI patients undergoing PCI.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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