Prediction of Reperfusion and Infarct Related Artery Patency after Thrombolysis in Acute Anterior Myocardial Infarction by Degree of P Wave Dispersion on ECG

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Keywords: *Ischaemic heart disease, Coronary artery, ECG, P wave.*

Abstract:

Background: *Early detection IRA patency following thrombolytic therapy is of great importance in terms of prognosis and identification of candidates for rescue percutaneous coronary intervention (PCI). P wave dispersion (PWD), a new parameter measured before and after thrombolytic therapy is supposed to predict successful reperfusion in patients with anterior acute myocardial infarction (AMI).*

Methods: *132 patients were selected and divided into two groups on the basis of ST Segment resolution (STR) after 120 minutes of thrombolysis. Group I: patients with STR >70%; Group II: patients with STR < 70%. P wave dispersion was measured in both groups before and after thrombolysis. All patients underwent coronary angiography (CAG). IRA was considered patent if TIMI flow grade was e"2.*

Results: *It was observed that diabetes mellitus and dyslipidemia were significantly higher in group II patients (p=0.04 and p=0.03, respectively). PWD before thrombolysis (PWD0) and 90 minutes after thrombolysis (PWD90) in both groups were statistically insignificant (p=0.45 and p=0.19, respectively). The mean level of PWD120 was statistically significant (p=0.001). After multivariate regression analysis PWD120 was found to be the significant predictor of IRA patency (OR = 1.101; 95% CI = 1.012 – 1.240; p = 0.01).*

Conclusion*: P wave dispersion in patients receiving thrombolytic therapy can be a predictor of successful reperfusion and patent IRA. PWD values, in combination with other reperfusion parameters, can contribute to the identification of rescue PCI candidates.*

(Cardiovasc. j. 2018; 10(2): 158-163)

Introduction:

Achieving optimal coronary flow following thrombolysis in myocardial infarction (TIMI) reduces mortality, preserves left ventricular function and improves survival following acute myocardial infarction (AMI).[1,2] The prognosis of patients with persistent occlusion of the IRA, despite thrombolytic therapy is poor compared with that of patients with recanalized coronary arteries. Therefore, early detection of successful reperfusion and IRA patency in patients who received thrombolytic therapy is of great importance in terms of prognosis and identification of candidates for rescue PCI.[3]

For this purpose, some parameters such as: relief of chest pain, early peak of cardiac biomarkers, appearance of reperfusion arrhythmia and various electrocardiographic (ECG) changes are used as noninvasive tools, among which ST segment resolution at 90 minutes is one of the most important markers of successful reperfusion and prognosis.[4]

P wave dispersion, a parameter measured before and after thrombolytic therapy is able to predict successful reperfusion in patients with acute anterior MI.[5] The P-max is the longest atrial conduction time and P-min is the shortest atrial conduction time measured in any of the 12 leads of the surface ECG.[6] PWD is calculated by subtracting the minimum P-min from the P-max.[7] A pathological P-wave duration is considered as e" 120 msec.[8]

PWD was found to be significantly increased during the anginal episodes irrespective of the presence of history of a previous myocardial infarction.[9] Furthermore, PWD showed higher values during the anginal episode in patients with left ventricular dysfunction independently of the presence of a previous myocardial infarction.[10] PWD at 120 minutes is significantly

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lower in patients with successful reperfusion and patent IRA.[5] P-max and PWD is higher in slow coronary flow patient.[11]

Methods:

This was an observational study conducted in Department of Cardiology, National Institute of Cardiovascular Diseases and Dhaka, Bangladesh from July, 2013 to July 2014 on the purposively sampled patients with acute MI (anterior) who received thrombolytic therapy. After judging inclusion and exclusion criteria total 132 patients were selected and divided with 66 patients in each group on the basis of ST Segment resolution (STR) after 120 minutes of thrombolysis after AMI. Group I: patients with STR >70%; Group II: patients with STR < 70%.

Streptokinase was used as a thrombolytic agent. 12 lead resting ECG was done at a paper speed of 25 mm/s and 10 mm standardization. All recordings were performed in the same quiet room during spontaneous breathing, following 20 minute of adjustment in the supine position. ST-segment deviation was measured with a handheld caliper and magnifying glass at 80 milliseconds after the J-point in all available leads. The TP-segment was considered the preferred iso-electric baseline and ST segment deviation was measured to the nearest 0.05 mV. ST segment resolution was calculated and expressed as a percentage with this formula: (baseline ST elevation-120 minute ST elevation)/ baseline ST elevation.

ECGs were recorded before thrombolysis and 90 & 120 minutes after onset of thrombolysis. The onset of the P wave was defined as the point of first visible upward slope from baseline for positive waveforms and as the point of first downward slope from baseline for negative waveforms. The return to the baseline was considered as the end of the P wave. Biphasic P waves were measured to the time of final return to baseline. If the onset or offset of the P wave were not clearly determined the lead was excluded from the analysis. P wave duration measurements were obtained manually by using calipers and magnifying lens for accurate definition of the ECG deflection. PWD of both groups was measured by subtracting P wave minimum from P wave maximum durations (Figure 1).

Transthoracic echocardiography was done for chambers size, wall motion abnormality, EF%, valvular, pericardial conditions. All patients underwent coronary angiography (CAG) during same hospital stay. Anterograde perfusion of the infarct-related artery was graded according to the classification system of the thrombolysis in myocardial infarction (TIMI) trial (grade 0 = no anterograde perfusion, grade 1 = minimal perfusion, grade 2 = partial perfusion and grade 3 = complete perfusion). IRA patency was considered if TIMI flow grade was 2 or 3.

The SPSS Statistical Software (17.0 version, SPSS Inc., Chicago, Illinois, USA) was used for data analysis. Continuous variables were expressed in mean & standard deviation and categorical variables as frequency and percentage. Student's t-test was used to compare normally distributed continuous variables and for the categorical variables the chi-square test was used. Multiple logistic regression analysis was performed to assess the PWD 120 minutes after onset of thrombolysis (PWD120) as a predictor of reperfusion and IRA patency. A p-value <0.05 was considered statistically significant.

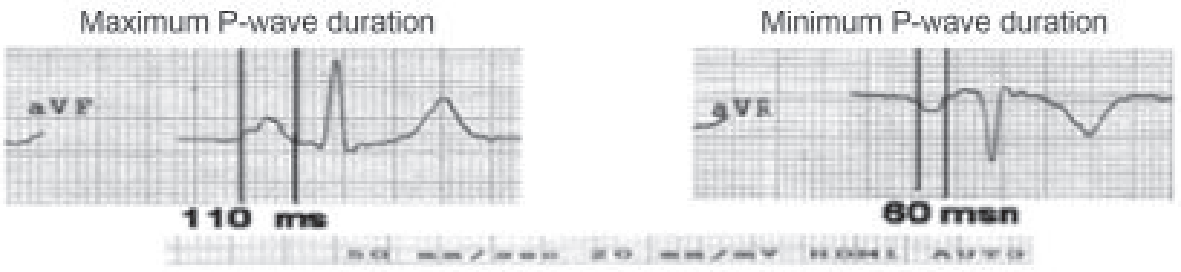

Fig.-1: *The maximum and minimum P-wave durations (P-max and P-min).*

Results:

Total 132 patients were studied. The mean age of the studied patients was 50.60±8.23 years. The mean age of group I was less than group II, but the difference between two groups was not statistically significant (p=0.06). Male female ratio was 4.3:1. No significant difference (p=0.82) was found between the groups in terms of sex distribution (Table I).

BMI demonstrates very close values in both groups with no significant difference between groups (p=0.33). Smoking is higher in group I than in group II but without statistical significance (p=0.36). It was observed that diabetes mellitus and dyslipidemia were significantly higher in Group II (p=0.04, p=0.03) (Table II).

Between the two groups, the differences of means of PWD0 and PWD90 were not statistically significant (p=0.45 and p=0.19, respectively). The difference of mean levels of PWD120 across the groups was statistically significant (p=0.001) (Table III).

It was observed that IRA patent patients were more in group I than group II (68.18% vs. 15.15%) which was statistically significant (p=0.001) (Table IV).

PWD120 was found to be the significant independent predictors to develop ST segment resolution (OR = 1.101; 95% CI = 1.012 – 1.240; p = 0.01) (Table V) and predictor of IRA patency (OR = 1.101; 95% CI = 1.012 – 1.240; p = 0.01) (Table VI) after multivariate analysis of the all studied independent variables.

Table-I

Comparison of the study groups by their demographic characteristics (N = 132).

Age in years	STR				Total(N = 132)		*p*-value
	Group I (n = 66)		Group II (n = 66)				
	Number	%	Number	%	Number	%	
< 40	14	21.21	11	16.67	25	18.94	[a]0.11[NS]
40 – 60	40	60.61	43	65.15	83	62.88	
> 60	12	18.18	12	18.18	24	18.18	
Mean ± SD	49.12±9.54		52.08±8.23		50.60±8.23		[b]0.06[NS]
Sex							
Male	53	80.30	54	81.82	107	81.06	[a]0.82[NS]
Female	13	19.70	12	18.18	25	18.94	

Group I= Patients with STR >70%
Group II = patients with STR < 70%
STR = ST segment resolution after 120 minutes of thrombolysis
NS= Not significant (p>0.05)
[a]p value reached from chi-squared test
[b]p value reached from unpaired t test

Table-II

Comparison of the study groups by their risk factors (N = 132).

BM(kg/m^2)	STR				Total(N = 132)		*p*-value
	Group I (n = 66)		Group II (n = 66)				
	Number	%	Number	%	Number	%	
Normal	31	46.97	28	42.2	59	18.94	[a]0.33[NS]
Overweight	22	33.33	19	28.49	41	62.88	
Obese	13	19.70	19	28.79	32	18.18	
Mean ± SD	23.42±3.67		24.78±4.88		24.10±4.23		[b]0.06[NS]
Risk Factors							
Smoking	45	68.18	40	60.61	85	64.39	[a]0.36[NS]
Hypertension	30	45.45	35	53.03	65	49.24	[a]0.28[NS]
Diabetes	25	37.88	37	56.06	62	46.97	[a]0.04[S]
Dyslipidemia	23	34.85	35	53.03	58	43.94	[a]0.03[S]
Family history	10	15.15	14	21.21	24	18.18	[a]0.36[NS]

Group I= Patients with STR >70%
Group II = patients with STR < 70%
STR = ST segment resolution after 120 minutes of thrombolysis
BMI = Body Mass Index
NS= Not significant (p>0.05)
S= Significant (p<0.05)
[a]p value reached from chi-squared test
[b]p value reached from unpaired t test

Table-III

Comparison of the study groups according to P wave dispersions (n=132).

PWD (millisecond)	STR		p value
	Group I (n = 66)	Group II (n = 66)	
PWD0	48.97±10.72	51.59±8.34	0.45^{NS}
PWD90	44.24±9.12	46.98±7.44	0.19^{NS}
PWD120	40.86±7.25	47.91±6.14	0.001^{S}

Group I= Patients with STR >70%
Group II = patients with STR < 70%
PWD = P Wave Dispersion
STR = ST segment resolution after 120 minutes of thrombolysis
PWD0 = PWD at 0 minute (before the of onset of thrombolysis)
PWD90 =PWD 90 minutes after onset of thrombolysis
PWD120 =PWD 120 minutes after onset of thrombolysis
NS= Not significant (p>0.05)
S= Significant (p<0.05)
p value reached from unpaired t test

Table-IV

Comparison of the study groups according to infarct related artery (IRA) patency (n=132)

BMI (kg/m^2)	STR				Total(N = 132)		p-value
	Group I (n = 66)		Group II (n = 66)				
	Number	%	Number	%	Number	%	
IRA patent	45	68.18	10	15.15	55	41.66	0.001^{S}
IRA occluded	21	31.82	56	84.85	77	58.44	

Group I= Patients with STR >70%
Group II = patients with STR < 70%
STR = ST segment resolution after 120 minutes of thrombolysis
IRA = Infarct Related Artery
S= Significant (p<0.05)
p value reached from chi-squared t test

Table-V

Multivariate logistic regression of determinants of ST-segment resolution.

Variables of interest	β	S.E.	p value	OR	95% CI
Smoking	0.253	0.441	0.56^{NS}	1.288	0.543 – 3.055
Hypertension	0.701	0.501	0.10^{NS}	1.066	0.519 – 2.503
Diabetes mellitus	0.367	0.506	0.46^{NS}	1.444	0.535 – 3.892
Dyslipidemia	0.203	0.249	0.66^{NS}	0.816	0.325-2.054
PWD120	0.912	0.654	0.01^{S}	1.101	1.012 – 1.240

Dependent variable: ST-segment resolution
Independent variables; smoking, hypertension, diabetes mellitus, dyslipidemia and PWD120
S = Significant
NS = Not significant

Table-VI

Multivariate logistic regression of determinants of infarct related artery patency

Variables of interest	β	S.E.	p value	OR	95% CI
Smoking	0.253	0.441	0.56^{NS}	1.288	0.543 – 3.055
Hypertension	0.701	0.501	0.10^{NS}	1.066	0.519 – 2.503
Diabetes mellitus	0.367	0.506	0.46^{NS}	1.444	0.535 – 3.892
Dyslipidemia	0.203	0.249	0.66^{NS}	0.816	0.325-2.054
PWD120	0.912	0.654	0.01^{S}	1.101	1.012 – 1.240

Dependent variable: infarct related artery patency
Independent variables: smoking, hypertension, diabetes mellitus, dyslipidemia and PWD120
S = Significant
NS = Not significant

Discussion:

In this study, the mean age of the successfully thrombolysed group was 49.12±9.54 and mean age of failed thrombolysis group was 52.08±8.23 years. Though higher age was associated with failed thrombolysis it was statistically insignificant (p=0.06). In a similar study conducted by Karabag et al. mean age observed higher in failed thrombolysis group.[5] Successful thrombolysis had higher percentage of male though statistically not significant (p=0.82). Another study showed the similar higher percentage of male in successful group.[6] Patients with higher BMI demonstrated successful thrombolysis as was found in the similar study conducted by Mahmoud.[6] Among the studied patients, hypertension, diabetes mellitus, dyslipidemia and family history of IHD were higher in group II than in group I except smoking which is higher in group I. It was observed that diabetes mellitus and dyslipidemia were significantly higher in Group II (p=0.04, p=0.03). There were other studies that yielded results was identical to this study.[6,10]

PWD before start of thrombolysis (PWD0) and PWD 90 minutes after the onset of thrombolysis in both groups were statistically insignificant (p=0.45 and p=0.19, respectively). The mean level of PWD120 was statistically significant (p=0.001). Similar observation was seen by another study.[5] The study conducted by Baykan, et al. showed that P wave dispersion was significantly higher in patients with AF than in patients without AF (P = 0.01).[12] Similar other study showed that P dispersion increased significantly during spontaneous angina (P < 0.001).[10] P wave dispersion was significantly higher in 60 patients with paroxysmal lone AF than in 40 healthy controls (p <0.0001) in another study.[13]

The multivariate regression analysis of odds ratios for characteristics of the subjects likely to cause IRA patency was studied. Out of the 5 variables, PWD120 was found to be the significant predictor of ST segment resolution as well as IRA patency. Karabag et al. also showed that PWD120 could predict IRA patency and ST-segment resolution on ECG (OR: 0.907, CI: 0.856 to 0.960; p=0.001; OR: 0.942, CI: 0,896 to 0,991; p=0.02, respectively).[5]

Study limitations

This was a purely observational study on patients who presented to hospital with acute MI (anterior) and who refused the option of primary PCI. We use streptokinase for thrombolysis which is less superior to other thrombolytics like tenecteplase due to unavailability of them. Purposive sampling was done instead of random sampling method in my study. Although 90 minutes after thrombolytic therapy is standard time for rescue PCI in most centers, PWD was measured at 120 minutes in our study. Most of our hypertensive patients were on antihypertensive medications. We could not exclude patients who were using drugs that might affect atrial conduction and PWD; there are no good data on the effect of antihypertensive agents on PWD.

Conclusion:

From this study, it may be concluded that low P wave dispersion in patients receiving thrombolytic therapy can be a predictor of successful reperfusion and patent infarct related artery. PWD values, in combination with other reperfusion parameters, can contribute to the identification of rescue PCI candidates.

Recommendations

Further prospective studies are needed to assess the temporality of the association between P wave dispersion value and successful reperfusion and IRA patency by ECG following thrombolysis of acute MI (Anterior) patients. Similarly, in future randomized clinical trials using large number of patients may be used.

Conflict of Interest - None.

References:

1. Fox KAA, Goodman SG, Klein W, Brieger D, Steg PG, Dabbous O, et al. Management of acute coronary syndromes. Variations in practice and outcome; findings from the Global Registry of Acute Coronary Events (GRACE). *Eur Heart J* 2002; 23:1177–1189.

2. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: Collaborative overview of early mortality and major morbidity results from all randomized trials of more than 1000 patients. *Lancet* 1994; 343: 311–322.

3. Ross AM, Lundergan CF, Rohrbeck SC, Boyle DH, van den Brand M, Buller CH, et al. Rescue angioplasty after failed thrombolysis: Technical and clinical outcomes in a large thrombolysis trial. GUSTO-1 Angiographic Investigators. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. *J Am Coll Cardiol* 1998; 31: 1511–1517.

4. Stewart JT, French JK, Theroux P, Ramanathan K, Solymoss BC, Johnson R, et al. Early noninvasive identification of failed reperfusion after intravenous thrombolytic therapy in acute myocardial infarction. *J Am Coll Cardiol* 1998;31:1499–505.

5. Karabag T, Dogan SM, Aydin M, Sayin MR, Buyukuysal C, Gudul NE, et al. The value of P wave dispersion in predicting reperfusion and infarct related artery patency in acute anterior myocardial infarction. *Clinical & Investigative Medicine* 2012; 35: 12–19.

6. Mahmoud K. Effect of coronary slow flow on dispersion of P-wave & QT-interval and its relationship with Thrombolysis in Myocardial Infarction frame count. *The Egyptian Heart Journal* 2013; 65: 175–180.

7. Agarwal YK, Aronow WS, Levy JA, Spodick DH. Association of interatrial block with development of atrial fibrillation. *Am J Cardiol* 2003;91:882.

8. Shturman A, Bickel A, Atar S. The predictive value of P-wave duration by signal-averaged electrocardiogram in acute ST elevation myocardial infarction. *Isr Med Assoc J* 2012; 14: 493–497.

9. Akin F, Firatli I, Katkat F, Gurmen T, Ayca B, Kalyoncuoglu M, et al. P-wave dispersion and its relationship with the severity of the disease in patients with stable coronary artery disease. *North Clin Istanb* 2014; 1: 65–70.

10. Dilaveris PE, Stefanadis CI. P Wave Dispersion: A Valuable Non-Invasive Marker of Vulnerability to Atrial Arrhythmias. *Hospital Chronicles* 2006; 1:130–137.

11. Akcay A, Acar G, Suner A, Sokmen A, Sokmen G, Nacar AB, et al. Effects of slow coronary artery flow on P-wave dispersion and atrial electromechanical coupling. *J Electrocardiol* 2009; 42:328–333.

12. Baykan M, Celik S, Erdol C, Durmus I, Orem C, Kucukosmanoglu M, et al. Effects of P-wave Dispersion on Atrial Fibrillation in Patients with Acute Anterior Wall Myocardial Infarction. *Ann Noninvas Electro* 2003; 8:101–106.

13. Dogan SM, Yildirim N, Gursurer M, Aydin M, Kalaycioglu E, Cam F. P-wave duration and dispersion in patients with coronary slow flow and its relationship with Thrombolysis in Myocardial Infarction frame count. *J Electrocardiol* 2008;41:55–59.