

Association between PR Segment Displacement with Adverse In-hospital Outcome after Thrombolysis in Patients with Acute ST Elevation Myocardial Infarction

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Abstract

Introduction: Atrial ischemia produces similar changes in the PR-segment as ventricular ischemia in the ST-segment. The occurrence of PR segment displacement on the admission ECG can predict the risk of developing adverse in-hospital outcomes, especially for ST-segment elevation myocardial infarction (STEMI) patients and is strongly correlated with the severity of STEMI. However, further studies are needed to see this relationship between PR segment displacement and in-hospital outcomes in patients with STEMI.

Method: This prospective observational study was conducted at the National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh, from February 2019 to September 2020 on 200 patients with two equally divided groups based on PR segment displacement: Group I with PR displacement ≥ 0.5 mm and Group II with PR displacement < 0.5 mm. Only the initial ECGs at the time of arrival to the emergency department were used to calculate PR segment displacement. A PR segment elevation or depression of ≥ 0.5 mm was considered significant. Arrhythmia, heart failure, cardiogenic shock, duration of hospital stay, and death were observed during the index hospitalization.

Results: Out of 200 patients, 112 had PR segment displacement. Among patients of PR segment displacement, PR segment depression (59.82%) was higher than elevation (40.18%). All of the atrial arrhythmias were observed more frequently in group I in comparison to group II, and among them, atrial fibrillation was significantly higher in group I (28% vs 10%; $p=0001$). Cardiogenic shock was also observed more in group I with significant PR depression than without significant PR depression (18% vs 8%; $p=0.03$). The mean hospital stay was significantly higher in group I than group II (Mean \pm SD = 6.05 \pm 1.84 vs 3.87 \pm 1.46 days; $p<0.001$). Incidence of ventricular arrhythmias, heart failure, atrial thrombus, and death didn't differ significantly between the groups ($p>0.05$). The odds ratios of hypertension, heart rate, and PR segment displacement were significant in univariate analysis. In multivariate analysis after adjusting for these variables, only PR segment displacement was found to be the independent predictor for developing adverse in-hospital outcomes, with an OR of 6.54.

Conclusion: Significant PR segment displacement is associated with adverse in-hospital outcomes, especially in the form of atrial fibrillation and cardiogenic shock in patients with ST elevation myocardial infarction after thrombolytic therapy.

Keywords: PR segment displacement, Hospital outcome, Thrombolysis, ST-segment elevation.

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Introduction

In the acute myocardial infarction (AMI), ST-segment elevation cannot predict the severity of the disease, atrial involvement, or overall effect [1]. It is well known that AMI may involve the atria, but clinicians have not paid special

attention to this fact. Atrial infarction is mostly diagnosed concomitantly with ventricular infarction. Its incidence in AMI varies significantly between studies, ranging from 0.7% to 42% [2,3]. In AMI, the electrocardiographic (ECG) sign of PR segment depression could signify extensive atrial ischemia or infarction, which is usually overlooked. The first case of atrial infarction was described in 1925, [4] and this was 17 years before Langendorf made the first ECG demonstration of atrial infarction [5]. Cushing et al. [6]

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reported the largest series of autopsy-proven atrial infarctions, including 31 of 182 cases of fatal MIs (17% incidence). The first antemortem diagnosis of atrial infarction was made by Hellerstein [7].

The ECG is the only means of diagnosing atrial infarctions before death [2]. The most commonly accepted ECG diagnosis of ATMI (atrial myocardial infarction) was defined by Liu et al. [8]. Agreeing to this definition, ATMI major and minor criteria were structured along with the basis on PR segment elevation or depression, abnormal P wave morphology, and the presence of a supraventricular arrhythmia. Diagnosis of atrial infarction can be reached only from ECG by a small, transient elevation and reciprocal depression of the PR segment, usually connected with alterations in the configuration of the P wave [9]. PR segment elevation of just 0.5mm or PR segment depression of 0.8 mm is strongly suggestive of atrial infarction [10]. Atrial ischemia produces similar changes in the PR-segment as ventricular ischemia in the ST-segment. Continuous monitoring of dynamic PR segment changes in patients with AMI is feasible and can detect concurrent atrial ischemia. When the patient is in sinus rhythm, ATMI often causes abnormal P waves and a PR segment [6]. Likewise, ignoring PR segment changes related to atrial infarction criteria and arrhythmias may result in delayed diagnosis of the atrial infarction [11]. PR segment displacement is suggestive of atrial infarction occurring concomitantly with STEMI. Previous studies reported that PR segment displacement in any lead, found in 31% of patients with STEMI, predicted both short-term and long-term poor outcomes [12].

Patients with ATMI have frequent cardiac and noncardiac complications. Profound PR segment depression ≥ 1 -2 mm in inferior leads was associated with a complicated hospital course and poor short-term effect in acute inferior MI [13]. The occurrence of PR segment displacements on the admission ECG can predict the hazard of developing supraventricular arrhythmias, particularly atrial fibrillation, during hospitalization for MI [14]. Supraventricular arrhythmias often complicate atrial infarction, and these arrhythmias, including atrial fibrillation, are the most common and may have hemodynamic consequences [15]. Supraventricular tachyarrhythmias have been established to occur more often in patients with concomitant atrial involvement compared to those with ventricular infarction alone (61–74% vs. 8%) [12]. The frequency of arrhythmias in atrial infarction may be as high as 70%, in contrast to about 20% in ventricular infarction [6]. Thromboembolic complications, such as pulmonary and systemic embolism, are also more common events with associated ATMI. In addition to the associated supraventricular arrhythmias, atrial infarction may present with lethal implications, such as thromboembolism and atrial rupture [16]. Early prediction of their occurrence is significant because they may influence the selection of therapy during the early

stages of the infarctions [17]. Therefore, this study aims to assess PR segment displacement in acute ST-elevation MI patients and predict in-hospital outcomes.

Methods

This prospective observational study was conducted at the National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh, from February 2019 to September 2020. The study protocol was accepted by the Ethical Review Committee of NICVD. A total of 200 patients admitted to the Department of Cardiology, NICVD, Dhaka, with the diagnosis of STEMI who were treated with thrombolytic therapy (Streptokinase) during index hospitalization and had no exclusion criteria considered for the study. Informed written consent was taken from each patient before enrollment. Meticulous history was taken, detailed clinical examination was performed, and recorded in a predesigned structured questionnaire. Demographic data, such as age, sex, was recorded. Risk factor profile, including smoking, hypertension, diabetes, dyslipidemia, and family history of coronary artery disease (CAD), was noted. Investigations like cardiac troponin I, serum creatinine, and random blood sugar (RBS) were carried out. Initial ECGs at the time of arrival to the hospital or the emergency department were used in the study. Variables collected from the ECG recordings include heart rhythm, PR segment displacements (elevation and depression), and types of STEMI. These ECGs were interpreted by the magnification of a still picture of the ECG. PR segment elevation or depression of ≥ 0.5 mm was considered significant. Patients were divided into two groups based on PR segment displacement. Those with a significantly displaced PR segment (≥ 0.5 elevations or depression) were categorized as group I, and those without a significantly displaced PR segment were categorized as group II. Arrhythmias, heart failure, cardiogenic shock, duration of hospital stay, and death were observed during the index hospitalization. All the data were recorded in the data collection sheet. The data obtained from the study were analyzed, and the significance of differences was estimated by using statistical methods. Continuous variables were expressed as mean value \pm standard deviation and compared using the unpaired Student's t-test. Categorical variables were compared using the chi-square test. Univariate logistic regression analysis was performed to specify the odds ratio (OR) for overall adverse in-hospital outcomes. Multivariate logistic regression analysis was done to investigate independent predictors of in-hospital outcomes. Statistical significance was assumed if $p \leq 0.05$ throughout the study. Statistical analysis was carried out by using SPSS 25.0.

Results

Table 1 showed that the mean age of the study population was 56.7 ± 8.2 years in Group I and 58.1 ± 8.4 years in Group II, with no significant difference ($p = 0.08$). Most of the study subjects were males. (Figure1). The male and female ratio was 2:1. There is no statistically significant difference ($p=0.32$) in

the sex distribution of the study patients. Group I patients had the highest percentage of hypertension (55%), followed by smoking (45%), diabetes mellitus (39%), dyslipidemia (15%), and family history of coronary artery disease (13%). On the contrary, in Group II, diabetes mellitus was predominant (44%), followed by hypertension (41%), smoking (40%), dyslipidemia (17%), and family history of coronary artery disease (11%). All the risk factors mentioned in Table 2 showed no statistically significant difference between the two groups ($p > 0.05$), except for hypertension ($p = 0.04$).

Table 1: Distribution of the study patients according to age

Age in years	Group I (n = 100)		Group II (n = 100)		Total (n=200)		p value
	Number	%	Number	%	Number	%	
35 – 44	4	4.0	4	4.0	8	4.0	
45 – 54	44	44.0	32	32.0	76	38.0	
55 – 64	31	31.0	35	35.0	66	33.0	
65 – 74	18	18.0	29	29.0	47	23.5	
75 – 84	3	3.0	0	0.0	3	1.5	
Age (Mean ±SD)	56.7±8.2		58.1±8.4		57.4±8.3		0.28 ^{ns}

SD: standard deviation; Group I: patients with PR segment displacement; Group II: patients without PR segment displacement; ns: not significant. P-value reached from an unpaired t-test.

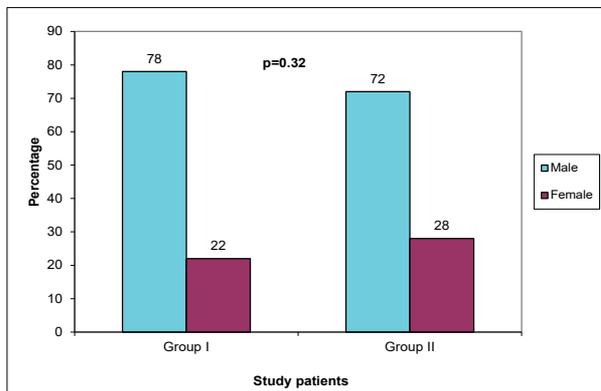


Figure 1: Gender distribution among the study patients by a bar diagram

Group I: patients with PR segment displacement; Group II: patients without PR segment displacement; ns= not significant. P-value reached from the Chi-square test.

Table 2: Distribution of the study patients according to cardiovascular risk factors

Risk Factors	Group I (n = 100)		Group II (n = 100)		Total (n=200)		p value
	Number	%	Number	%	Number	%	
Smoking	45	45.0	40	40.0	85	42.5	0.47 ^{ns}
Hypertension	55	55.0	41	41.0	96	48	0.04 ^s
Diabetes mellitus	39	39.0	44	44.0	83	41.5	0.48 ^{ns}
Dyslipidemia	15	15.0	17	17.0	32	16	0.69 ^{ns}
Family history of premature CAD	13	13.0	11	11.0	24	12.0	0.66 ^{ns}

CAD: coronary artery disease; Group I: patients with PR segment displacement; Group II: patients without PR segment displacement; ns: not significant; s: significant. Data was analyzed using the Chi-Square test.

The heart rate was 91.2±19.4 beats per minute in Group I and 80.2±14.7 beats per minute in Group II (Table 3), with a statistically significant difference ($p=0.01$). Anterior wall MI was found in about 39% of Group I and 43% of Group II (Table 4). On the contrary, non-anterior wall MI was found in 61% and 57% in Group I and Group II, respectively. No significant difference was found among the patients in terms of the site of MI ($p=0.56$). Regional Wall Motion Abnormality (RWMA) was observed in 39% and 35% of Group I and Group II (Table 5), respectively, with no statistically significant difference ($p=0.65$). The mean left ventricular ejection fraction (LVEF) was 54.6 ± 5.4% in Group I & 52.2 ± 3.3% in Group II ($p=0.17$).

Table 3: Distribution of the study patients by heart rate status

Parameters	Group I (n = 100)		Group II (n = 100)		p value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Heart rate/minute	91.2±19.4	80.2±14.7	80.2±14.7	80.2±14.7	0.001 ^s
	(60-150) *		(60-110) *		

SD: standard deviation; Group I: patients with PR segment displacement; Group II: patients without PR segment displacement; s: significant. The figure in parentheses indicates the range. P-value reached from an unpaired t-test

Table 4: Distribution of the study patients by the site of MI

Site of MI	Group I (n = 100)		Group II (n = 100)		Total (n=200)		p value
	Number	%	Number	%	Number	%	
Anterior	39	39.0	43	43.0	82	41.0	0.56 ^{ns}
Non-anterior	61	61.0	57	57.0	118	59.0	

MI: myocardial infarction; Group I: patients with PR segment displacement; Group II: patients without PR segment displacement; ns: not significant; s: significant. Data was analyzed using the Chi-Square test.

Table 5: Comparison of two groups by echocardiography

VARIABLES	Group I (n = 100)		Group II (n = 100)		p value
	Number	%	Number	%	
RWMA					
Present	39	39.0	35	35.0	a _{0.65} ns
Absent	68	68.0	65	65.0	
LVEF in %					
36 – 44 (Moderate)	5	5.0	4	4.0	b _{0.17} ns
45 – 54 (Mild)	40	40.0	44	44.0	
≥ 55 (Normal)	55	55.0	52	52.0	
Mean ± SD	54.6 ± 5.4		52.2 ± 3.3		

RWMA: regional wall motion abnormality; LVEF: left ventricular ejection fraction; SD: standard deviation; Group I: patients with PR segment displacement; Group II: patients without PR segment displacement; ns: not significant. a=P value reached from using the Chi-Square test. b=P value reached from unpaired t-test

Among patients who had PR segment displacement, about 60% had PR segment depression, while 40% had PR segment elevation (Table 6). PR segment depression was more commonly observed in limb leads, while PR segment elevation was more commonly observed in the precordial leads. Table 7 depicts a comparison of patients by in-hospital outcome. Heart failure developed in 21% of Group I and 18% of Group II subjects with a statistically insignificant difference ($p=0.59$). In atrial arrhythmias, AF occurred in 28% and 10% of patients in Group I and Group II, respectively, with a statistically significant difference ($p=0.001$). Ventricular arrhythmias were found to be similar in both groups of patients, with no significant difference ($p>0.05$). Cardiogenic shock developed in 18% of patients in Group I and 8% in Group II patients with a statistically significant difference ($p=0.03$). It was observed that the mean hospital stay period was higher in Group I than in Group II, which was 6.05 ± 1.84 vs. 3.87 ± 1.46 days. The mean difference was statistically significant ($p<0.001$). Finally, 15% of patients died in Group I and 8% of patients in Group II, with statistically no significant difference ($p=0.12$). Out of the 3 variables, PR segment displacement was found to be the independent predictor for developing adverse in-hospital outcomes with an Odds ratio (OR) being 6.54 (Table 8).

Table 6: Distribution of PR segment elevation and depression among patients with PR segment displacement

Characteristics	PR segment displacement	
	Number	%
PR segment elevation	45	40.18
Leads (n=45)		
Limb leads	22	48.9
Precordial leads	23	51.1
PR segment depression	67	59.82
Leads (n=67)		
Limb leads	37	55.2
Precordial leads	30	44.8

Group I: Patients with PR segment displacement.

Table 7: Comparison of patients by the in-hospital outcome

In-hospital outcome	Group I (n=100)		Group II (n=100)		Total (n=200)		p value
	Number	%	Number	%	Number	%	
Atrial Arrhythmias							
AF	28	28.0	10	10.0	38	19.0	0.001*
AT	5	5.0	1	1.0	6	3.0	0.09 ^{ns}
Atrial extrasystole	4	4.0	1	1.0	5	2.5	0.17 ^{ns}
PSVT	3	3.0	0	0.0	3	1.5	0.08 ^{ns}
Ventricular arrhythmia							
VT	5	5.0	7	7.0	12	6.0	0.55 ^{ns}
VF	2	2.0	2	2.0	4	2.0	1.00 ^{ns}
Heart failure	21	21.0	18	18.0	39	19.5	0.59 ^{ns}
Cardiogenic shock	18	18.0	8	8.0	26	13.0	0.03*
Atrial thrombus	3	3.0	0	0.0	3	1.5	0.08 ^{ns}
Hospital stays	6.05 ± 1.84		3.87 ± 1.46				$p<0.001^*$
[Mean \pm SD	(2 – 9)		(2 – 8)				
Range (Min-Max)]							
Death	15	15.0	8	8.0	23	11.5	0.12 ^{ns}

AF: atrial fibrillation; AT: atrial tachycardia; PSVT: paroxysmal supraventricular tachycardia; VT: ventricular tachycardia; VF: ventricular fibrillation; SD: standard deviation; Group I: patients with PR segment displacement; Group II: patients without PR segment displacement; ns: not significant; s: significant. Data were analyzed using the Chi-Square test and Fisher's exact test. b= p-value reached from unpaired t-test.

Table 8: Factors related to the adverse in-hospital outcome as a dependent variable

Variables of interest	Multivariate analysis		
	OR	95% CI of OR	p value
Hypertension	1.18	0.543 – 2.580	0.67 ^{ns}
Heart rate	1.06	0.201 – 9.801	0.09 ^{ns}
PR segment displacement	6.54	1.910 – 19.44	0.001 ^s

OR: odds ratio; CI: confidence interval; s: significant; ns: not significant.

Discussions

Baseline characteristics of the study subjects were similar between the two groups in this study, except for hypertension, which was more prevalent in patients in group I.

In the present study, the age range spanned from 35 to 84 years, with the majority of patients falling within the 45-54 year age group. The average age was 56.7 ± 8.2 years for group I and 58.1 ± 8.4 years for group II, which aligns with the findings of Lu et al. [12]. Conversely, a different study by Jim et al. [13] reported a mean age of 67.9 ± 10.4 years in the PR-segment depression group and 64.9 ± 13.1 years in the control group. Male patients were predominant in this study population (75%). Lu et al. [12] also found male predominance. A similar observation was also noted in several other studies [13,18].

In this study sample, hypertension emerged as the most prevalent risk factor (48%), followed by smoking (42.5%), diabetes (41.5%), dyslipidemia (16%), and a family history of coronary artery disease (12%). Similarly, the study conducted by Lu et al. [12] reported hypertension as the leading risk factor (74.5%), with smoking (57.1%) ranking second. However, their findings indicated a higher prevalence of a family history of premature CAD (45%) compared to diabetes (33%). On the other hand, Jim et al. [13] also highlighted hypertension as the predominant risk factor (55%). However, it was accompanied by hyperlipidemia and diabetes, with a family history of premature CAD not being recorded in their study. In the current study, statistical analysis revealed no significant differences in the prevalence of cardiac risk factors between the two groups ($p > 0.05$), except for hypertension. Hypertension was significantly more common in Group I compared to Group II (55 vs. 41), and this difference was found to be statistically significant ($p < 0.04$).

Among group I patients, the mean heart rate was 91.2 ± 19.4 beats per minute (bpm), and among group II subjects, the mean heart rate was 80.2 ± 14.7 bpm in the current study, and statistically significant differences were found in relation to heart rate between the study groups ($p=0.01$). This finding differs from the study of Jim et al. [13], where the mean heart rate on presentation was higher (111 ± 27 beats/min).

In this present study, anterior MI was less common in both groups than non-anterior MI. Anterior MI was found in 39% of group I and 43% of group II. On the contrary, non-anterior MI was found in 61% and 57% of group I and group II, respectively. These differences in the prevalence of types of MI between the groups were not statistically significant ($p > 0.05$). Although this finding differs from the study by Lu et al [12], where they found anterior MI was the predominant presentation (54.45%). Several Bangladeshi studies on STEMI also found a lower number of anterior MI than non-anterior MI [19-21].

All the patients of this study were evaluated by echocardiography to see the LVEF and RWMA. The mean LVEF was $54.6 \pm 5.4\%$ in Group I and $52.2 \pm 3.3\%$ in Group II. Statistically, no significant difference in LVEF was found among the study groups ($p = 0.17$). Similar findings were observed by studies of both Lu et al. [12] and Jim et al. [13].

In this current study, among Group I patients, PR segment depression (59.82%) was higher than elevation (40.18%), and PR segment depression was more commonly observed in limb leads than precordial leads, while PR segment elevation was more commonly observed in precordial leads than limb leads. A similar finding was also observed by Lu et al. [15] in their study. They also concluded that the presence of PR depression in limb and precordial leads was associated with higher 1-year mortality in anterior wall STEMI patients but not in non-anterior wall STEMI patients [12].

In the present study, the adverse outcome was more frequently observed in group I patients in comparison to group II. Among the atrial arrhythmias, atrial fibrillation (19%) was more frequently observed, followed by atrial tachycardia (3%), atrial extra systole (2.5%), and paroxysmal supraventricular tachycardia (1.5%). All these atrial arrhythmias were observed more frequently in group I in comparison to group II, and among them, atrial fibrillation was observed significantly higher in the group with the PR displacement (28% vs 10%; $p = 0.001$). Nielsen et al [14] also observed that atrial fibrillation is the predominant arrhythmia in their study. Lu et al. [12] also observed supraventricular arrhythmia as the predominant arrhythmia in their study, though they didn't mention which type is more common. But Jim et al. [13] found atrial tachycardia as the predominant arrhythmia and more than atrial fibrillation in their study.

In this study, among the ventricular arrhythmias, hemodynamically significant ventricular tachycardia and ventricular fibrillation were analyzed. Ventricular tachycardia was more common in group II than in group I (7 vs 5), and these differences were not significant ($p = 0.55$) between the two groups. Ventricular fibrillation was observed similarly in numbers in groups I and II (2 vs 2, $p = 1.00$).

In this current study, heart failure was observed in 19.5% of patients. There was no significant difference with respect to the occurrence of heart failure between the groups ($p = 0.59$). The study of Nielsen et al. [14] also observed more heart failure in groups who fulfilled major criteria of atrial infarction, including significant PR depression, than the other group (80.9% vs 47%). They also observed heart failure more in patients with supraventricular arrhythmia (65.7%).

Cardiogenic shock was also observed more in Group I than in Group II in this study. This difference between the two groups in relation to cardiogenic shock is statistically significant ($p = 0.03$). This finding is like both Lu et al. [12] and Jim et al. [13] studies. The loss of atrial 'kick' may lead to decreased ventricular filling pressures, causing decreased cardiac output and significant hemodynamic consequences, such as cardiogenic shock. These patients will be preload dependent and may benefit from aggressive fluid loading [12].

In this present study, Thrombosis has been observed more in group I patients than in group II patients, though this difference is not statistically significant (3% vs 0%; $p = 0.08$). Both Lu et al. [12] and Nielsen et al. [14] observed a higher rate of thrombosis and thromboembolism in the atrial infarction group of their study.

In this current study, it was observed that the duration of hospital stay was higher in group I than in group II (6.05 ± 1.84 & 3.87 ± 1.46 days in group I and group II, respectively). The mean difference was statistically significant ($p < 0.001$). This finding is similar to the study of Lu et al. [12], where they observed that the median length of hospital stay was 5 days in the total population of that study.

Death is higher in group I patients than in group II patients in this present study (15% vs 8%), but the differences between the two groups in relation to death were not significant ($p = 0.12$). These findings are like the study of Nielsen et al. [14], where they also observed no significant difference in mortality between the two groups (3 vs 12, $p > 0.05$), but these findings differ from the studies conducted by Lu et al. [12] and Jim et al. [13]. In the study by Jim et al. [13], the presence of PR-segment depression was associated with an increase in in-hospital mortality (44.4 vs. 11.7%, $p = 0.015$), and in the study by Lu et al. [12], the 30-day mortality (14% vs. 9% $p < 0.05$) and 1-year mortality (33% vs. 12% $p < 0.001$) were statistically significant.

In this current study, binary logistic regression analysis was done to identify variables that were independently associated with at least one adverse outcome. The odds ratios of hypertension, heart rate, and PR segment displacement were significant in univariate analysis. In multivariate analysis after adjusting for these variables, only PR segment displacement was found to be the independent predictor for developing adverse in-hospital outcomes, with

an OR being 6.54. Lu et al. [12] also observed a similar result in their study. After adjusting for age, ejection fraction, peak troponin I level, and left main disease, PR displacement in any lead was associated with increased 1-year mortality (adjusted OR 6.22 (2.23–18.64)) in that study.

There were several limitations of the study. As purposive sampling was done so there could be a chance of selection bias. The study population was heterogeneous, including age, gender, the time interval from symptom onset to hospital admission, and ECG types of STEMI, blood sample collection for random blood sugar, and fasting lipid profile. Tachycardia may interfere with the measurement of the PR segment, and this effect could not be totally excluded. As the PR segment tended to resolve spontaneously, it is possible that this ECG sign may not be seen in patients who presented late. The sample size was small, so it may not reflect the true scenario. For the identification of significant arrhythmia, patients were observed in coronary care unit (CCU) for 24 hours only; later, it was diagnosed only by ECG based on the patient's complaints of palpitation, so some arrhythmias may be missed. Ventricular extrasystole and idioventricular rhythm were also observed but not analyzed because they are frequently observed due to successful thrombolysis and are benign in course.

Conclusion

Significant PR segment displacement is associated with adverse in-hospital outcomes, especially in the form of atrial fibrillation and cardiogenic shock in patients with ST elevation myocardial infarction after thrombolytic therapy. Correct identification of this subset of patients through early identification of PR displacement could alert the physician to the potential for future complications.

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