Effect of Reperfusion on P-Wave Duration and P-Wave Dispersion in Acute Myocardial Infarction: Primary Angioplasty Versus Thrombolytic Therapy

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Summary

Atrial fibrillation is a common arrhythmia occurring in about 10-20% of patients with acute myocardial infarction. P-wave dispersion and P-wave duration have been used to evaluate the discontinuous propagation of sinus impulse and the prolongation of atrial conduction time respectively. This study was conducted to compare the effects of reperfusion either by thrombolytic therapy or primary angioplasty on P wave duration and dispersion in patients with acute anterior wall myocardial infarction.

We have retrospectively evaluated 72 consecutive patients (24 women, 48 men; aged 58 ±12 years) experiencing a first acute anterior wall myocardial infarction (AMI). Patients were grouped according to the reperfusion therapy received (primary angioplasty (PTCA) versus thrombolytic therapy). Left atrial diameter and left ventricular ejection fraction (LVEF) were determined by echocardiography in all patients. Electrocardiography was recorded from all patients on admission and on pach day of hospitalization. Maximum (P max) and minimum (P min) P wave durations and P wave dispersions (PWd) were calculated before and after treatment.

There were no significant differences between the groups regarding age, gender, left ventricular ejection fraction (LVEF), left atrial diameter and volume, cardiovascular risk factors and duration from symptom onset to treatment. PWd and P wave durations were significantly reduced after PTCA (mean P max was 113±11 ms before and 95±17ms after the treatment [p=0.007]. Mean PWd was 46±12 ms before and 29±10 ms after the treatment (p=0.001). Also, P max and PWd were significantly lower in PTCA group (for P max 97±22 ms versus 114±16 ms and for PWd 31±13 ms versus 55±5 ms, respectively).

Primary angioplasty reduces P max and P wave dispersion. ***(Türk Kardiyol Dern Arş 2004; 32: 302-308)***

Key words: *Primary angioplasty, P wave duration, P wave dispersion*

Özet

Akut Miyokard Enfarktüslü Hastalarda Reperfüzyon Yöntemlerinin P-Dalga Süresi ve Dispersiyonuna Etkisi

Atriyal fibrilasyon akut miyokard enfarktüslü hastalarda %10-20 sıklıkla görülen bir aritmidir. P dalga süreleri ve dispersiyonu sinus noddan çıkan uyarının atriyal yayılımının bozulmasını incelemede kullanılmaktadır. Bu çalışma akut ön duvar miyokard enfarktüsü geçirmiş hastalarda primer anjioplasti ve trombolitik tedavinin P dalga süre ve dispersiyonuna etkisini araştırmaktadır.

Akut ön duvar miyokard enfarktüsü geçiren 24 kadın, 48 erkek toplam 72 hasta çalışmaya alındı. Hastalar primer anjioplasti ve trombolitik tedavi almak üzere randomize edildi. Klinik, ekokardiyografik ve EKG değerleri incelendi. Tedavi öncesi ve sonrası P dalga süreleri ve dispersiyonu karşılaştırıldı.

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Yaş, cinsiyet, sol ventrikül ejeksiyon fraksiyonu, sol atriyum çapları ve kardiyovasküler risk faktörleri açısından karşılaştırıldıklarında her iki grupta anlamlı istatistiksel farklılık bulunmadı. Primer anjioplasti grubunda tedaviden sonar P dalga süreleri ve dispersiyonu anlamlı olarak azalmış ve her iki grup karşılaştırıldığında p max ve dispersiyon azalması anjioplasti grubunda istatistiksel olarak daha fazla saptandı.

Primer anjioplasti, P dalga süreleri ve dispersiyonunu trombolitik tedaviye göre anlamlı olarak azaltır. ***(Türk Kardiyol Dern Arş 2004; 32: 302-308)***

Anahtar kelimeler: *Primer anjiyoplasti, P dalga süresi, P dalga dispersiyonu*

Atrial fibrillation remains a common complication of acute MI in the thrombolytic era. P-wave dispersion (PWd) can be defined as the difference between maximum and minimum P wave duration. Prolonged P-wave durations (PWD) and PWd have been reported to carry an increased risk for atrial fibrillation (AF) in AMI patients after thrombolytic therapy (TT) [1-6]. Early coronary reperfusion has been shown to be effective in reducing electrophysiological instability by decreasing QT dispersion, in the recovery phase after acute MI [7]. And it has been shown that early coronary reperfusion is associated with decreased incidence of atrial fibrillation after acute MI [8,9]. There is not any data in the literature comparing the efficacy of different reperfusion methods on the PWD in acute myocardial infarction.

The aim of the present study was to examine the efficacy of different reperfusion methods; primary PTCA and thrombolytic therapy, on P max, P min and PWd in patients with acute anterior MI.

PATIENTS and METHODS

Patients: Between 2002 and 2004, 164 patients were admitted to our hospital within 6 hours after the onset of AMI. AMI was defined by the presence of typical chest pain, ST segment elevation on admission ECG compatible with acute MI and significant serum enzyme elevations. Among 164 patients with ST elevation MI, 72 patients fulfilling the inclusion criteria (48 males and 24 females with a mean age of 54±11 years) were included the study. Exclusion criteria were; presence of atrial fibrillation or flutter either before or later to the assigned treatment, bundle branch block or any other intra-ventricular conduction abnormalities, severe requiring permanent pacemaker insertion, pre-excitation on admission or at the 24th hour's ECG, cardiogenic shock, presence of either hypertrophic or dilated cardiomyopathy, previously known congestive heart failure, congenital cardiac abnormalities, patients who required rescue angioplasty/stenting, severe valvular heart disease, previous beta blocker and other anti-arrhythmic drug usage, absence of successfully reperfusion criteria after PTCA or thrombolytic therapy and presence of unmeasurable P waves in more than 4 leads on any ECG. All of the patients were treated with either by primary angioplasty or thrombolytic therapy. From the 72 patients matching the selection criteria, 40 were treated with primary PTCA and stenting (group A, 40 patients) and 32 had thrombolytic agents (streptokinase) (group B, 32 patients).

The choice of treatment method was completely randomized due to another study comparing primary PTCA versus thrombolytic therapy conducted in the same center, which had no on-site surgical back up. Low-flow nasal oxygen, 5-15μ intravenous nitroglycerin, oral aspirin (100-325 mg) and intravenous beta-blocker (metoprolol totally 15mg by intravenous route in 15-30 minutes and followed by 25-50 mg /day according to heart rate and blood pressure) were administered to all patients in each group. Anti-arrhythmic agents and calcium blockers were not administered. Heparin was given according to treatment arm to which the patient was assigned.

Angiography and primary angioplasty procedure: Coronary angiography was performed in patients treated with primary PTCA before the procedure. In these patients, anterograde perfusion of the infarct-related artery was graded according to the classification system of the TIMI trial (grade 0 = no anterograde perfusion, grade 1 = minimal perfusion, grade 2 = partial perfusion, grade 3 = complete perfusion)[4]. Coronary angiography was not performed in patients who were randomized to thrombolytic treatment in the acute phase of MI unless recurrent

ischemia. 300mg clopidogrel was administered orally to all patients after randomization. Procedures were performed using standard angioplasty technique with an 8 French (Fr) guiding catheter via the femoral artery approach. A bolus of 100 IU/kg of heparin was administered intra-arterially after insertion of the vascular access sheath achieving a target therapeutic aPTT level. Target lesions were initially treated with appropriate balloon pre-dilatation in all patients followed by routine intra-coronary stenting. Angiographic success was defined as complete restoration of distal flow (TIMI-III) and absence of residual stenosis up to 20%. Clinical success was defined as angiographic success plus absence of death and urgent surgery, resolution of chest pain and ST segment elevations.

After successful stent implantation, heparin was not routinely administered unless there was a clinical indication, such as a large residual dissection or massive intracoronary thrombosis. The sheaths were removed in the same day. Ambulation was allowed 6 h after the sheath was removed. Clopidogrel 75 mg once daily were continued for 4 weeks and aspirin 100-300 mg once daily was continued indefinitely. Electrocardiograms (ECG) were recorded immediately after the procedure, then daily before discharge. If the patient had recurrent chest pain after the procedure, creatine kinase-myocardial band (CK-MB) level was measured and additional ECG was recorded.

Thrombolytic therapy protocol: All patients randomized to thrombolytic therapy received streptokinase as standard care. Streptokinase was given with intravenous route 1, 5 Million Units in about sixty minutes. Heparin was given as an intravenous bolus before the thrombolytic drug, followed by an infusion 4 hours after the thrombolytic therapy for 24 hours with the dose adjusted to rise the activated partial thromboplastin time between 60 and 80 s. For patients with persistent or recurrent chest pain, or hemodynamic instability, emergency catheterization was planned. Reperfusion after thrombolytic therapy was assessed by clinical criteria defined as complete relief of chest pain, resolution of ECG abnormalities (ST segment resolution) and development of reperfusion arrhythmias.

ECG analysis: A 12-lead surface ECG was obtained from all patients before the randomization to angioplasty or thrombolytic therapy and at 24th hour after the treatment. First ECG's were obtained prior to intravenous beta-blocker. All the ECG's were recorded at a paper speed of 25 mm/with 1 mV/cm standardization. Patients were allowed to breath freely but not to speak or cough during recordings. All ECG's were stored in a digital system. A computer-based ECG system was used, which recorded all 12 ECG leads simultaneously at a sampling rate of 1200 Hz and with 12-bit analog-to-digital conversion defined by Dilaveris et al [3]. For each lead, the average complex was calculated, and P-wave duration was measured manually from the average complexes displayed on a high-resolution computer screen.

Analysis of ECG and P waves were performed by two of the investigators independently (by H.A. and H.G.), without knowledge of the patient's clinical diagnosis. The start and the end of the P waves were marked with the cursor on a high-resolution computer screen. P max was defined as the maximum P-wave duration in any of the measured leads (P max), P min was defined as the minimum P-wave duration in any of the measured leads and PWd was defined as the difference between P max and P min.

The onset of the P wave was defined as the junction between isoelectric line at the beginning of the P wave deflection and the offset of the P wave was defined as the junction between the end of the P wave and the isoelectric line. If the onset or offset of the P wave were not clearly determined the lead was excluded from the analysis. Maximum P wave duration and minimum P wave duration (P minimum) were both measured from the 12-lead ECG and then P wave dispersion defined as the difference between P max and P min was calculated.

Echocardiographic evaluation: All patients underwent a complete two-dimensional transthoracic echocardiographic and Doppler study in the left lateral decubitus position from multiple windows. Echocardiographic evaluations were performed at 24th hours in majority of patients. All studies were performed with Vingmed Vivid-3 echocardiograph and a 2.5 MHz transducer. Echocardiographic measurements were performed according to the recommendations of the American Society of Echocardiography. Studies were recorded on compact disks for storage and review.

Two-dimensional echocardiographic calculations were obtained by parasternal long axis (PSL), apical three and four chamber views. Left ventricular ejection fraction was calculated by Teicholz formula. Left atrial maximal and minimal volume calculated and left atrial ejection fraction were calculated as the ratio of end diastolic area to end-systolic area of the left atrium using apical three chamber views.

Statistical Analysis: The results were presented as mean ± standard deviation. The statistical analysis was performed using the Statistical Package For Social Sciences software (SPSS for Windows). Differences between groups (primary PTCA versus thrombolytic therapy) were calculated by the unpaired t-test. Comparisons of P maximum, P minimum, and P dispersion before and after treatment were done by the paired t-test. Frequencies were compared using chi-square analysis. P value <0.05 was considered to be statistically significant.

RESULTS

Clinical characteristics of the two study groups and the comparisons between them are shown in Table 1. Any significant differences were not detected between group A and group B regarding to age, gender, cardiovascular risk factors and time from symptom onset to treatment. In group A, there were 28 patients with one-vessel disease (LAD), 12 patients with two-vessel disease (LAD and LCX) (Data not shown). All patients underwent angioplasty procedure only for infarct related artery. Distally TIMI-III perfusion was achieved in all patients.

Tablo 1. Clinical characteristics of group A and B

Characteristics	Group A (n: 40)	Group B (n: 32)	P value
Age (year)	53 ± 10	56±7	0.053
Sex (Male/Female)	30/10	18/14	0.354
Smoking (%)	44	39	0.346
Hypertension (%)	41	37	0.226
Diabetes Mellitus (%)	20	27	0.413
History of familial CAD (%)	34	37	0.768
Obesity (%)	24	20	0.612
Dyslipidemia (%)	31	29	0.276
Time to therapy (hours)	3.2	3.6	0.650
Systolic blood pressure (mmHg)	132±21	127±18	0.345
Diastolic blood pressure (mmHg)	83±16	81±19	0.671
Diastolic blood pressure (mmHg)	83±16	81±19	0.671

(CAD: coronary artery disease)

LVEF, left ventricular end-systolic and end-diastolic diameters, left atrial diameters and volumes, systolic and diastolic blood pressures and heart rate were not significantly different between the two groups (Table 2).

There was not any significant difference between group A and group B in P max, P min and PWd before both revascularization procedures. But, P max and PWd were found to be significantly lower in group A than in group B after the treatment (P max was 97±22 msn in group A versus 114±16 ms in group B and p=0.002. PWd was 31±13 ms in-group A versus, 55±5 ms in-group B and p=0.001) (Table 3). P max and PWd were significantly decreased after the treatment in group A (113±11 ms prior-PTCA versus 97±22ms after-PTCA, p=0.007 for P max and 46±12 ms prior-PTCA versus 29±10 ms after-PTCA, p= 0.001 for PWd, respectively) (Table 4). On the other hand, any statistically significant change was not detected in-group B as compared before and after the treatment (116±13 ms prior-TT versus 114±16ms after-TT, p=0.450 for P max and 57±8 ms prior-TT versus 55±5 ms after-TT, p=0.343 for PWd, respectively).

DISCUSSION

This study examines the effects of reperfusion either by primary angioplasty or by thrombolytic therapy on P wave duration and dispersion in patients with acute anterior myocardial infarction. It has been shown that only primary PTCA leads significant reduction on PWd and P dispersion in patients with acute anterior MI. This study has also showed that primary PTCA has more favorable effects on reducing P-wave duration and P dispersions at the end of the first 24 hours in patients with acute anterior MI, compared to thrombolytic therapy.

Tablo 2. Echocardiographic variables in-group A and B after treatment

Characteristics	Group A (n: 40)	Group B (n: 32)	P value
LV Diastolic diameter (mm)	52±9	56±7	0.742
LV systolic diameter (mm)	34±6	35±8	0.965
LA diameter (mm)	37±5	38±8	0.493
LA volume (ml)	46±16	47±14	0.367
LV Ejection fraction (%)	56±7	52±10	0.554

(LV: left ventricle, LA: left atrium)

Clinical significance of atrial fibrillation in acute MI: Atrial fibrillation is one of the most common supraventicular arrhythmias in the setting of acute myocardial infarction, occurring in around 5-18% of all patients [1-7]. The arrhythmia develops for many different reasons, including left ventricular dysfunction with haemodynamic impairment [5,8-11], atrial ischaemia or infarction (particularly in patients with early onset atrial fibrillation in the course of acute myocardial infarction), right ventricular infarction, pericarditis, excessive release of catecholamines, chronic lung disease, acute hypoxia, drugs (for example, the use of sympathomimetic agents), and hypokalaemia [11-13]. Atrial fibrillation is usually abrupt in onset and can cause rapid haemodynamic instability through one of three mechanisms: loss of the atrial component of the cardiac output; increased ventricular response rate with the decreased diastolic filling time; or irregular ventricular filling [14,15].

Atrial fibrillation (AF) can adversely affect clinical outcomes following percutaneous coronary interventions, coronary artery bypass grafting, other major non-cardiac surgery and acute myocardial infarction [9-16].

Clinical significance of P wave duration, P wave dispersion: For about ten years, it is known that PWd is an electrocardiographic marker for prediction of atrial fibrillation and it is associated with the inhomogeneous and discontinuous propagation of sinus impulses [3-9]. It can be defined as the difference between maximum and minimum P-wave duration. Prolongation of intra-atrial and interatrial conduction time and inhomogenous propagation of sinus impulses are known electrophysiologic characteristics of atria prone to fibrillation. Moreover, the correlation between the presence of intra-atrial conduc-

Table 3. Comparison of p wave durations before and after treatment according to the revascularization methods

Variables	PCI Group A	Trombolitic Therapy Group B	P
P max (ms), before treatment	113±11	116±13	0.371
P minimum (ms), before treatment	66±10	60±12	0.189
P wave dispersion (ms) before treatment	46±12	57±8	0.361
P max (ms), after treatment	97±22	114±16	**0.002**
P minimum (ms), after treatment	68±12	61±9	0.336
P wave dispersion (ms), after treatment	31±13	55±5	**0.001**

Table 4. Comparison of p wave durations in group A and group B before and after treatment

Variables	Before Treatment	After Treatment	P
P max (ms), Group A	113±11	97±22	**0.007**
P minimum (ms), Group A	66±10	68±12	0.369
P wave dispersion (ms), Group A	46±12	31±13	**0.001**
P max (ms), Group B	116±13	114±16	0.450
P minimum (ms), Group B	60±12	61±9	0.794
P wave dispersion (ms), Group B	57±8	55±5	0.343

tion abnormalities and the induction of paroxysmal AF has been well documented [3-9]. This electrophysiologic characteristic results in increased PWD on electrocardiographic measurements. Therefore, PWd can be used to classify patients with a high risk of AF during sinus rhythm [12]. Dilaveris et al. reported the effects of ischemia on P wave duration and dispersion in patients with anginal episodes [17]. Baykan et al also showed that P maximum and P dispersion are significant predictive factors of AF in patients with acute anterior wall MI [2].

Previous studies reported significant decrease in the incidence of atrial fibrillation during acute MI by thrombolytic therapy and primary angioplasty procedures [8-9]. Results of this trials found that predictors of atrial fibrillation after acute myocardial infarction were; increased age, KILLIP class and decreased LVEF [8-11]. Several studies reported that increased PWd and P wave durations can predict atrial fibrillation [2, 6,18-20]. But there is not any reported trial in the literature comparing the effects of primary angioplasty and thrombolytic therapy on P wave duration and dispersion.

In the present study only patients with anterior acute MI were included, because of the sinus and atrio-ventricular node arteries arise mainly from right coronary artery. Our results showed significant reductions on P max and PWd by successfully reperfusion after primary PTCA. These results may be related with the prompt restoration of distal flow by PTCA and quick healing of ischemia. And it may be related with abrupt restoration of left ventricular ejection fraction although LVEF values were not significantly different in both groups.

Multi-center randomized trials indicate that primary angioplasty in acute myocardial infarction (AMI) lowers the rates of death, stroke, recurrent ischemia and re-infarction compared with fibrinolytic therapy [21]. A new favorable effect of primary PTCA over thrombolytic therapy may be the lower incidence of atrial fibrillation although our findings need to be confirmed by prospective larger scale studies.

Limitations: This study has several limitations; most important limitation is small sample size in both groups. The other limitations are as follow; absences of rhythm follow up, absence of coronary angiography in thrombolytic therapy group.

Conclusion: Primary angioplasty has a more favorable effect on reducing P wave duration and dispersion when compared to thrombolytic therapy in acute MI.

REFERENCES

1. Crenshaw BS, Ward SR, Granger CB, Stebbins AL, Topol EJ, Califf RM: Atrial fibrillation in the setting of acute myocardial infarction: the GUSTO-I experience. Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries. J Am Coll Cardiol 1997; 30: 406-13

2. Baykan M, Celik S, Erdol C, et al: Effects of P-wave dispersion on atrial fibrillation in patients with acute anterior wall myocardial infarction. Ann Noninvasive Electrocardiol. 2003; 8: 101-6

3. Dilaveris PE, Gialafos EJ, Chrissos D, et al: Detection of hypertensive patients at risk for paroxysmal atrial fibrillation during sinus rhythm by computer-assisted P wave analysis. J Hypertens 1999; 17: 1463-70

4. Chesebro JH, Knatterud G, Roberts R, et al: Thrombolysis in myocardial infarcion (TIMI) trial, Phase I: a comparison between intravenous plasminogen activator and intravenous streptokinase. Circulation 1987; 76: 142; 54

5. Dilaveris PE, Gialafos EJ, Andrikopoulos GK, et al: Clinical and electrocardiographic predictors of recurrent atrial fibrillation. Pacing Clin Electrophysiol 2000; 23: 352-8

6. Dilaveris PE, Gialafos EJ, Sideris S, et al: Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. Am Heart J 1998; 135: 733-8

7. Endoh Y, Kasanuki H, Ohnishi S, Shibata N, Hosoda S: Influence of early coronary reperfusion on QT interval dispersion after acute myocardial infarction. Pacing Clin Electrophysiol 1997; 20:1646;53

8. Nielsen FE, Sorensen HT, Christensen JH, Ravn L, Rasmussen SE: Reduced occurrence of atrial fibrillation in acute myocardial infarction treated with streptokinase. Eur Heart J 1991; 12: 1081-3

9. El-Omar MM, Dangas G, Mehran R, et al: Usefulness of atrial fibrillation as a marker of outcome after percutaneous coronary intervention. Am J Cardiol 2003; 91: 232-4

10. Hunt D, Sloman G, Penington C: Effects of atrial fibrillation on prognosis of acute myocardial infarction. Br Heart J 1978; 40: 303-7

11. Pizzetti F, Turazza FM, Franzosi MG, et al: Incidence and prognostic significance of atrial fibrillation in acute myocardial infarction: the GISSI-3 data. Heart 2001; 86: 527-32

12. Cristal N, Peterburg I, Szwarcberg J: Atrial fibrillation developing in the acute phase of myocardial infarction. Prognostic implication. Chest 1976; 70: 8-11

13. Sugiura T, Iwasaka T, Ogawa A, et al: Atrial fibrillation in acute myocardial infarction. Am J Cardiol 1985; 56: 27-9

14. Klass M, Haywood LJ: Atrial fibrillation associated with acute myocardial infarction: a study of 34 cases. Am Heart J 1970; 79: 752-60

15. Beck OA, Hochrein H: Atrial fibrillation and flutter as a complication of acute myocardial infarction. Dtsch Med Wochenschr 1976; 101: 1148-53

16. Guidera S, Steinberg J: The signal-averaged P wave duration: a rapid and noninvasive marker of risk of atrial fibrillation. J Am Coll Cardiol 1993; 21: 1645; 51

17. Dilaveris PE, Andrikopoulos GK, Metaxas G, et al: Effects of ischemia on P wave dispersion and maximum P wave duration during spontaneous anginal episodes. Pacing Clin Electrophysiol. 1999; 22: 1640-7

18. Klein M, Evans SJL, Blumberg S, Cataldo L, Bodenheimer MM: Use of P wave-triggered, P-wave signal-averaged electrocardiogram to predict atrial fibrillation after coronary artery bypass surgery. Am Heart J 1995; 129: 895;901

19. Dilaveris PE, Gialafos JE: P-wave dispersion: a novel predictor of paroxysmal atrial fibrillation. Ann Noninvasive Electrocardiol 2001; 6: 159-65

20. Rosiak M, Bolinska H, Ruta J: P wave dispersion and P wave duration on SAECG in predicting atrial fibrillation in patients with acute myocardial infarction. Ann Noninvasive Electrocardiol 2002; 7: 363-8

21. Weaver WD, Simes RJ, Betriu A, et al: Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitave review. JAMA 1997, 278: 2093-8