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

Ramazan Akdemir, M.D.,* Hakan Ozhan, M.D.,* Huseyin Gunduz, M.D.,† Ali Tamer, M.D.,† Mehmet Yazici, M.D.,* Enver Erbilen, M.D.,* Sinan Albayrak, M.D.,* Serkan Bulur, M.D.,* and Cihangir Uyan, M.D.†

*From the *Department of Cardiology, Düzce Faculty of Medicine, Abant İzzet Baysal University, Konuralp Düzce, Turkey; and †Izzet Baysal Medical School, Abant İzzet Baysal University, Bolu, Turkey*

Background: Atrial fibrillation (AF) is a common arrhythmia occurring in about 10–20% of patients with acute myocardial infarction (AMI). P-wave dispersion (PWd) and P-wave duration (PWD) 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.

Methods: We have evaluated 72 consecutive patients retrospectively (24 women, 48 men; aged 58 ± 12 years) experiencing acute anterior wall myocardial infarction (AMI) for the first time. 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 every day during hospitalization. Maximum (P max) and minimum (P min) P-wave durations and P-wave dispersions were calculated before and after the treatment.

Results: There were not any significant differences between the groups regarding age, gender, left ventricular ejection fraction, left atrial diameter and volume, cardiovascular risk factors, and duration from symptom onset to treatment. P-wave dispersions and P-wave durations were significantly decreased after PTCA [Mean P max was 113 ± 11 ms before and 95 ± 17 ms 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 vs 114 ± 16 ms and for PWd 31 ± 13 ms vs 55 ± 5 ms, respectively).

Conclusions: Primary angioplasty reduces the incidence of AF by decreasing P max and P-wave dispersion.

A.N.E. 2005;10(1):35–40

primary angioplasty; P-wave duration; P-wave dispersion

Atrial fibrillation (AF) remains a common complication of acute myocardial infarction (AMI) in the thrombolytic era. P-wave dispersion (PWd) can be defined as the difference between maximum and minimum P-wave duration (PWD). Prolonged P-wave durations and PWd have been reported to carry an increased risk for AF in AMI patients after thrombolytic therapy.[1–6] Early coronary reperfusion has been shown to be effective in reducing electrophysiological instability by decreasing QT dispersion in the recovery phase after AMI.[7] And it has been shown that early coronary reperfusion is associated with decreased incidence of atrial fibrillation after AMI.[8,9] There are no data in the literature comparing the efficacy of different reperfusion methods on the P-wave duration in AMI.

The aim of the present study was to examine the efficacy of different reperfusion methods; primary PTCA and thrombolytic therapy, on P max,

Address for reprints: Ramazan Akdemir, M.D., Abant İzzet Baysal University, Düzce School of Medicine, 81620, Konuralp Düzce, Turkey. Fax: +90 380 541 40 64; E-mail: rakdemir@yahoo.com, ramazanakdemir@hotmail.com

P min, and PWd in patients with acute anterior MI.

MATERIALS AND METHODS

Patients

Between 2003 and 2004, 164 patients were admitted to our hospital within 6 hours after the onset of AMI. Acute myocardial infarction was defined by the presence of typical chest pain, ST-segment elevation on admission electrocardiograms (ECG) compatible with AMI, and significant serum enzyme elevations. Among 164 patients with ST elevation myocardial infarction, 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: the presence of atrial fibrillation or flutter either before or after the assigned treatment, bundle branch block or any other intraventricular conduction abnormalities requiring permanent pace-maker insertion, preexcitation on admission or at the 24th hour ECG, cardiogenic shock, presence of either hypertrophic or dilated cardiomyopathy, previously known as 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, presence of any complications such as pericarditis or acid-base imbalance. All of the patients were treated by either 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, 5–15 μgr intravenous nitroglycerin, oral aspirin (100–325 mg), and intravenous beta-blocker (metoprolol totally 15 mg 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. Antiarrhythmic 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, and grade 3 = complete perfusion).[4] Coronary angiography was not performed in patients who were randomized to thrombolytic treatment in the acute phase of myocardial infarction unless recurrent ischemia. Oral 300 mg clopidogrel was administered 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 predilatation in all patients followed by routine intracoronary 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 on the same day. Ambulation was allowed 6 hours after the sheath was removed. Clopidogrel 75 mg, once daily, was continued for 4 weeks and aspirin 100–300 mg, once daily, was continued indefinitely. Electrocardiograms 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 intravenous route 1, 5 Million Units about 60 minutes. Heparin was given as an intravenous bolus injection before the thromboltyic 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 seconds. 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 from chest pain, resolution of ECG abnormalities (ST-segment resolution), and development of reperfusion arrhythmias.

Electrocardiogram Analysis

A 12-lead surface ECG was obtained from all patients before randomization to angioplasty or thrombolytic therapy and at 24th hour after the treatment. First ECGs were obtained prior to intravenous beta-blocker. All ECGs were recorded at a paper speed of 25 mm with 1 mV/cm standardization. Patients were allowed to breathe 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 is calculated, and P wave duration is 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 the knowledge of 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 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 wave duration and minimum P-wave duration (P min) 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 hour 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, apical three and four chamber views. Left ventricular ejection fraction (LVEF) 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 are 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 vs 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. The 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 their comparisons are shown in Table 1. Any significant differences were detected between group A and group B regarding age, gender, cardiovascular risk factors, and time from symptom onset to treatment. In group A, there were 28 patients with one-vessel disease (LAD) and 12 patients with two-vessel disease (LAD and LCX) (data not shown). All patients had undergone angioplasty

Table 1. Clinical Characteristics of Groups A and B

Characteristics	Group A (PCI Group, n = 40)	Group B (TT Group, 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 (hour)	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.

procedure for only infarct-related artery. Distally TIMI-III perfusion was achieved in all patients.

Left ventricular ejection fraction (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 ms in group A vs 114 ± 16 ms in group B and P = 0.002. PWd was 31 ± 13 ms in group A vs 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 vs 97 ± 22 ms after-PTCA, P = 0.007 for P max and 46 ± 12 ms prior-PTCA vs 29 ± 10 ms after-PTCA, P = 0.001 for PWd, respectively (Table 4). Any statistically significant change was not detected in group B as compared before and after the treatment (116 ± 13 ms prior-TT vs 114 ± 16 ms after-TT, P = 0.450 for P max and 57 ± 8 ms prior-TT vs 55 ± 5 ms after-TT, P = 0.343 for PWd, respectively).

Table 2. Echocardiographic Variables in Groups 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.

Table 3. Comparison of P-wave Durations Before and After Treatment According to the Revascularization Methods

Variables	PCI Group A	Thrombolytic Therapy Group B	P Value
P max (ms), before treatment	113 ± 11	116 ± 13	0.371
P min (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 min (ms), after treatment	68 ± 12	61 ± 9	0.336
P-wave dispersion (ms), after treatment	31 ± 13	55 ± 5	0.001

DISCUSSION

This study examines the effects of reperfusion either by primary angioplasty or by thrombolytic

Table 4. Comparison of P-Wave Durations in Group A and Group B Before and After Treatment

Variables	Before Treatment	After Treatment	P Value
P max (ms), Group A	113 ± 11	97 ± 22	0.007
P min (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 min (ms), Group B	60 ± 12	61 ± 9	0.794
P-wave dispersion (ms), Group B	57 ± 8	55 ± 5	0.343

therapy on P-wave duration and dispersion in patients with acute anterior myocardial infarction. It has been shown that only primary PTCA leads to significant reduction in PWd and P dispersion dispersions in patients with acute anterior MI. This study has also showed that primary PTCA has a more favorable effect 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.

Clinical Significance of Atrial Fibrillation in Acute Myocardial Infarction

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 hemodynamic impairment,[5,8–11] atrial ischemia or infarction (particularly in patients with early onset in the course of AMI), right ventricular infarction, pericarditis, excessive release of catecholamines, chronic lung disease, acute hypoxia, drugs (e.g., the use of sympathomimetic agents), and hypokalemia.[11–13] Atrial fibrillation is usually abrupt in onset and can cause rapid hemodynamic 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 can adversely affect clinical outcomes following percutaneous coronary interventions, coronary artery bypass grafting, other major noncardiac surgery, and acute myocardial infarction.[9–16]

Clinical Significance of P-Wave Duration, P-Wave Dispersion

For about 10 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 dispersion. Prolongation of intra-atrial and interatrial conduction time and inhomogeneous propagation of sinus impulses are known electrophysiologic characteristics of atria prone to fibrillation. Moreover, the correlation between the presence of intra-atrial conduction abnormalities and the induction of paroxysmal atrial fibrillation 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 atrial fibrillation during sinus rhythm.[12] Dilaveris et al. reported the effects of ischemia on P-wave duration and P dispersion in patients with anginal episodes.[17] Baykan et al. also showed that P max and P dispersion are significant predictive factors of atrial fibrillation in patients with acute anterior wall myocardial infarction.[2]

Previous studies reported significant decrease in the incidence of atrial fibrillation during AMI 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 are no reported trials in the literature comparing the effects of primary angioplasty and thrombolytic therapy on P-wave duration and P dispersion.

In the present study, only patients with anterior AMI were included in the study group, because the sinus and atrioventricular node arteries arise mainly from right coronary artery. Our results showed significant reduction in P max and PWd by successful reperfusion after primary PTCA. These results may be related to the prompt restoration of distal flow by PTCA and quick healing of ischemia. And it may be related to abrupt restoration of LVEF although LVEF values were not significantly different in both groups. Cavusoglu et al.[21] demonstrated that reperfusion therapy with primary PTCA or thrombolytic agents reduces QT and QTc dispersions in patients with AMI, and they concluded that shorter QT and QTc dispersions with primary PTCA after 24-hour treatment could be attributed to the higher TIMI grade 3 patency rate achieved by primary PTCA. We think that complete and accurate reperfusion by primary PTCA results in significant reduction in the electrical instability of atrium.

Multicenter randomized trials indicate that primary angioplasty in AMI lowers the rates of death, stroke, recurrent ischemia, and re-infarction compared with fibrinolytic therapy.[22] 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. So, any subgroup analysis was not done. The other limitations are absences of rhythm follow-up in both groups and coronary angiography in thrombolytic therapy group.

CONCLUSION

In the lights of previous reports, reperfusion therapy decreases the incidence of atrial fibrillation during AMI. Results of this study showed that this reduction may occur through reduction in P-wave duration and P dispersion. Primary angioplasty has a more favorable effect on reducing in P-wave duration and P dispersion when compared to thrombolytic therapy in AMI.

REFERENCES

1. Crenshaw BS, Ward SR, Granger CB, et al. 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(2):406–413.
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;8:101–106.
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;17:1463–1470.
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;76:142–154.
5. Dilaveris PE, Gialafos EJ, Andrikopoulos GK, et al. Clinical and electrocardiographic predictors of recurrent atrial fibrillation. Pacing Clin Electrophysiol 2000;23:352–358.
6. Dilaveris PE, Gialafos EJ, Sideris S, et al. Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. Am Heart J 1998;135:733–738.
7. Endoh Y, Kasanuki H, Ohnishi S, et al. Influence of early coronary reperfusion on QT interval dispersion after acute myocardial infarction. Pacing Clin Electrophysiol 1997;20:1646–1653.
8. Nielsen FE, Sorensen HT, Christensen JH, et al. Reduced occurrence of atrial fibrillation in acute myocardial infarction treated with streptokinase. Eur Heart J 1991;12:1081–1083.
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;91:232–234.
10. Hunt D, Sloman G, Penington C. Effects of atrial fibrillation on prognosis of acute myocardial infarction. Br Heart J 1978;40:303–307.
11. Pizzetti F, Turazza FM, Franzosi MG, et al. On behalf of the GISSI-3 Investigators: Incidence and prognostic significance of atrial fibrillation in acute myocardial infarction: The GISSI-3 data. Heart 2001;86:527–532.
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;56:27–29.
14. Klass M, Haywood LJ. Atrial fibrillation associated with acute myocardial infarction: A study of 34 cases. Am Heart J 1970;79:752–760.
15. Beck OA, Hochrein H. Atrial fibrillation and flutter as a complication of acute myocardial infarction. Dtsch Med Wochenschr 1976;101:1148–1153.
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;21:1645–1651.
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;22:1640–1647.
18. Klein M, Evans SJL, Blumberg S, et al. 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;6:159–165.
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;7:363–368.
21. Cavusoglu Y, Gorenek B, Timuralp B, et al. Comparison of QT dispersion between primary coronary angioplasty and thrombolytic therapy for acute myocardial infarction. Isr Med Assoc J 2001;3(5):333–337.
22. Weaver WD, Simes RJ, Betriu A, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: A quantitative review. JAMA 1997;278:2093–2098.