Amount of ST wave resolution in patients with and without spontaneous coronary reperfusion in the infarct -related artery after primary PCI: an observational study

Primer PKG'den sonra enfarkt ilişkili arterde spontan reperfüzyon saptanan ve saptanmayan hastalarda ST segment rezolüsyon miktarı: Gözlemsel bir çalışma

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ABSTRACT

Objective: In patients with ST-elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI), a patent infarct-related artery (IRA) on initial angiography was associated with better angiographic results and improved prognosis compared with patients without spontaneous reflow. The role of systematic emergency PCI in patients with spontaneous reperfusion during myocardial infarction is debated. We compared the amount of ST wave resolution (STR) in patients with and without spontaneous coronary reperfusion (SCR) in the infarct related artery.

Methods: This study was designed as an observational cohort study. One hundred sixty-one consecutive patients (121 males, 40 females, with a mean age of 56±10 years) who had STEMI and treated with primary PCI without previous thrombolytic therapy were included in the study. All patients were treated with primary PCI within 12 hours from the onset of the symptoms and had stent implantation in the culprit lesion. ST wave resolution was measured as percent resolution of ST segment elevation from electrocardiogram (ECG), before and after PCI, classified as complete (>70%), partial (30% to 70%), or absent (<30%). SCR was defined as a TIMI grade III flow in the IRA on baseline coronary angiogram. The amount of ST wave resolution (STR) in patients with and without SCR in the IRA was compared. We used Chi-square test, Student's t-test and the Mann-Whitney U test for statistical analysis.

Results: At the baseline coronary angiography 40 (25%) patients had SCR and 121 patients (75%) had TIMI flow grade 0, 1 or 2 (non-SCR group). ST segment resolution amount was significantly higher in patients without SCR (53±17 versus 13±23 mm; p<0.001). In fact; in five patients whom had patent infarct related artery in initial angiography, ST segment elevation increased according to pre-PCI ECG.

Conclusion: Mean ST wave resolution was lower in patients with spontaneous coronary reperfusion who were treated with primary PCI compared to their counterparts who did not have spontaneous coronary reperfusion on initial coronary angiography.

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Key words: Spontaneous coronary reperfusion, stent implantation, myocardial infarction, percutaneous coronary intervention

ÖZET

Amaç: Acil perkütan koroner girişim (PKG) yapılan ST elevasyonlu miyokart enfarktüslü hastalarda (STEMI), ilk anjiyografide, enfarkt ilişkili arterde (İİA) saptanan spontan koroner açıklık (SKA), spontan reperfüzyonun olmadığı hastalarla kıyaslandığında daha iyi anjiyografik sonuç ve prognozla ilişkilidir. Spontan reperfüze olan MI hastalarında sistematik acil PCI'nin rolü tartışılmalıdır. Enfarkt ilişkili arterde spontan reperfüzyon gerçekleşen ve gerçekleşmeyen hastalarda ST rezolüsyon (STR) miktarını karşılaştırdık.

Yöntemler: Bu çalışma gözlemsel kohort çalışması olarak dizayn edildi. Çalışmaya ST elevasyonlu MI geçirmiş ve trombolitik tedavi uygulanmayıp primer PCI yapılan ortalama yaşı 56±10 yıl olan 161 hasta dahil edildi. Tüm hastalar semptom başlangıcından 12 saat içinde primer PKG'e alındı ve sorumlu lezyona stent implantasyonu yapıldı. ST rezolüsyonu, PKG öncesi ve sonrası elektrokardiyogramlarda (EKG) ST segment elevasyonunun yüzdesel gerilemesi olarak hesaplandı. >%70 tam rezolüsyon, %30 -%70 arası parsiyel rezolüsyon olarak adlandırıldı. <%30 rezolüsyon olarak kabul edilmedi. Spontan koroner reperfüzyon, yapılan ilk anjiyoda enfarkt ilişkili arterde TIMI-III akım saptanması olarak kabul edildi.

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Enfarkt ilişkili arterde spontan reperfüzyon olan ve olmayan hastalarda ST segment rezolüsyon miktarı karşılaştırıldı. İstatistiksel analizler için Ki-kare testi, Student's t-testi, Mann-Whitney U testleri kullanıldı.
Bulgular: Yapılan bazal anjiyoda 40 hastada (%25) spontan reperfüzyon, 121 hastada (%75) TIMI 0, 1 veya 2 akım saptandı (SKA olmayan grup). Spontan reperfüzyon olmayan hastalarda ST rezolüsyonu anlamlı olarak yüksek saptandı (53±17 ye karşı 13±23 mm; p<0.001). Hatta, yapılan ilk anjiyografisinde enfarkt ilişkili arteri açık saptanan beş hastada yapılan girişim sonucu PKG öncesi EKG'ye göre ST elevasyonunda artış saptandı.
Sonuç: Ortalama ST segment rezolüsyonu, başlangıç koroner anjiyografide spontan koroner reperfüzyon saptanıp primer PKG uygulanan hastalarda, spontan koroner reperfüzyon saptanmayan hastalara göre daha düşük olarak saptandı.
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Anahtar kelimeler: Spontan koroner reperfüzyon, stent implantasyonu, miyokart enfarktüsü, perkütan koroner girişim

Introduction

Spontaneous coronary reperfusion (SCR) of the infarct-related artery (IRA) occurs in 7-27% of patients experiencing acute ST elevation myocardial infarction (STEMI) (1). In patients with STEMI undergoing primary percutaneous coronary intervention (PCI), a patent infarct-related artery on initial angiography was associated with better angiographic results and improved prognosis compared with patients without spontaneous reflow (2-7). Resolution of electrocardiographic ST-segment elevation after reperfusion therapy for acute myocardial infarction has been correlated with clinical outcomes and recovery of left ventricular function (8, 9). ST segment resolution (STR) is believed to be a measure of microvascular reperfusion (10, 11).

To date, the question whether the classic treatment that we provide for patients with STEMI is applicable to patients with SCR remains controversial. Patients admitted to the hospital due to STEMI with clinically proven SCR may not need PCI (12). Little is known about the prevalence, clinical course and optimal management of patients presenting with clinical signs of spontaneous reperfusion (SCR).

Therefore, we hypothesized that SCR might have different effect on microvascular reperfusion as assessed by amount of ST segment resolution; in patients with and without SCR in the infarct related artery.

Methods

Study design and population

This observational cohort study consisted of one hundred sixty-one consecutive patients (121 males, 40 females, with a mean age of 56±10 years) who had STEMI and treated with primary PCI without previous thrombolytic therapy were included in the study between Düzce University May 2009 and April 2011. All patients were treated with primary PCI within 12 hours from the onset of the symptoms and had stent implantation in the culprit lesion. The patients who were selected for either medical therapy or bypass surgery on the basis of anatomic and clinical considerations and who had bundle branch block or with cardiogenic shock were excluded.

Clinical and demographical variables

Age, gender, blood pressure, heart rate, presence of diabetes or hypertension, smoking status and chest pain duration was determined in all patients at admission. Blood samples for biochemistry analysis including lipid panel and electrocardiographic (ECG) recordings were undertaken. To determine the enzymatic infarct area, multiple blood samples to measure creatine kinase (CK)-MB levels (for every 3-hours during the first 24 h and for every 6-hours for the next 2 days, and then daily until discharge) were obtained.

Treatment modalities

All patients received aspirin (500 mg), loading dose of clopidogrel (600 mg) and heparin (100 U/kg) intravenously before the procedure. Glycoprotein IIB-IIIA inhibitors were used in none of the patients because of the lack of providing in our country. STEMI was defined as typical chest pain >30 minutes with ST-segment elevation >1 mm in two or more contiguous leads. Patients who presented >12 h from the onset of symptoms were not included.

Electrocardiographic measurement and analysis

All patients had their ECG recorded in the emergency unit and if the patients whom chest pain decreased before undergoing PCI, were taken ECG again and this ECG was accepted as basal ECG for evaluating STR. STR was defined according to the following criteria (8). ST segment elevation ≥2 mm in ≥2 contiguous leads on an electrocardiogram performed just before PCI and paired electrocardiograms at baseline and ≤4 hours after PCI that were adequate for interpretation. Patients who had left bundle branch block, ST-segment elevation <2 mm and inadequate electrocardiographic data (paced rhythm, artifacts, or electrocardiograms >4 hours or missing) were excluded. Amount of STR was measured manually by 1 of the 3 investigators blinded to the angiographic data using ECG calipers as previously described (9). STR was measured as percent resolution of ST wave elevation from ECG, before and after PCI, classified as complete (>70%), partial (30% to 70%), or poor (<30%).

Coronary angiography and PCI

Coronary angiography was performed using standard techniques. Multiple projections of the coronary arteries were recorded digitally. Angiograms were reviewed by two independent expert interventional cardiologists and a third reviewer was involved when discrepancies emerged. The Thrombolysis in Myocardial Infarction (TIMI) flow was assessed in every patient. Spontaneous coronary reperfusion was defined as a TIMI grade III flow in the infarct related artery on baseline coronary angiogram. PCI was performed according to standard techniques. We implanted the same type stent (Driver-Stent®/Medtronic CardioVascular, Santa Rosa, California, USA) in all patients. Angiographic "success" was

defined as the achievement of a minimum stenosis diameter reduction to less than 20% in the IRA with TIMI flow grade 3 (13). Time to treatment was defined as the time from the onset of symptoms to balloon inflation.

Statistical analysis

Statistical analysis was executed by an independent statistician, using SPSS 18 software (SPSS Inc., Chicago, IL, USA). Data are expressed as mean±SD for continuous variables and frequencies and percentage for categorical variables. The Chi-square test was used to compare categorical variables. Student's t-test and the Mann-Whitney U test were used for the comparison of continuous variables. A p value of <0.05 was considered significant.

Results

Clinical characteristics

At the baseline coronary angiography 40 (25%) patients had SCR and 121 patients (75%) had TIMI flow grade 0, 1 or 2 (non-SCR group). Baseline characteristics of the two groups of patients are shown in Table 1.

Compared with patients without SCR at baseline, the patients with SCR before PCI were younger, had a higher prevalence of prior angina (p<0.05 for all) and had less evidence of heart failure (Killip>1) at presentation (Table 1). In angiographic analysis, patients with better preprocedural flow had a lower prevalence of multivessel disease and better procedural success rate (p<0.05 for all). The level of peak values of plasma CKMB and fasting plasma glucose was significantly higher (p<0.05 for all) in patients without SCR than those patients with SCR. The two groups were similar with respect to sex distribution, body mass index, frequencies of diabetes mellitus, hypercholesterolemia, family history of coronary artery disease, incidence of previous AMI and medications. In addition, the groups were similar in terms of serum levels of total cholesterol, creatinine, mean platelet volume, platelet number, white blood cells and serum urea.

Amount of ST segment resolution in patients with and without SCR in the infarct related artery

Complete, partial and poor STR were seen in 24 (19.8%), 77 (63.6%), and 20 (16.5%) in the patients without SCR and 0 (0%), 7 (17.5%) and 33 (82.5%) in the patients with SCR, respectively. ST segment resolution amount was significantly higher in patients without SCR (53±17 versus 13±23 mm; p<0.001) (Table 1, Fig. 1). Surprisingly; in five patients whom had patent infarct related artery in initial angiography, ST segment elevation increased according to pre PCI ECG.

Discussion

The main finding of the current study is that ST segment resolution amount was significantly lower in patients with SCR (13±23 versus 53±17 mm; p<0.001). In fact, in five patients who

Table 1. Baseline demographic and clinical characteristics

Variables	SCR absent (n=121)	SCR (n=40)	p*
Age, years	57.2±11.6 (35-82)	52.6±9.1 (36-70)	0.021
Female sex, %	23.9	27.5	NS
Body mass index, kg/m^2	26.9±3.9 (18-39)	26.4±2.9 (19-32)	NS
Hypertension, %	41.4	46.5	NS
Diabetes, %	14.8	10.3	NS
Hyperlipidemia, %	38.4	31.6	NS
Current cigarette use, %	54.8	48.5	NS
Prior bypass surgery, %	2.4	2.5	NS
Prior myocardial infarction, %	12.2	15.4	NS
Prior angina, %	24.8	5.0	0.005
Previous medications			
Aspirin, %	19.4	30.0	NS
Ticlopidine or clopidrogel, %	3.3	0	NS
Beta-blockers, %	19.0	22.5	NS
Statin, %	17.3	20.0	NS
ACE inhibitors, %	35.5	37.5	NS
Calcium antagonist, %	16.5	17.5	NS
Heart failure on admission (Killip >1), %	11.5	2.5	NS
Admission systolic blood pressure, mm Hg	124.1±26.5 (72-220)	130.9±26.6 (76-200)	NS
Admission heart rate, beats/min	83.2±23.7 (30-120)	79±16.9 (40-160)	NS
Time to treatment, h	3.1±2.1 (1-9)	3.6±1.9 (1-8)	NS
Angiographic characteristics			
Infarct vessel=LAD, %	55.4	52.5	NS
Infarct vessel=CX, %	11.5	10.0	NS
Infarct vessel=RCA, %	33.1	37.5	NS
Three-vessel disease, %	57.8	37.5	0.029
Procedural (PPCI) success, %	87.6	97.5	0.039
CKMB peak, IU/L	262.3±176.4 (42-1827)	189.3±121.3 (39-894)	0.028
Fasting plasma glucose, mg/dl	137.2±66.2 (72-300)	110.2±36.5 (79-350)	0.001
Serum creatinine, mg/dl	0.76±0.15 (0.4-2.8)	0.83±0.16 (0.2-2.1)	NS
Total cholesterol, mg/dl	194.4±44.1 (95-380)	189.5±34.9 (117-237)	NS
Platelets, (1x1000)	254.5±60.8 (36-373)	247.3±62.5 (129-448)	NS
Mean platelet volume, fl	8.1±0.8 (6.2-10.8)	8.0±0.8 (6.5-10.6)	NS
White Blood cells, (1x1000)	14.1±9.4 (10.6-22.8)	13.9±8.9 (9.9-19.8)	NS
Serum uric acid level, mg/dl	5.5±1.5 (2.8-14.1)	5.1±1.3 (3.4-8.3)	NS
ST segment resolution, mm	53±17	13±23	<0.001

Values are presented as mean±SD (range) or percentage
*unpaired Student t- test, Mann-Whitney U test and Chi-square test
ACE - angiotensin-converting enzyme, CKMB - creatine kinase, CX - circumflex coronary artery, LAD - left anterior descending artery, PPCI - primary percutaneous coronary intervention, RCA - right coronary artery, SCR - spontaneous coronary reperfusion

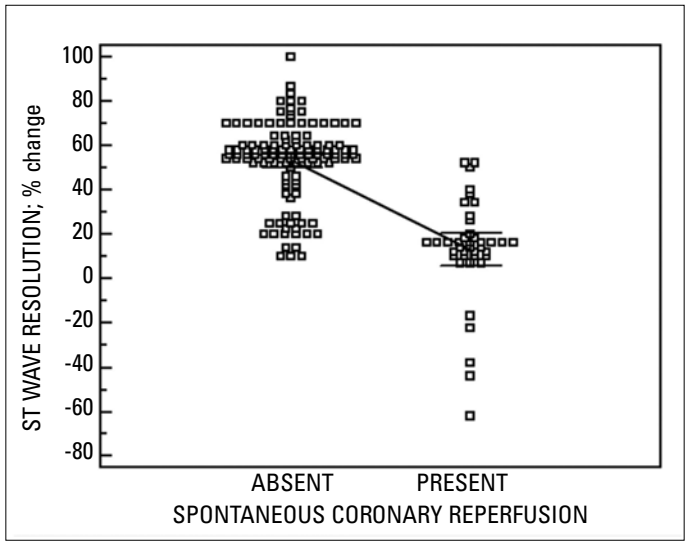

Figure 1. The amount of ST wave resolution in patients with and without spontaneous coronary reperfusion after primary percutaneous coronary intervention

had patent infarct related artery in initial angiography, ST segment elevation increased according to pre-PCI ECG.

Spontaneous coronary reperfusion was noted in 40 of 161 (22%) patients with STEMI who were admitted within 12 hours of symptom onset. Thus, the prevalence of STR was 22% in the present study, which was similar with the findings in previous angiographic series (4-7). Also, consistent with the previous studies (3-7), we found a significant relationship between preprocedural TIMI flow and enzymatic infarct size. Patients with preprocedural SCR had a smaller enzymatic infarct size, compared with the patients who did not have preprocedural SCR. Also, better procedural success rate was observed in patients with SCR.

Patients presenting with clinical features of SCR have a better prognosis (1-7) and an excellent in-hospital outcome, with evidence of less myocardial damage than patients in whom reperfusion therapy was required to achieve TIMI-3 patency. The major threat to these patients is considered to be re-infarction due to re-occlusion of the IRA, since the large area of viable myocardium is potentially at risk. Although patients with SCR showed a higher incidence of re-ischemia, this did not mean as an increased incidence of myocardial infarction or malignant arrhythmias. These results agreed with findings by Steg et al. (14), who studied the clinical course of 47 consecutive patients with STEMI in whom spontaneous TIMI 3 flow was found in the infarct related artery before any intervention and were managed conservatively, without emergency PCI. Of these 47 patients, 17% had recurrent ischemia requiring emergency PCI in 3/4, but none had reinfarction. Importantly, of 39 patients who underwent scheduled predischarge repeated angiography, 11 (constituting 1/4 of the entire cohort of patients with SCR) had residual stenosis <50% and therefore PCI were not required in these patients. Uriel et al. (12) studied to determine the optimal PCI time for patients admitted to the hospital due to STEMI with clinically proven SCR. Cardiac catheterization was executed early (<24 hours from pain onset) in 26 patients and late (>24 hours) in 55. Pre PCI angiographic TIMI flow 2-3 was seen in >95% in both groups. Myocardial infarction and angina pectoris at 30 days occurred more frequently in the early catheterization group (p=0.039), however no difference in any major adverse cardiac events was detected during long-term follow-up (491±245 days). There was not a single reinfarction episode during an observation period of 6579 patient hours. This is in contrast with the 10-20% reocclusion of the IRA observed in patients with STEMI, post-thrombolysis (15).

No trial has addressed the question whether patients with clinical diagnosis of STEMI and SCR had benefit from early PCI or whether PCI should be delayed. It is possible that delayed PCI may be safer, after a "cooling down" period, potential thrombus resolution and plaque stabilization. Also, stent implantation in culprit lesion on patent infarct related artery, may cause microembolisation by fragmentation of thrombi and may damage microvascular perfusion. Furthermore, reocclusion rate of the IRA in the patients with SCR was not observed at higher rates as it was feared (6, 7, 12, 14).

Study limitations

The study has a small cohort and larger scale prospective studies with more patients should be done in order to maintain more accurate prognostic information.

Conclusion

Mean ST wave resolution was lower in patients with spontaneous coronary reperfusion who were treated with primary PCI compared to their counterparts who did not have spontaneous coronary reperfusion on initial coronary angiography. Especially, presence of ST wave elevation after PCI in 5 patients instead of ST wave normalization should urge investigators to design prospective studies about routine stenting in patients with SCR in the baseline angiography.

Conflict of interest: None declared.

Authors contributions: Concept - E.Ç.E; Design - E.Ç.E., I.E., Supervision - I.E.; Material - Y.A., A.K., S.Y.; Data collection &/or processing - Y.A., A.K., S.Y.; Analysis &/or interpretation - Y.A., A.K., E.Ç.E., I.E., I.E., S.Y.,; Literature search -Y.T., E.Ç.E., I.E.; Writing - Y.T., E.Ç.E., I.E.; Critical review - Y.T., E.Ç.E., I.E., Y.A., A.K.

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