

THE EFFECT OF CLINICAL CHARACTERISTICS, TREATMENT APPROACHES, CLINICAL OUTCOMES IN RESCUE PERCUTANEOUS CORONARY INTERVENTION AFTER FAILED THROMBOLYSIS

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Kurtarıcı perkütan girişim (PKG), akut miyokard infarktüsü (MI) hastalarında trombolitik tedavinin başarısız olmasının ardından yapılan mekanik revaskülarizasyon tedavisidir. Kurtarıcı PKG'nin kısa süre içinde infarktten sorumlu arterde kan akımını sağlama avantajı olmasına rağmen, son yapılan çalışmalarda mortalite ve morbiditeye etkileri hakkında şüpheli sonuçlar vardır. Bu nedenle, kendi hasta popülasyonumuzda, kurtarıcı PKG yapılan olguların klinik özellikleri, tedavi yaklaşımları ve klinik sonuçlarını tanımlamayı amaçladık.

Bu tanımlayıcı çalışmaya, Gazi Üniversitesi Kardiyoloji Departmanı'nda ST yükselmeli miyokard infarktüsü nedeniyle trombolitik tedavi uygulanan ve başarısız olması üzerine kurtarıcı PKG uygulanan 37 hasta alındı. Klinik özellikler, tedavi yaklaşımları ve kısa- dönem klinik sonuçlar kaydedildi. Revaskülarizasyon işlemi öncesi ve sonrası koroner anjiogramlar kantitatif koroner anjiogram tekniği (QCA) ile değerlendirildi.

Çalışma popülasyonunda, 34 (%90) erkek hasta vardı ve yaş ortalaması 56.6±10.7 bulundu. Hipertansiyon 16 (%43), diabetes mellitus (DM) 5 (%13.5), sigara kullanımı 23 hastada mevcuttu. Semptom başlangıcında kurtarıcı PKG'ye geçen süre ortalama 7.5±5.2 saattir. Kurtarıcı PKG sırasında 4 hasta (%10) kardiyak arrest oldu, 2 hastada

(%5) acil koroner arter bypass ameliyatı (KABG) gerekti. Olguların Sol ön inen koroner arter %49'unda, sirkumfleks arter %19'unda, sağ koroner arter %32'sinde infarktten sorumlu arter (IRA) olarak bulundu. Tüm hastalarda PKG öncesinde trombus izlendi. Koroner stent %89 oranında yerleştirildi. İntraaortik balon pompası ve glikoprotein IIb/IIIa inhibitörleri 7 (19%) hastada uygulandı. Hastanede- içi mortalite 2(%5) hastada izlendi. Kanama komplikasyonu 5 (%11) hastada görüldü ve vasküler girişim alanındaydı. Girişim öncesi IRA 26 (70%) hastada tamamen tıkalıydı. IRA'nın tamamen tıkalı olduğu hastalar ve diğerleri arasında önemli fark yoktu. Göğüs ağrısının başlamasından itibaren 5 saat içinde girişim yapılan hastalarda >5 saat alınanlara göre işlem öncesi kantitatif anjiyografik değerler daha iyi bulundu (p<0.05), ancak işlem sonrası değerler arasında iki grup arasında fark yoktu. Kurtarıcı PKG sonrası, TIMI III kan akımı 23 (%62) hastada izlendi.

Çalışma popülasyonumuzda hasta özellikleri, tedavi yaklaşımları ve mortalite hızı, glikoprotein IIb/IIIa inhibitörleri kullanımı dışında son dönemdeki bilgilerle uyumlu bulundu.

Anahtar Kelimeler: Kurtarıcı perkütan, Koroner girişim, Başarısız trombolitik tedavi

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INTRODUCTION

In the setting of acute myocardial infarction (MI) thrombolytic therapy is a common reperfusion management. However thrombolytic therapy fails to

restore blood flow in infarct related coronary artery (IRA) in a large number of patients^{1,2}. Rescue percutaneous coronary intervention (PCI) is known as a mechanical revascularization procedure after failed thrombolytic therapy in patients with acute MI. Despite rescue PCI has advantages in restoring flow in IRA promptly, there are conflicting results on mortality and morbidity in recent studies³⁻⁶. Therefore we aimed to describe the clinical characteristics, treatment approaches, clinical outcomes in whom rescue PCI was applied after failed thrombolytic therapy and also

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Table 1: Clinical characteristics, treatment strategies of the patients

Age	56.6±10.7	
Male gender	34 (90%)	
DM	5 (%13.5)	
HT	16 (43%)	
Smoking	23 (63%)	
Dyslipidemia	8 (22%)	
MI localization	anterior	20 (54%)
	inferior	7 (19%)
	inferoposterior	3 (8%)
	inferolateral	1 (2,7%)
	inferoposterolateral	2 (5,4%)
	inferior with	
	right ventricle	4 (10,8%)
Infarct related artery	LAD	18 (49%)
	Cx	7 (19%)
	RCA	13 (32%)
Stent implantation	33 (89%)	
Intraaortic balloon and pump insertion	6 (%16)	
Treatment with glycoprotein IIb/IIIa	7 (19%)	

DM: Diabetes mellitus, HT: Hypertension, MI: Myocardial infarction, LAD: Left anterior descending artery, CX: Circumflex artery, RCA: Right coronary artery

to define the parameters which have significant effects on the success of the procedure.

METHODS

37 patients in whom thrombolytic therapy failed and therefore rescue PCI was applied from 2000 through 2006 were enrolled into this descriptive study. MI was defined by the ischemic chest pain lasting more than 30 min with typical ST segment elevation on electrocardiogram. Failure of thrombolytic therapy was determined as persistent ST segment elevation with or without persistent chest pain (>60 min) after initiation of thrombolytic therapy. Exclusion criterias were cardiogenic shock, contraindications for thrombolytic therapy, pregnancy. All patients were treated with thrombolytic agents. The demographic characteristics, infarct localization, preferred thrombolytic agent, procedural properties and treatment approaches, short term clinical outcomes (death, requirement to CABG operation, heart failure, bleeding complications) were recorded. Coronary angioplasty and stent implantation were performed with standart techniques. All patients received 300 mg clopidogrel as initial dose and 75 mg/day thereafter with 100 mg/day aspirin. During PCI heparin was administered with a target activated clotting time 250-300 s and 200-250 s in patients who received glycoprotein IIb/IIIa inhibitors. As a glycoprotein IIb/IIIa inhibitor, tirofiban was applied 10 µg/kg bolus followed by infusion with 0.15 µg/kg/min maintenance dosage.

Coronary angiograms were evaluated with QCA technique. Quantitative angiographic analysis (QCA) of the percentage of minimal lumen diameter (MLD) stenosis, lesion length, and reference lumen diameter (RLD) were performed by using a digital- detection algorithm. Contrast filled catheter was used as calibration standart; RLD, MLD, TIMI frame count, Myocardial blush grade (MBG) were calculated before and after the PCI.

Angiographic thrombus score was defined as 0=absence of the thrombus, 1=luminal hazziness, 2=presence of thrombus that is smaller than the half of the vessel diameter, 3=presence of the thrombus that was between the half and the twice of the vessel diameter, 4=thrombus that was more than the twice of the vessel diameter after the passage of the guide wire. Thrombus score 3 and 4 together were defined as 'high thrombus score'.

Statistical Analysis

Continuous data were reported as mean± SD, while categorical variables were reported as percentage (%). Chi-square or Fisher's Exact test was used in the comparison of the categorical variables. Continuous variables were compared with t-test. Comparisons between before and after angiographic criteria were performed using the Wilcoxon sign test. A p value <0.05 was considered significant. All statistical calculations were made with the SPSS 11.5 software package.

Table 2: The comparison of the QCA parameters of 11 patients with partial occlusion before procedure

	Before PCI (n:11)	After PCI (n:11)	p
TFC	40.73±13.4	30.64±19.72	0.09
MBG 0	1 (9.1 %)	1 (9.1%)	
MBG I	7 (63.6%)	2 (18.2%)	
MBG II	3 (27.3%)	6 (54.6%)	<0.001
MBG III	0 (0%)	2 (18.2%)	
TIMI flow 0	3 (27.3%)	0 (0%)	
TIMI flow I	7 (63.6%)	2 (18.2%)	
TIMI flow II	1 (9.1%)	4 (36.4%)	<0.001
TIMI flow III	0 (0%)	5 (45.5%)	
% of stenosis	72.85±8.72	13.44±6.63	<0.0001
MLD	91.94±4.85	25.82±10	<0.0001
RLD	0.42±0.17	7.56±2.91	<0.0001
Lesion length	6.12±2.46	9.94±3.31	<0.0001

Table 3: The comparison of the postprocedural QCA parameters of the patients with preprocedural partially or totally occluded IRA

	Not totally occluded (n:11)	Totally occluded (n:24)	p
TFC	30.64±19.72	40.26±23.04	0.221
MBG 0	1 (9.1%)	2 (8.3%)	
MBG I	2 (18.2%)	9 (37.55%)	
MBG II	6 (54.6%)	12 (50%)	0.101
MBG III	2 (18.2%)	1 (4.15%)	
TIMI flow 0	0 (0%)	0 (0%)	
TIMI flow I	2 (18.2%)	9 (37.5%)	
TIMI flow II	4 (36.4%)	8 (33.3%)	0.240
TIMI flow III	5 (45.5%)	7 (29.2%)	
% of stenosis	13.44±6.63	12.72±8.86	0.794
MLD	25.82±10.00	23.06±14.36	0.521
RVD	7.56±2.91	6.89±3.30	0.554
Lesion length	9.94±3.31	8.88±3.33	0.393

RESULTS

Between 2000 and 2006, rescue PCI was performed in 37 patients. The clinical characteristics with some treatment strategies are seen in Table 1. 12 patients (32%) received streptokinase and 25 patients (68%) received t-PA. The mean time from onset of chest pain to rescue PCI was 7.5±5.2 hours. High thrombus score was found in 20 patients (88.2%). During rescue PCI 2 patients (5%) died, 2 patients required emergency CABG operation (due to guidewire failure to cross the lesion). IRA was totally occluded in 26 patients (70%) before rescue PCI. The QCA parameters, MBG and TFC of patients with partial occlusion before the procedure (11 patients, %30 of the whole population) improved significantly after the procedure (Table 2). The baseline characteristics of the patients were similar between the patients with or without totally occluded IRA; postprocedural angio-

graphic parameters show no difference either (Table 3). Patients in whom rescue PCI was performed within 5 hours from the onset of chest pain had better quantitative angiographic values before the procedure ($p<0.05$), but the postprocedure values were similar with the others. After procedure TIMI III blood flow in IRA was observed in 23 patients (%65). As short term clinical outcome, 27 patients (73%) were discharged without complications, 4 (11%) had heart failure, 5 (15%) had minor bleeding in a vascular access site without need for transfusion, 4 patients (11%) died and 2 (5.4%) had recurrent ischemia. Patients with heart failure and recurrent ischemia were successfully treated.

DISCUSSION

The early studies compared angioplasty and conservative treatment in patients with acute MI after

failed thrombolysis and found that the mortality rate was similar between groups⁴⁻⁶. Mc Kendall et al. demonstrated an improved survival at 1 year with rescue PCI⁷. In the MERLIN trial, rescue PCI and conservative approach to the patients with acute anterior and inferior MI was compared, after failed thrombolysis with streptokinase; similar mortality rate between groups with higher stroke incidence in PCI group at 30 days were found³.

In this present study, patient characteristics were concordant with other studies. 70% of patients had a totally occluded IRA before rescue PCI. In RESCUE II trial patients with partial reperfusion were investigated, it has been shown that time window in rescue PCI for successful procedure must be less than 8 h⁸⁻¹¹. Our mean time between onset of chest pain and PCI was 7.5±5.2 h. In a meta analysis of RESCUE I & RESCUE II Trials, benefit of rescue PCI was shown^{10,11}.

STOPAMI- 4 trial compared angioplasty with stenting as rescue PCI and demonstrated stenting was more beneficial. In this trial abciximab was used in 97%¹². We performed stent implantation in 97% and administered tirofiban as a glycoprotein IIb/IIIa inhibitor in 19% of study population. Tirofiban, a small molecule, has a shorter half life than abciximab. For procedural efficacy tirofiban loading dose is required. Advantages of tirofiban are cost effectiveness and less haemorrhagic complications¹³. Xu L et al evaluated the effect of tirofiban in primary PCI and showed that tirofiban initiation 36 min before procedure had better results than later (during procedure) initiation¹⁴. The TARGET study compared the effect of tirofiban and abciximab in elective PCI and found that reduction in the primary composite endpoint in the abciximab group with increased bleeding complications. The routine dose of tirofiban during PCI is 10 µg/kg bolus followed by 0.15 µg/kg/min maintenance infusion¹⁵. In a head to head comparison, Mukherjee et al found that in PCI, abciximab was superior to tirofiban therapy with the recommended dose of 10-microg/kg bolus followed by a 0.15-microg/kg/min infusion¹⁶. In some studies it has been shown that tirofiban treatment with standart regimen failed to demonstrate significant effect on cardiovascular outcome because of inadequate effectiveness on early inhibition of platelets^{13,17,18}. Valgimigli et al found that tirofiban with high dose regimen had beneficial effects in patients with high risk PCI¹⁹. For efficacy with tirofiban treatment loading dose is required and it may cause delay in the setting of rescue PCI. Abciximab might have been a better choice in rescue PCI for early efficacy,

however only available glycoprotein IIb/IIIa inhibitor in our market is tirofiban.

In REACT trial incidences of death and severe heart failure were decreased in PCI group versus conservative treatment group⁵. Contrarily ASSENT-4 trial showed increased mortality rate in rescue PCI group with tenecteplase²⁰. PCI with thrombolytic therapy increased stroke and bleeding. In our study in-hospital mortality and heart failure rate were 11%. These results are concordant with RESCUE II¹⁰, MERLIN, REACT trials^{3,5,7}.

Thromboembolic stroke rate was 4% in MERLIN trial and %1.4 in REACT trial. In our study stroke was not observed however frequencies of streptokinase and glycoprotein IIb/IIIa inhibitors were lower. The rate of glycoprotein IIb/IIIa inhibitors use was 7% in RESCUE II, 3% in MERLIN, 80% in REACT trial. We administered tirofiban as a glycoprotein IIb/IIIa inhibitor in 19%. As thrombolytic treatment 12 patients (32%) received streptokinase and 25 patients (68%) t-PA. Streptokinase use was 97% in MERLIN and 86% in REACT trial.

Bleeding complications were frequent in MERLIN trial. In our study only 5 patients had minor bleeding in vasculer access site. The frequent use of streptokinase which has long half-life in MERLIN trial was thought as a possible reason of increased bleeding complications.

Study Limitations

Small sample size and low rate use of tirofiban are the major limitations. Our study was not randomized according to use of glycoprotein IIb/IIIa inhibitors. All of them have limited to detect the effect of tirofiban in rescue PCI.

CONCLUSION

Patients characteristics, treatment approaches and mortality rate of our study population is well-matched with current data except glycoprotein IIb/IIIa inhibitor use. The low ratio of TIMI III blood flow after rescue PCI may be explained lower use rate of glycoprotein IIb/IIIa inhibitors in our population. In our country, only tirofiban is available. Loading dose and sufficient time is required for its efficacy. Tirofiban is less preferred in this setting for preventing delay in restoring of blood flow in IRA. It is hard to say more about this subject with a small study group. For optimal tirofiban dose and timing in rescue PCI, further studies are required.

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