Primary percutaneous coronary intervention in patients admitted with cardiogenic shock and ST-elevation myocardial infarction: prognosis and predictors of in-hospital mortality

Kardiyojenik şokla başvuran ST yükselmeli miyokart enfarktüslü hastalarda primer perkütan koroner girişim: Prognoz ve hastane içi mortalitenin belirleyicileri

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Objectives: We investigated the efficacy and outcome of primary percutaneous coronary intervention (PCI) in patients admitted with cardiogenic shock and ST-elevation myocardial infarction (STEMI).

Study design: We reviewed 91 consecutive patients (66 males, 25 females; mean age 61±11 years) treated with primary PCI for cardiogenic shock due to STEMI. All clinical, angiographic data, and in-hospital and long-term outcomes were collected. The patients were classified into two groups depending on the presence (n=59, 64.8%) or absence (n=32, 35.2%) of in-hospital mortality.

Results: Hospital nonsurvivors were older (mean age 62.7±11.1 vs. 57.7±11.4 years; p=0.04) and exhibited higher frequencies of diabetes mellitus (DM), renal failure, and history of myocardial infarction. Multi-vessel disease (p=0.004) and circumflex artery involvement (p=0.03) were more frequent and the rates of tirofiban administration (p=0.02) and stenting (p=0.007) were lower in nonsurvivors. Procedural success rate was substantially lower in nonsurvivors (39% vs. 84.4%; p<0.001). Of 32 survivors, cardiovascular mortality occurred in only three patients (9.4%) during a median follow-up of 26 months. In multivariate regression analysis, unsuccessful procedure (OR 7.2, 95% CI 1.77-29.27; p=0.006) and DM (OR 3.92, 95% CI 1.13-13.62; p=0.03) were the independent predictors of in-hospital mortality.

Conclusion: Mortality rate is considerably higher and successful procedure yields a two-fold decrease in in-hospital mortality in patients with cardiogenic shock complicated by STEMI. Unsuccessful procedure and DM represent as two independent predictors of in-hospital mortality.

Key words: Angioplasty, transluminal, percutaneous coronary; hospital mortality; myocardial infarction/therapy/ complications; prognosis; shock, cardiac/therapy/mortality; stents.

Amaç: Bu çalışmada, kardiyojenik şokla başvuran ST yükselmeli miyokart enfarktüslü (STYME) hastalarda pri-mer perkütan koroner girişimin (PKG) etkinliği ve sonuçları değerlendirildi.

Çalışma planı: Çalışmaya STYME’ye bağlı kardiyojenik şok nedeniyle primer PKG uygulanan adres 91 hasta (66 erkek, 25 kadın; ort. yaş 61±11) alınmıştı. Tüm klinik ve anjiyografik verilerle birlikte hastane içi ve uzun dönem sonuçlar geriye dönük olarak toplandı. Olgular, hastane içi dönemde mortalite gelişen (n=59, %64.8) ve gelişme-yen (n=32, %35.2) hastalar olarak iki gruba ayrıldı.

Bulgular: Hastane içi mortalite gelişen grupa yaş (ort. 62.7±11.1 ve 57.7±11.4; p=0.04) ve diabetes mellitus (DM), renal yetersizlik ve miyokart enfarktüsü öyküsü sıkılığı daha yüksekti. Çoklu damar hastalığı (p=0.004) ve sirkumfeks arter tutulumu (p=0.03) mortalite gelişen grupta; tirofban (p=0.02) ve stent kullanıma (p=0.007) sahılmak grubunda daha yüksek oranlardı. İşlem başarısı mortalite gelişen grupta anlamlı derecede düşük bulundu (%39 ve %84.4%; p<0.001). Yaşanın 32 hastanın ortanca 26 aylık takibe sisizada yalnızca üç hasta (%9.4) kardiyovasкурler ölüm görüldü. Çok değişkenli analizde, başarısız işlem (odds oranı 7.2, %95 güven aralığı 1.77-29.27; p=0.006) ve DM (odds oranı 3.92, %95 güven aralığı 1.13-13.62; p=0.03) hastane içi mortalitenin bağımsız belirleyicileri olarak bulundu.


Anahtar sözcükler: Anjiyoplasti, translüminal, perkütan koroner; hastane mortalitesi; miyokart enfarktüsü/tedavi/ komplikasyon; prognoz; şok, kardiyojenik/tedavi/mortalite.
Cardiogenic shock is highly associated with cardiovascular mortality. The incidence ranges from 5-10% in patients who had previous ST-elevation myocardial infarction (STEMI).\[^{1,2}\] Primary percutaneous coronary intervention (PCI) is an effective reperfusion strategy in STEMI patients, decreasing the cardiovascular mortality rate, compared to thrombolytic therapy.\[^{3,4}\] Although primary PCI has several beneficial effects on mortality, cardiogenic shock is still the main cause of death in STEMI patients. Therefore, it is critical to understand the risk factors for cardiovascular mortality in cardiogenic shock patients who underwent primary PCI.

In this paper, we investigated the independent markers of in-hospital mortality, considering the in-hospital and long-term results in patients with cardiogenic shock complicated by STEMI and underwent primary PCI.

**PATIENTS AND METHODS**

**Patient population.** Between October 2003-March 2008, a total of 2644 consecutive patients who were admitted to emergency unit with the diagnosis of STEMI and underwent primary PCI within the first 12 hours after the onset of symptoms (within the first 18 hours after the onset of symptoms for patients with hemodynamic instability and persistent chest pain) were evaluated retrospectively. Ninety one with cardiogenic shock (66 men, 25 women; mean age 61±11) were included in the study. The parameters used to diagnose STEMI were as follows: (i) ST-segment elevation in the consecutive ≥2 leads (≥2mm in precordial leads; ≥1 mm in extremity leads) or emerging left bundle branch block (LBBB); (ii) ischemic chest pain for longer than 30 minutes; (iii) ≥2-fold increase in the level of serum creatinine phosphokinase myocardial band (CK-MB). Patients were also divided into two groups, including patients with/without in-hospital mortality (n=59; n=32, respectively). The study protocol was approved by the Local Ethics Committee.

**Data analysis.** Demographic characteristics of the patients, history of cardiovascular disease, risk factors (smoking, hypercholesterolemia, diabetes mellitus, hypertension) and pain-to-balloon and door-to-balloon times were obtained from the hospital records. Daily blood sample results of all the patients on admission and thereafter were obtained from the medical records. Information about the type of STEMI was obtained from records of the electrocardiogram performed on admission.

**Coronary angiography, primary angioplasty and stent implantation.** All patients received a loading dose of clopidogrel 300 and aspirin 300 mg before the procedure. Angiographic data obtained from the archives of Catheterization Lab were assessed. Emergency coronary angiography and angioplasty were performed through the femoral artery. A bolus of heparin 10000 U was administered intravenously to all patients after femoral artery puncture. Flow in the infarct-related coronary artery was evaluated according to the TIMI (Thrombolysis In Myocardial Infarction) classification. The acute phase procedural success was defined as a decrease in narrowing of ≥50% in the infarct-related coronary artery at the end of every procedure and the provision of TIMI III flow. All of the patients were sent to Coronary Intensive Care Unit following primary PCI. They were administered 1000 IU/h heparin infusion (or 1 mg/kg subcutaneous enoxaparin, bid) with the treatment of aspirin 100 mg and clopidogrel 75 mg once daily. The use of glycoprotein IIb/IIIa inhibitor was at the discretion of the surgeon.

**Definitions.** The criteria for the diagnosis of cardiogenic shock were as follows: (i) persistent systolic blood pressure <90 mmHg or requiring for vasodilators to set a systolic blood pressure of >90 mmHg; (ii) presence of signs of end-organ hypoperfusion (urine excretion <30 mL/h; cold or sweaty extremity; fluctuating mental state); (iii) clinical signs indicating an increase in the left ventricular end-diastolic pressure (physical examination and chest x-ray showing pulmonary congestion).\[^{5}\] The pain-to-balloon time was defined as the time lapse between the start of symptoms and post-balloon angioplasty coronary reperfusion, whereas the door-to-balloon time was the time lapse between hospital visit and post-balloon angioplasty coronary reperfusion. Recurrent infarction was defined as the repeated increase in the CK-MB level with a repeated increase in the ST segment. Target vessel revascularization was defined as repeated PCI or coronary artery bypass grafting (CABG) due to stenosis or occlusion in the infarct-related coronary artery. Cardiovascular mortality was defined as unexpected sudden death or death related to acute MI, heart failure or arrhythmia. Multivessel disease was defined as the presence of more than 50% occlusion in at least two main epicardial coronary arteries or the left main coronary artery. Glomerular filtration rate (GFR) was estimated using the Modification of Diet in Renal Disease (MDRD) GFR equation and renal failure was defined as GFR <60 ml/min/1.73m\(^2\).\[^{6}\] The use of oral hypoglycemic or insulin therapy at the time of presentation was considered as a diagnosis of diabetes mellitus, whereas the use of antihyperlipidemic drugs or a total cholesterol level of ≥200 mg/dl was defined as the diagnosis of hypercholesterolemia.

**Statistical analysis.** Statistical analysis of the data was performed using the SPSS 15.0 program. Numerical data were expressed in mean±standard deviation, whereas categorical data were expressed in percentages. The
Mann-Whitney U-test was used to compare numerical values between the groups, whereas Chi-square test was used to evaluate the differences between categorical variables. Also, retrospective multivariate stepwise Cox regression analysis was used to investigate the independent predictor of in-hospital mortality, one of the clinical and angiographic variables. Procedural failure, renal failure, multivessel disease, history of myocardial infarction, DM, use of glycoprotein IIb/IIIa inhibitors, stent implementation and >70 years of age were included in the Cox regression model. A p value of <0.05 was considered statistically significant.

RESULTS

Clinical and demographic characteristics. Demographic and clinical characteristics of the patients are shown in Table 1. In-hospitality was more common among the older patients (mean age 62.7±11.1 and 57.7±11.4; p=0.04) with the history of DM, renal failure and MI. The incidence of diabetes mellitus, hypertension, and history of cigarette smoking was similar in both groups. No significant difference was found in terms of anterior MI development between the groups (65.6% vs. 57.6%; p=0.55). In addition, the incidence of PCI (6.3% vs. 18.6%) and CABG (0% vs. 7.2%) was higher in the in-hospital mortality patient group.

Angiographic and procedural characteristics. Angiographic and procedural characteristics are shown in Table 2. The incidence of circumflex artery lesions causing myocardial infarction was higher in the in-hospital mortality group (0% vs. 15.3%; p=0.03), while no significant difference was found in terms of distribution of coronary arteries between the
groups. On the other hand, the use of tirofiban and stent implantation was higher in the patients who did not experience in-hospital mortality (p=0.02 and p=0.007, respectively) with a higher rate of success (84.4% vs. 39%; p<0.001). Furthermore, pain-to-balloon and door-to-balloon times were similar between the groups, however the incidence of multivessel disease was higher in the in-hospital mortality group (25% vs. 55.9%; p=0.004).

In-hospital and long-term results. In-hospital events are shown in Table 3. In-hospital mortality was seen in 59 of 91 patients (64.8%) with cardiogenic shock undergoing primary PCI. Cardiovascular mortality occurred within the first 24 hours in 61% of the patients (n=36) and after 24 hours in 39% of the patients (n=23). Ventricular tachycardia / fibrillation and complete AV block were more common in the in-hospital mortality group (p=0.03 and p=0.02, respectively). On the other hand, there was no significant difference in target vessel revascularization and reinfarction between two groups.

Considering the success rate, the incidence of procedural failure was two-fold higher in the in-hospital mortality group, compared to those who did not experience in-hospital mortality (46% vs. 87.8%; p<0.001). In addition, the use of intraaortic balloon was significantly lower in patients who did not experience in-hospital mortality (85.3% vs. 58%; p=0.004). Thirty-two patients who were discharged from the hospital were followed over 26 months and only 3 patients (9.4%) experienced cardiovascular mortality.

Univariate and independent predictors of in-hospital mortality. Univariate and independent predictors of in-hospital mortality are shown in Table 4. In the univariate analysis, procedural failure, renal failure, multivessel disease, history of MI, DM, use of tirofiban and stent implementation were the main factors, influencing the in-hospital mortality rate considerably. On contrast, only procedural failure (OR 7.2, CI 95% 1.77-29.27; p=0.006) and DM (OR 3.92, CI 95% 1.13-13.62; p=0.03) were the independent predictors of the in-hospital mortality in the multivariate analysis.

DISCUSSION

The study investigating the efficacy and outcomes of primary PCI in STEMI patients with cardiogenic shock on admission concluded that (i) in-hospital mortality rate was very high in patients with cardiogenic shock complicated by STEMI; (ii) successful primary PCI decreased in-hospital mortality by 50%; (iii) pro-

Table 3. In-hospital events

<table>
<thead>
<tr>
<th></th>
<th>In-hospital mortality</th>
<th>No in-hospital mortality</th>
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<tbody>
<tr>
<td></td>
<td>(n=59)</td>
<td>(n=32)</td>
</tr>
<tr>
<td>Number</td>
<td>Percent (%)</td>
<td>Number</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>2</td>
<td>3.4</td>
</tr>
<tr>
<td>Target vessel revascularization</td>
<td>3</td>
<td>5.1</td>
</tr>
<tr>
<td>Ventricular tachycardia/fibrillation</td>
<td>39</td>
<td>66.1</td>
</tr>
<tr>
<td>Use of intraaortic balloon pump</td>
<td>53</td>
<td>89.8</td>
</tr>
<tr>
<td>Complete AV block</td>
<td>12</td>
<td>20.3</td>
</tr>
<tr>
<td>Requiring hemodialysis</td>
<td>2</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Table 4. Univariate and multivariate analyses of independent predictors of in-hospital mortality

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>CI 95%</th>
<th>p</th>
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<tbody>
<tr>
<td>Univariate analysis</td>
<td></td>
<td></td>
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<tr>
<td>Procedural failure</td>
<td>8.45</td>
<td>2.84-25.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal failure</td>
<td>5.25</td>
<td>1.76-15.6</td>
<td>0.003</td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>3.96</td>
<td>1.52-10.28</td>
<td>0.005</td>
</tr>
<tr>
<td>Previous MI</td>
<td>3.92</td>
<td>0.81-19.03</td>
<td>0.08</td>
</tr>
<tr>
<td>DM</td>
<td>3.30</td>
<td>1.23-8.78</td>
<td>0.01</td>
</tr>
<tr>
<td>Tirofiban use</td>
<td>0.32</td>
<td>0.12-0.83</td>
<td>0.02</td>
</tr>
<tr>
<td>Stent implantation</td>
<td>0.21</td>
<td>0.06-0.69</td>
<td>0.01</td>
</tr>
<tr>
<td>Multivariate analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedural failure</td>
<td>7.20</td>
<td>1.77-29.27</td>
<td>0.006</td>
</tr>
<tr>
<td>DM</td>
<td>3.92</td>
<td>1.13-13.62</td>
<td>0.03</td>
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It is a well-known phenomenon that coronary reperfusion can be established rapidly and efficiently through primary PCI in STEMI patients. However, a few number of patients admitted to hospital, presenting with cardiogenic shock; therefore the efficacy of the procedure reduces. Coronary lesions which are considered complex lesions, requiring more complicated interventions, are more common in patients with cardiogenic shock. In addition, hemodynamic instability which is present in patients with cardiogenic shock is one of the main drawbacks for an effective coronary reperfusion after primary PCI. As a result, the success rate has been reported to be significantly lower in patients with cardiogenic shock who underwent primary PCI, compared to those without cardiogenic shock.

In our study, multivariate analysis showed that procedural failure and DM were the main independent predictors of in-hospital mortality.

Klein et al. also reported that lack of use of a glycoprotein IIb/IIIa inhibitor or stent was the independent risk factors of cardiovascular mortality in patients with cardiogenic shock complicated by STEMI who underwent primary PCI. Similarly, Chan et al. found that the success rate of angiography was higher and cardiovascular mortality rate was lower in the patients receiving a glycoprotein IIb/IIIa inhibitor with coronary stenting. Also, the incidence of using glycoprotein IIb/IIIa inhibitors with coronary stenting was significantly lower in patients who experienced in-hospital mortality in this study (87.5% vs. 59.3% for stenting, p=0.007; 46% vs. 22% for glycoprotein IIb/IIIa inhibitors, p=0.002). Although multivariate analysis did not show any association, univariate analysis demonstrated an independent association between the use of glycoprotein IIb/IIIa inhibitor with coronary stenting and cardiovascular mortality (p=0.01 and p=0.02, respectively).

Review of the literature has shown different mortality rates for patients with cardiogenic shock who underwent primary PCI, in-hospital mortality was higher in our study, compared to others. This may be explained by higher incidence of comorbidities such as DM, multivessel disease and renal failure, likely having a direct on in-hospital mortality was higher among our study population. A total of 49.5% of the patients had DM; 45.1% had multivessel disease and 59.3% had renal failure on admission (GFR <60 mL/min/1.73 m2). In addition, the incidence of glycoprotein IIb/IIIa inhibitors used was lower than the others. In our study, only tirofiban was also used as a glycoprotein IIb/IIIa inhibitor, compared to other studies using abciximab. Considering the recommendation of ACC/AHA guidelines stating that abciximab is class Ia and tirofiban is class IIb, lower incidence of tirofiban use may be considered as another reason for in-hospital mortality in our study.

In our study, the incidence of intraaortic balloon pump use was significantly higher in the patient group with procedural failure, compared to those who

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underwent a successful procedure (58% vs. 85.3; p=0.004). In addition to beneficial effects of intraaortic balloon pump on hemodynamic stability in patients with cardiogenic shock, it has been shown that the left ventricular support devices can be also useful.[28] Therefore, the left ventricular support devices may be considered as an alternative, particularly for the patients who are unresponsive to PCI and intraaortic balloon pump therapy.

Compared to in-hospital mortality, higher long-term survival rate in the patients who were discharged following primary PCI was another result of our study. During the 26-month-follow-up, death related to CVD was seen only 3 of 32 patients who were discharged following primary PCI. The mortality rate was 9.4% during the long-term follow-up, while the incidence of target vessel revascularization was 1% and the incidence of reinfarction was 4.8%.

**Study limitations.** There are some limitations of this study which should be considered when interpreting the study results. First, this study was a unicenter and retrospective which led to some disadvantages. Second, the use of glycoprotein IIb/IIIa inhibitors and stent implantation were at the discretion of the physician, not randomized to all patients. This could also have an influence on the final results. Third, open coronary arteries following primary PCI and TIMI flow do not always indicate tissue-level perfusion. The studies using contrast echocardiography and PET scan have shown that tissue-level perfusion cannot be maintained in a one third of the patients, despite TIMI III flow.[26] In case of no-reflow, it is well-known that complications of post-MI and left ventricular dilatation are more common.[27] In addition, evaluation of only TIMI flow grade was another limitation of our study. If myocardial blush grade, ST-segment depression or contrast echocardiography were used together with TIMI flow grade, additional data could have been obtained. Finally, we did not assess the hemodynamic profile for the diagnosis of cardiogenic shock to make reperfusion of the infarct-related artery as soon as possible. As a result, those patients had to be diagnosed with cardiogenic shock based on only clinical parameters.

In conclusion, the in-hospital mortality rate is significantly higher in patients with cardiogenic shock complicated by STEMI. In addition, successful procedures yield a two-fold decrease in in-hospital mortality in those patients. On the other hand, procedural failure and DM are two independent predictors of in-hospital mortality.

**REFERENCES**


