

## Relationship between in-Hospital Mortality and Renal Dysfunction after Primary Percutaneous Coronary Intervention in Turkish Geriatric Patients with ST-elevation Myocardial Infarction

### ST yükselmeli Miyokard İnfarktüsülü Türk Geriatrik Hastalarda Primer Perkütan Koroner Girişim Sonrası Hastane İçi Mortalite ile Renal Disfonksiyon Arasındaki İlişki

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#### ABSTRACT

Geriatric population (>80 years) has an increased mortality risk due to several reasons including more extensive coronary artery disease (CAD) and impaired renal function. We investigated the relationship between in-hospital mortality and renal dysfunction in geriatric patients with ST-elevation myocardial infarction (STEMI) who underwent primary percutaneous intervention (PCI). We included 203 geriatric patients with STEMI who underwent primary PCI. Patients were divided into 2 groups; group 1 comprised 42 patients who died in the hospital after MI, and group 2 included 161 patients who were discharged following primary PCI. The risk factors of the patients were determined. We calculated coronary artery disease prevalence by Gensini risk score, renal function by creatinine clearance (CrCl), and compared 2 groups. The patients in group 1 who died in hospital after STEMI were older; they had more extensive CAD and lower CrCl (age:  $82 \pm 5$  yr,  $78 \pm 7$  yr,  $p < 0.001$ ; Gensini score:  $70 \pm 30$ ,  $42 \pm 26$ ,  $p = 0.001$ ; CrCl:  $46 \pm 17$  mL/min,  $65 \pm 18$  mL/min,  $p < 0.001$ ). When multivariate analysis was performed with logistic regression, we found to be CrCl, HDL-cholesterol, and Gensini scores to be the independent predictors of in-hospital mortality (CCL: OR 1.057 (1.029-1.086),  $p = 0.001$ ); HDL: OR 1.077 (1.021-1.136),  $p = 0.007$ , Gensini score: OR 0.969 (0.952-0.985),  $p = 0.001$ ). Renal dysfunction increases in-hospital mortality in elderly patients with STEMI undergoing primary PCI. Renal dysfunction in elderly patients with MI is an important risk factor that increases in-hospital mortality like other cardiovascular risk factors.

**Keywords:** Geriatric population, ST elevation myocardial infarction, renal function, creatinine clearance, Gensini score.

#### ÖZET

Geriatric popülasyon (>80 yaş), daha yaygın koroner arter hastalığı (KAH) ve bozulmuş böbrek fonksiyonu gibi çeşitli nedenlerden dolayı artmış mortalite riskine sahiptir. Primer perkütan girişim (PCI) uygulanan ST yükselmeli miyokard enfarktüsü (STEMI) olan geriatrik hastalarda hastane içi mortalite ile böbrek fonksiyon bozukluğu arasındaki ilişkiyi araştırdık. Primer PCI uygulanan STEMI'li 203 geriatrik hastayı dahil ettik. Hastalar 2 gruba ayrıldı; grup 1, Miyokard infarktüsü (MI) sonrası hastanede ölen 42 hastadan, grup 2 ise primer PKG sonrası taburcu edilen 161 hastadan oluşuyordu. Hastaların risk faktörleri belirlendi. Koroner arter hastalığı prevalansını Gensini risk skoru ile, renal fonksiyonu kreatinin klirensi (CrCl) ile hesapladık ve 2 grubu karşılaştırdık. Grup 1'de STEMI sonrası hastanede ölen hastalar daha yaşlıydı; daha yaygın KAH ve daha düşük CrCl'ye sahiptiler (yaş:  $82 \pm 5$  yıl,  $78 \pm 7$  yıl,  $p < 0.001$ ; Gensini skoru:  $70 \pm 30$ ,  $42 \pm 26$ ,  $p = 0.001$ ; CrCl:  $46 \pm 17$  mL/dk,  $65 \pm 18$  mL/dak,  $p < 0.001$ ). Lojistik regresyon ile çok değişkenli analiz yapıldığında CrCl, HDL-kolesterol ve Gensini skorlarının hastane içi mortalitenin bağımsız öngördürücüleri olduğunu bulduk (CCL: OR 1.057 (1.029-1.086),  $p = 0.001$ ); HDL: OR 1.077 (1.021-1.136),  $p = 0.007$ , Gensini skoru: OR 0.969 (0.952-0.985),  $p = 0.001$ ). Primer PKG uygulanan STEMI'li yaşlı hastalarda renal disfonksiyon hastane içi mortaliteyi artırmaktadır. MI'lı yaşlı hastalarda böbrek fonksiyon bozukluğu, diğer kardiyovasküler risk faktörleri gibi hastane içi mortaliteyi artıran önemli bir risk faktördür.

**Anahtar Kelimeler:** Geriatrik popülasyon, ST yükselmeli miyokard infarktüsü, böbrek fonksiyonu, kreatinin klirensi, Gensini skor

## INTRODUCTION

Cardiovascular disease (CVD) is one of the important causes of death in western countries.<sup>1</sup> The risk of cardiovascular disease is high in renal failure.<sup>2-4</sup> It is also known to increase the risk of chronic kidney disease (CKD), myocardial infarction (MI), and cardiovascular mortality.<sup>5,6</sup> Twenty to 50% of patients with acute ST-elevation myocardial infarction (STEMI) are over 65 years of age. More than 60% of deaths due to MI occur in this age group.<sup>7</sup> The frequency of chronic kidney disease increases with age and increases cardiovascular morbidity and mortality due to ventricular arrhythmia, heart failure, which is one of the in-hospital complications.<sup>8</sup>

We investigated the factors associated with in-hospital mortality in elderly patients undergoing primary percutaneous intervention (PCI) for STEMI.

## METHODS

Our study is a retrospective study, we included 203 geriatric patients who underwent MI and primary PCI between October 2016 and October 2018.

We received the ethics committee approval of the study at non-interventional clinical studies ethics committee of Recep Tayyip Erdogan University (Local Ethical Committee) (Decision no: 2016/13). Patients were participated in a random and consecutive manner. Forty-two patients died in the hospital and 161 patients were discharged. We identified risk factors for these two groups. Coronary artery disease (CAD) severity was assessed by Gensini risk scoring<sup>9</sup>, renal function was assessed by creatinine clearance (CrCl), and two groups were compared. We used logistic regression analysis to determine in-hospital mortality predictors after primary PCI. Acute STEMI was diagnosed as having two of the following three criteria:<sup>10</sup>

1- ST-segment elevation in consecutive  $\geq 2$  leads ( $\geq 2$  mm in chest lead,  $\geq 1$  mm in extremity lead). 2- Ischemic chest pain lasting over 30 minutes. 3- Serum creatinine kinase myocardial band (CK-MB) level increased at least two times of normal range. Patients who presented in the subacute period (symptom onset  $> 12$  hours), had MI, 3 months past, or underwent coronary artery bypass graft (CABG) surgery or PCI revascularization, had myocardial infarction from the left main coronary artery, and had emergency CABG surgery were excluded from the study. An informed consent form was signed by all patients. Blood samples required for

randomization were taken from the patients by direct venous puncture. Serum creatinine (Cr) and biochemical parameters were analyzed in a standard laboratory using an appropriate method. In the study, the accuracy of the biomarker measurements of the centers and the clinical laboratory measurement were evaluated with a significant quality measure. We used the Cockcroft-Gault equation to calculate CrCl as follows:  $(\{140 - \text{in age}\} \times \text{body weight in kg}) / \{72 \times \text{Cr mg/dL}\} \times 0.85$  (female gender). In our study, according to the age of the patient population, we divided the patients into two groups as CrCl  $> 45$  mL/min and CrCl  $< 45$  mL/min. The study was conducted in accordance with the 1975 Helsinki Declaration in accordance with the ethical rules.

Primer Percutaneous Coronary Intervention Procedure: Aspirin (300 mg) and clopidogrel (300 mg) were given orally at emergency, and 100 U / kg (max 10.000 U) heparin was administered after femoral artery puncture. Primary PCI (balloon angioplasty and/or stent implantation) was performed on infarcted arteries after coronary angiography. During the procedure, coronary artery flow (Thrombolysis in Myocardial Infarction (TIMI) classification) was used.<sup>11</sup>

Successful stent angioplasty procedure was considered as achieving less than 20% residual stenosis and TIMI-III flow after stent placement. Recurrent infarction was defined as recurrent cardiac enzyme and ST segment elevation associated with chest pain lasting over 30 minutes after the first 24 hours of infarction. Major bleeding was defined as hemorrhage causing a decrease in hemoglobin level  $> 5$  g/dL or any grade of intracranial hemorrhage. We made comparisons between groups in terms of basic clinical features, PCI success, and in-hospital outcomes (death, recurrent infarction, stroke, and major bleeding). Table 1 includes the main characteristics of the study population.

### Statistical Analysis

Continuous variables were calculated as mean  $\pm$  standard deviation (SD) and categorical variables as percentages. Normally distributed continuous variables were compared with Student's t-test, non-normally distributed ones were compared with Mann-Whitney U-test. Categorical variables were compared with the Chi-square test. p value  $< 0.05$  was considered statistically significant. SPSS 16.0 program was used in Statistical analysis, (SPSS Inc., Chicago, IL).

**Table 1.** Main characteristics of the study population

Parameters (N=203)	Group1 (N=42)	Group 2 (N=161)	P value
Age (years $\pm$ SD)	82 $\pm$ 5	78 $\pm$ 7	0.001
Sex (male), n (%)	23 (11)	85 (42)	0.8
Gensini score	70 $\pm$ 30	42 $\pm$ 26	0.001
Hypercholesterolaemia, n (%)	12 (6)	77 (38)	0.03
Smoking, n (%)	7 (3)	11 (5)	0.06
HT, n (%)	21 (10)	92 (45)	0.5
Diabetes mellitus, n (%)	11 (5)	43 (21)	0.2
Alanin aminotransferaz (ALT)	31 $\pm$ 25	25 $\pm$ 18	0.8
Hgb (g/dL)	12.7 $\pm$ 2.2	13.1 $\pm$ 1.5	0.9
Glucose (mg/dL)	112 $\pm$ 46	115 $\pm$ 38	0.2
Total Cholesterol (mg/dL)	166 $\pm$ 38	177 $\pm$ 42	0.25
LDL (mg/dL)	103 $\pm$ 32	113 $\pm$ 36	0.25
HDL (mg/dL)	34 $\pm$ 7	41 $\pm$ 9	0.001
Triglyceride (mg/dL)	126 $\pm$ 45	112 $\pm$ 52	0.3
Creatinine clearance	46 $\pm$ 17	65 $\pm$ 18	0.001
<b>TIMI flow</b>			0.001
TIMI 0	13 (6)	10 (5)	
TIMI 1	10 (5)	6 (3)	
TIMI 2	6 (3)	16 (8)	
TIMI 3	13 (6)	161 (79)	
<b>Myocardial infarction (MI)</b>			0.01
Anteroseptal MI	27(13)	69 (64)	
Inferior MI	15(7)	92 (45)	

**Table 2.** The correlations of parameters with hospital mortality.

Parameters	Gensini score	Age	HDL	Creatinine clearance	Hospital mortality
Gensini score	-	r=0.246 p=0.001	r=-0.179 p=0.01	r=-0.263 p=0.001	r:0.439 p:0.001
Age	r=0.246 p=0.001	-	r=0.119 p=0.09	r=-0.452 p=0.001	r:0.273 p:0.001
HDL	r=-0.179 p=0.01	r=0.119 p=0.09	-	r=-0.128 p=0.07	r:-0.282 p:0.001
Creatinine clearance	r=-0.263 p=0.001	r=-0.452 p=0.001	r=0.128 p=0.07	-	r:-0.413 p:0.001
Hospital mortality	r:0.439 p:0.001	r:0.273 p:0.001	r:-0.282 p:0.001	r:-0.413 p:0.001	-

## RESULTS

In group 1, patients who died after MI, renal function (CrCl) was worse, the severity of coronary artery disease (Gensini score) and age were higher according to group 2 (age: 82  $\pm$  5 yr, 78  $\pm$  7 yr, p<0.001; Gensini score: 70  $\pm$  30, 42  $\pm$  26, p: 0.001; CrCl: 46  $\pm$  17 mg/min, 65  $\pm$  18 mg/min, p<0.001). HDL levels were lower in group 1 and were statistically significant. (HDL: 34  $\pm$  7 mg/dL, 41  $\pm$  9 mg/dL, p <0.001). Other basal characters were similar in both groups.

### Explanations of abbreviations

(TIMI: Thrombolysis in myocardial infarction, HT: Hypertension,

**HDL:** High density lipoprotein cholesterol,

**LDL:** Low density lipoprotein cholesterol,

**Hgb:** Hemoglobin,

**Gensini score:** Gensini score was used to evaluate the severity of atherosclerosis. The most severe stenosis in each of the 8 coronary segments was graded from 1 to 4 (1%-49% lumen diameter reduction: 1 point; 50%-74% stenosis, 2 points; 75%-99% stenosis, 3 points; and 100% occlusion 4 points) to give a total score ).

Hospital mortality correlated positively with Gensini score and advanced age, while negatively correlated with HDL and creatinine clearance (Table 2). Age: r:0.273, p:0.001; Gensini score: r:0.439, p:0.001; creatinine clearance r:-0.413, p:0.001; HDL: r:-0.282, p<0.001.

Hospital mortality correlated positively with Gensini score and advanced age, while negatively correlated with HDL and creatinine clearance. There were positive correlations between in-hospital mortality with age and coronary artery disease prevalence, and negative correlations between in-hospital mortality with CrCl and HDL (age: r: 0.273, p: 0.001; Gensini skor: r: 0.439, p: 0.001; CrCl: r: -0.413, p: 0.001; HDL: r: -0.282, p: 0.001). Table 3 shows the results of multivariate analysis with logistic regression in hospital mortality. As a result of logistic regression multivariate analysis used to determine in-hospital mortality, crcl, HDL level and Gensini score were independent predictors of in-hospital mortality (CrCl: OR 1.057 (1.029-1.086), p = 0.001; HDL: OR 1.077 (1.021-1.136), p = 0.007; Gensini score: OR 0.969 (0.952-0.985), p = 0.001).

**Table 3.** Results of multivariate analysis with logistic regression for hospital mortality.

Independent Variables	P value	Odds Ratio (95% confidence interval)
Gensini score	0.001	0.969 (0.952-0.985)
HDL	0.007	1.077 (1.021-1.136)
Age (year)	0.14	0.933 (0.852-1.023)
Creatinine clearance	0.001	1.057 (1.029-1.086)
Constant	0.455	17.976
R <sup>2</sup> (Cox & Snell/ Nagelkerke)		0.3 / 0.469

In univariate analysis, determinants with a p value <0.05 were taken into the logistic regression analysis by the input method. When we performed multiple logistic regression analysis, hospital mortality was associated to group 1 creatinine clearance (CCL), (OR 1.057 (1.029-1.086), p = 0.001), HDL, (OR 1.077 (1.021-1.136), p = 0.007), Gensini score, (OR 0.969 (0.952-0.985), p = 0.001); and it was independent from group 2 creatinine clearance, HDL and Gensini score (Table 3).

## DISCUSSION

In our study, it was revealed that renal dysfunction is an important risk factor increasing in-hospital mortality in geriatric patients with ST-elevation MI and primary PCI. In geriatric patients with atherosclerosis, MI, acute coronary syndrome, renal failure increases mortality and morbidity and is closely related, and there are similar studies. Clinicians' fear of elderly patients is due to their high complication rates and more fragility.<sup>12</sup> The prevalence of CKD increases in correlation with age. So; While it is 4% at the age of 20-39, it increases to 47% after the age of 70.<sup>13</sup> CKD is also an important risk factor for diseases such as heart failure and ventricular arrhythmias, which are important in the morbidity and mortality of cardiovascular diseases.<sup>14,15</sup> We found a significant increase in mortality, especially in elderly patients with renal failure who had MI. Current guidelines recommend intervention and treatment in patients with STEMI and renal dysfunction in the same way as other STEMI patients, taking into account some precautions during the administration of contrast dye and some drugs.<sup>16</sup> Aging causes both structural and functional changes in the kidneys. Reduction of renal

blood flow and a number of nephrons with aging cause CKD by decreasing glomerular filtration rate.

Chronic kidney disease (CKD) is set in 5 stages of increasing severity with a decrease in glomerular filtration rate leading to end stage renal disease (ESRD) requiring a treatment of substitution, dialysis or transplantation. CKD is frequent, it increases with age, and affects one person out of 10 in the general population, and only 4 per 100,000 will reach end-stage renal disease (ESRD). As soon as it occurs, CKD is associated with increased cardiovascular comorbid conditions.<sup>17</sup>

Chronic renal disease has a high mortality and morbidity, especially due to cardiovascular diseases. Cardiovascular risk increases exponentially as the CKD stage progresses. For example, cardiovascular risk increases 2 to 4 times in a patient in stage 3, and 10 to 50 times in a patient in stage 5.<sup>18</sup>

In recent studies, aggressive revascularization strategies have been shown to provide more survival and absolute risk reduction in terms of better quality of life in patients over 75 years of age than younger patients.<sup>19-21</sup>

The main finding of our study, coronary artery revascularization in elderly patients with low CrCl was found to be more applicable, safe and associated with better outcome than medical treatment. This was also the case in elderly patients who were susceptible to bleeding, contrast nephropathy, in-hospital bleeding, and toxic effects from treatment. Studies in this area, especially in geriatric patients, have also achieved similar results to our study. as follows: In patients with ST-segment elevation MI (STEMI) and without STEMI, patients with kidney disease have a higher mortality than patients with preserved kidney function.<sup>22-24</sup> Currently, primary PCI in STEMI patients is included in the recommended reperfusion strategy and also in those with renal dysfunction. Since primary PCI is an emergency treatment in STEMI patients, renal function and CrCl levels are unknown in these patients during the procedure. Records show that most patients are diagnosed outside the hospital and referred directly to the catheterization laboratory, with the first blood samples taken prior to contrast injection for biochemical testing.<sup>25</sup> While guidelines recommend evaluation of risk-benefit ratio with severity of renal dysfunction, an early invasive approach remains the best strategy for patients with acute coronary syndrome with CKD.<sup>26</sup>

In our study, patients with renal dysfunction who underwent primary PCI were fewer in number than

patients without renal dysfunction. In our study, as in other studies, the presence of CKD increases short-term and long-term mortality. This situation, the presence of RI, has seen a higher 30-day increase in mortality, similar to previous studies. In addition, the presence of kidney disease in STEMI and non-STEMI patients has been associated with an increase in 9-month mortality, depending on all causes.<sup>27-30</sup> According to our study, RI (renal insufficiency) is an independent predictor of increasing 1-year mortality.

Renal dysfunction increases mortality during hospitalization in elderly patients who underwent primary percutaneous coronary intervention and had myocardial infarction. Renal dysfunction in elderly patients with MI, like other cardiovascular risk factors, increases mortality during hospitalization. Taking these factors into account and taking precautions in geriatric patients with MI would play an important role in reducing in-hospital mortality.

## CONCLUSION

Renal dysfunction increases in-hospital mortality in elderly patients with STEMI undergoing primary PCI. Renal dysfunction in elderly patients with MI is an important risk factor that increases in-hospital mortality like other cardiovascular risk factors.

## Limitations

Our findings can be affected by data quality and confounding variables. In addition, our study is open to bias regarding unmeasurable factors. We tried to reduce the bias caused by these unknown variables as much as possible. ST-elevation MI patients with cardiogenic shock that might be subject to the study were not excluded. Our systematic access to additional information about creatinine values or contrast-induced nephropathy was limited in the days after primary PCI was performed.

## Ethics Committee Approval

Ethics Committee the ethics committee approval of the study at non-interventional clinical studies ethics committee of Recep Tayyip Erdogan University (Local Ethical Committee) (Decision no: 2016/13).

## Informed Consent

Informed consent was obtained from the patients who participated in this study.

## Conflict of Interest

The authors have no conflict of interest to declare.

## Financial Disclosure

The authors declared that this study has received no financial support.

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