ORIGINAL ARTICLE

Effect of acute kidney injury on long-term mortality in patients with ST-segment elevation myocardial infarction complicated by cardiogenic shock who underwent primary percutaneous coronary intervention in a high-volume tertiary center

Yüksek hacimli üçüncü basamak merkezde ST segment yükselmeli miyokart enfarktüsü ile başvuran primer perkütan koroner girişim yapılan ve kardiyojenik şok gelişen hastalarda akut böbrek hasarının uzun dönem mortaliteye etkisi

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ABSTRACT

Objective: Acute kidney injury (AKI) is a reflection of both renal and cardiac reserve in patients with ST-segment elevation myocardial infarction (STEMI), but there is a lack of evidence related to the effect of AKI on long-term mortality in patients with STEMI. This study was an investigation of the prognostic value of AKI for long-term mortality in patients with STEMI complicated by cardiogenic shock (CS) and primary percutaneous coronary intervention (PPCI).

Methods: This retrospective analysis evaluated the long-term prognostic impact of AKI on 492 patients with STEMI complicated by CS who were treated with PPCI. AKI was defined as ≥0.3mg/dL increase in serum creatinine within 48 hours or a ≥50% increase in serum creatinine in 7 days, or a reduction in urine output (documented oliguria of less than 0.5mL/kg per hour >6 hours. Patients were grouped according to the incidence of AKI and long-term mortality was compared. Cox regression analysis was used to determine independent prognostic factors of long-term mortality.

Results: In Cox regression analysis, the age- and sex- adjusted hazard ratios (HRs) were higher for all-cause mortality in patients with AKI. [HR: 4.556; 95% confidence interval: (CI) 2.370–8.759]. After adjustment for confounding variables, the relative risk was greater for patients with AKI in comparison with patients without AKI (HR: 2.207; 95% CI: 1.150–4.739). Age (HR: 1.060, 95% CI: 1.027–1.094; p<0.001), left ventricular ejection fraction (HR: 0.952, 95% CI: 0.916–0.989; p=0.012), blood urea nitrogen level (HR: 1.019, 95% CI: 1.005–1.034; p=0.010), and AKI (HR: 2.244, 95% CI: 1.077–4.676; p=0.031) were found to be independent factors to determine long-term mortality.

Conclusion: The results of this study demonstrated that AKI was an independent prognostic factor for long-term mortality among patients with STEMI complicated by CS and treated with PPCI.

ÖZET

Amaç: Akut böbrek hasarı (ABH) ST segment yükselmeli miyokart enfarktüsü (STYME) hastalarında renal ve kardiyak rezervi yansıtır, ama STYME hastalarında ABH'nın uzun dönem mortaliteye olan etkisi konusunda kanıt azdır. Bu çalışmada, STYME ile primer perkütan koroner girişim (PPKG) uygulanan ve kardiyojenik şok (KŞ) gelişen hastalarda ABH'nın uzun dönem mortaliteye olan etkisini araştırdık.

Yöntemler: Bu geriye dönük çalışmada, ABH'nın STYME nedeniyle primer perkütan koroner girişim uygulanan ve KŞ gelişen 492 hastadaki uzun dönem prognoza etkisi değerlendirildi. Serum kreatininde 0.3 mg/dL veya fazla artış, serum kreatininde %50 veya fazla artış veya idrar çıkışında azalma (6 saatten uzun süredir idrar çıkışı 0.5 mL/kg'dan az olan dökümente oligüri) ABH olarak tanımlandı. Hastalar ABH görülmesine göre iki gruba ayrıldı ve bu gruplar arasında uzun dönem mortalite karşılaştırıldı. Cox regresyon analizi uzun dönem mortalitenin bağımsız prognostik faktörlerini belirlemek için kullanıldı.

Bulgular: Cox regresyon analizindeki yaş ve cinsiyet düzeltilmiş risk oranları (HR) ABH gelişen hastalarda tüm nedenli ölümler için anlamlı olarak yüksekti (HR 4.55; %95 güven aralığı [GA] 2.370–8.759). Karışıklığa neden olan faktörler düzeltildiğinde, ABH gelişen hastalar ABH gelişmeyen hastalar ile karşılaştırıldığında HR anlamlı olarak yüksekti. (HR 2.207; %95 GA 1.150–4.739) yaş (p<0.001, HR 1.060, %95 GA 1.027–1.094), ejeksiyon fraksiyonu (p=0.012, HR 0.952, %95 GA 0.916–0.989), BUN (p=0.010, HR 1.019, %95 GA 1.005–1.034) and ABH (p=0.031, HR 2.244, %95 GA 1.077–4.676) uzun dönem mortaliteyi belirleyen bağımsız faktörler olarak bulundu.

Sonuç: Çalışmamız ABH'nın, STYME nedeniyle PPKG uygulanan ve KŞ gelişen hastalarda uzun dönem mortalite için bağımsız prognostik faktör olduğunu göstermiştir.

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ST-segment elevation myocardial infarction (STEMI) remains a leading cause of death worldwide despite improvements in medical and invasive approaches to management. Patients admitted to emergency departments with STEMI categorized as Killip class III or IV are the group with the highest in-hospital morbidity and mortality. Killip class IV STEMI, cardiogenic shock (CS), is characterized by a fatal myocardial contractile deterioration causing failure to provide sufficient cardiac output despite an adequate pre-load. The incidence of CS in STEMI ranges from 4.9% to 7.9% in different observational cohorts.[1,2] The mortality rate of CS is considerably higher in patients with an unsuccessful invasive procedure or the presence of diabetes, chronic renal failure, or higher serum levels of lactate or glucose.[3,4]

Baseline renal dysfunction and acute kidney injury (AKI) are strong predictors of in-hospital and long-term adverse cardiovascular outcomes after STEMI.[5] In patients with STEMI, AKI is associated with contrast volume, hemodynamic impairment, inflammation, bleeding, and nephrotoxic agents.[6,7] A scoring system which evaluates 8 factors developed to predict the risk of contrast-induced AKI after percutaneous coronary intervention has been validated in patients with STEMI.[8] The impact of cardiac pump efficiency in the development of AKI is included in this score. AKI has been directly linked to cardiac pump function due to a strong association with hypotension, congestive heart failure, and intra-aortic pump (IABP) use. Even though AKI is an indicator of renal and cardiac reserve in patients with STEMI, there is a lack of evidence with regard to the effect of AKI on long-term mortality in patients with STEMI. The aim of this study was to assess the prognostic value of AKI for long-term mortality in patients with CS who underwent primary percutaneous coronary intervention (PPCI).

METHODS

Patient and study design

A total of 492 consecutive patients of all ages with acute STEMI complicated by CS who underwent PPCI between January 2013 and January 2017 were enrolled in this retrospective study. The patients were all admitted to the emergency department of a single tertiary heart center. The study inclusion criteria were (1) men or women over 18 years of age, (2) diagnosis of STEMI complicated by CS during emergency department admission, (3) transfer to the catheterization laboratory within 12 hours after symptom onset, and (4) absence of any other possible etiology causing hypotension, such as severe fluid depletion or sepsis. Patients who were on dialysis (n=3) and who underwent urgent coronary artery bypass graft (CABG) (n=28) after coronary angiography were excluded in order to provide standardization and to appropriately test the effect of AKI on long-term mortality.

Abbreviations:

AKI	*Acute kidney injury*
BUN	*Blood urea nitrogen*
CABG	*Coronary artery bypass graft*
CI	*Confidence interval*
CS	*Cardiogenic shock*
EF	*Ejection fraction*
HR	*Hazard ratio*
IABP	*Intra-aortic pump*
LVEF	*Left ventricular ejection fraction*
MI	*Myocardial infarction*
PAD	*Peripheral artery disease*
PPCI	*Primary percutaneous coronary intervention*
STEMI	*ST-segment elevation myocardial infarction*
TIMI	*Thrombolysis in Myocardial Infarction*

Baseline demographic characteristics and related clinical information were obtained from each patient at the time of admission. Transthoracic echocardiography was performed by an expert in cardiovascular imaging using a GE Vivid 7 system (GE Healthcare, Inc. Chicago, IL, USA). Left ventricular ejection fraction (LVEF) was calculated using the Simpson method.[9] The pulmonary artery peak systolic pressure was calculated using the simplified Bernoulli equation.[10] A standard 12-lead electrocardiogram (Cardiovit AT-10 Plus, filter 150 Hz, 25 mm/s, 10 mm/mV; Schiller AG, Baar, Switzerland) was recorded prior to PPCI.

Blood values obtained from venous blood samples taken at hospital admission were recorded. The white blood cell count and hemoglobin level were measured as part of the automated complete blood count using a Coulter LH 780 hematology analyzer (Beckman Coulter Inc., Brea, CA, USA). Biochemical measurements were performed using kits and calibrators from Siemens Healthcare Diagnostics Products (Marburg, Germany).

Angiography was performed using non-ionic iohexsol contrast dye (Omnipaque 300; GE Healthcare, Inc. Chicago, IL, USA). Adenosine diphosphate-receptor blockers were administered as a loading dose and the type of antiplatelet agent added to acetylsalicylic acid was left to the interventional cardiologist.

No single standard treatment was implemented to prevent contrast nephropathy. The duration and pressure of balloon inflation, the number of inflations, and the choice of specific interventional equipment, including the balloon and stent, were left to the discretion of the interventional cardiologist performing the procedure. Long-term mortality was determined by a trained study coordinator using data from the mortality notification system of the Ministry of Health.

The study population was divided in 2 according to the presence of AKI during the hospitalization period. SYNTAX I and II scores were calculated by 2 cardiologists blinded to the study population using the online version of the SYNTAX score calculator (www.syntaxscore.com).

This study was conducted in April 2018 with the permission of the scientific committee of Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital in accordance with the regulations in Turkey.

Definitions

In-hospital mortality was defined as death from any cause during hospitalization. Long-term mortality was defined as death from any cause after discharge. CS was defined as systolic blood pressure <90 mmHg not responsive to fluid resuscitation and/or heart rate correction for at least 1 hour or the need for vasopressor/inotropic therapy to maintain systolic blood pressure >90 mmHg for at least 1 hour and believed to be secondary to cardiac dysfunction and associated with at least 1 of the following: 1) signs of pulmonary edema, 2) signs of hypoperfusion (cool clammy skin, oliguria, or altered sensorium), or 3) cardiac index <2.2 L/minute. Hypertension was defined as systolic pressure >140 mmHg, diastolic pressure >90 mmHg, or previously diagnosed hypertension. Diabetes mellitus was defined as the use of insulin or anti-diabetic agents in the patient's medical history or a fasting glucose level >126 mg/dL. Hyperlipidemia was defined as serum total cholesterol ≥240 mg/dL, serum triglyceride ≥200 mg/dL, low-density lipoprotein cholesterol ≥130 mg/dL, or previously diagnosed hyperlipidemia. Mechanical complications included ventricular septal rupture, papillary muscle rupture, and free wall rupture. An absolute increase in serum creatinine of ≥0.3 mg/dL and a ≥50% increase in serum creatinine (1.5-fold from baseline, or a reduction in urine output of documented oliguria <0.5 mL/kg per hour for more than 6 hours) was defined as AKI.[11] LVEF was measured using transthoracic echocardiography. Chronic obstructive pulmonary disease was defined according to the European System for Cardiac Operative Risk Evaluation definition of the use of long-term bronchodilators or steroids for lung disease.[12] The definition of peripheral artery disease (PAD) used was that of the Arterial Revascularization Therapies Study Part I.[13]

Follow-up

The primary endpoint of the study was the incidence of long-term mortality. In-hospital mortality was also noted.

Statistical analysis

Data analysis was performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to test the distribution pattern. The data were presented as mean±SD for those with a normal distribution and median (interquartile range) for non-normally distributed continuous variables. The number of cases and percentages were used for categorical data. The Mann-Whitney U test was applied for comparisons of data that were not normally distributed. Categorical data were analyzed using Fisher's exact test when 1 or more cells had an expected frequency of 5 or less. Otherwise, Pearson's chi-square test was applied. The mean survival time of the 2 groups was compared using the Kaplan-Meier survival method. Differences between the groups were analyzed with the log-rank test. A Cox proportional regression model was used for multivariable analysis. The hazard ratio (HR) indicated the relative risk of death in the AKI(+) group compared with the AKI(-) group. Confounders in the multivariate analysis of predictors of long-term mortality were considered in the multivariable models. Two multivariable models were used: The variables used as covariates in model I were age and sex, and the variables in model II were age, sex, smoking status, hypertension, diabetes mellitus, previous myocardial infarction (MI), previous CABG, PPCI, chronic renal failure, PAD, anterior MI, Thrombolysis in Myocardial Infarction (TIMI) 3 flow after intervention, ejection fraction (EF), and admission levels of creatinine and blood urea nitrogen (BUN). Univariate Cox regression analysis was used to quantify the association of a variable with long-term mortality. Variables found to be statistically significant

(p<0.25) in univariate analysis were used in a multivariate Cox regression analysis using the enter method in order to determine the independent prognostic factors of long-term mortality in patients with STEMI complicated by CS who underwent PPCI. A p value <0.05 was considered statistically significant.

RESULTS

A total of 492 (mean age 68.7±12.5 years; 62.3% male) patients with STEMI complicated by CS were evaluated in this study. The patients were analyzed according to the incidence of AKI during hospitalization and were grouped as (+) or (-) for AKI (Table 1). The patients in the AKI(+) group were older, and there was a greater prevalence of diabetes, chronic renal failure, and anterior MI than in the AKI(-) group (p=0.035, p<0.001; p=0.002, p<0.001 respectively) The AKI(-) group demonstrated a greater frequency of TIMI 3 flow in the culprit artery after intervention (p=0.008). The left anterior descending artery was the culprit artery significantly more often in the AKI(+) group (p<0.001). IABP use was greater in the AKI(+) group (p=0.041). In-hospital and long-term mortality were statistically greater in the AKI(+) group (p<0.001 and p<0.001, respectively).

Table 2 presents the comparison of the medical treatment, echocardiographic, and laboratory findings of the study population according to the incidence of AKI. Adrenaline-infusion treatment was used more frequently in the AKI(+) group (p<0.001). The SYNTAX I and II scores were significantly greater among the patients with AKI (p=0.007 and p<0.001, respectively) The EF was statistically lower in patients without AKI (p<0.001). Admission levels of serum leukocytes, BUN, creatinine, aspartate aminotransferase, and lactate were higher in the AKI(+) group (p=0.028, p=0.017, p<0.001, p=0.002, and p<0.001, respectively).

Figure 1 illustrates the finding that the 5-year Kaplan-Meier overall survival rate for patients with and without AKI was 70.3% and 91.9%, respectively. The mean length of survival for the patients in the AKI(+) group was 47.3±2.29 months [95% confidence interval (CI): 42.8-51.8] and 57.6±1.17 months (95% CI: 55.3–59.9) for patients in the AKI(-) group. The patients were followed up for a mean period of 35 months (range:1-63 months). Patients without AKI had a significantly higher survival rate in comparison with patients who did have AKI (log-rank test: 19.85; p≤0.001). Cox regression analysis revealed that the age- and sex-adjusted HR was significantly greater for all-cause mortality in patients with AKI (HR: 4.556, 95% CI: 2.370–8.759). After adjustment for a number of confounding variables, the relative risk was attenuated, but remained statistically significantly elevated for patients with AKI in comparison with patients without AKI (HR: 2.207, 95% CI: 1.150–4.739) (Table 3). Age; the presence of diabetes mellitus, chronic renal failure, or PAD; smoking; TIMI 3 flow after intervention; EF; level of hemoglobin, creatinine, BUN; and the presence of AKI were found to have prognostic significance in univariate Cox regression analysis (Table 4). In multivariate Cox regression analysis using the enter method, age (HR: 1.060, 95% CI: 1.027–1.094; p<0.001), EF (HR: 0.952, 95% CI: 0.916–0.989; p=0.012), BUN level (HR: 1.019, 95% CI: 1.005–1.034; p=0.010), and AKI (HR: 2.244, 95% CI: 1.077–4.676; p=0.031) were found to be independent factors to determine long-term mortality (Table 4).

DISCUSSION

Research considering an association between AKI and STEMI and CS is limited. Our long-term follow-up study evaluating AKI in patients with STEMI complicated by CS revealed AKI to be an independent prognostic factor for long-term mortality. Age, EF, BUN level, and AKI were all demonstrated to be independent factors impacting long-term mortality. The severity of AKI originates from the underlying pathophysiology and the effect on several neurohormonal systems.

The incidence of AKI in patients with STEMI complicated by CS has been reported to be 33% and 55% of patients in limited cohort studies.[14,15] We included a larger number of patients with CS and the AKI incidence was 49.7%. AKI tended to appear in patients with the most severe hemodynamic deterioration among those with CS and was related to higher rates of in-hospital mortality and morbidity. Among patients with AKI, those who required renal replacement therapy had poorer outcomes when compared with the group who did not.[14,16] Thus, recommendations for contrast-induced nephropathy should be considered carefully to prevent AKI, especially in patients with CS. Adequate hydration, using low-osmolar or iso-osmolar contrast media, minimizing con-

Table 1. Comparison of demographic and clinical characteristics of patients according to the presence of acute kidney injury

	AKI(-) (n= 247)	AKI(+) (n=245)	*p*
Age (years)	67.6 (57.0–79.0)	69.9 (60.0–80.0)	0.035
Female/male gender, n (%)	98 (39.7) / 149 (60.3)	87 (35.5) / 158 (64.5)	0.340
Hypertension, n (%)	115 (46.6)	119 (48.6)	0.655
Diabetes mellitus, n (%)	67 (27.1)	98 (40.0)	0.002
Smoking, n (%)	84 (34.0)	89 (36.3)	0.590
Hyperlipidemia, n (%)	57 (23.1)	59 (24.1)	0.793
Previous myocardial infarction, n (%)	41 (16.6)	44 (18.0)	0,690
Previous cerebrovascular accident, n (%)	9 (3.6)	11 (4.5)	0.805
Previous coronary artery bypass graft, n (%)	24 (9.7)	19 (7.8)	0.541
Previous percutaneous coronary intervention, n (%)	61 (24.7)	52 (21.2)	0.360
Congestive heart failure, n (%)	40 (16.2)	43 (17.6)	0.688
Chronic obstructive pulmonary disease, n (%)	15 (6.1)	16 (6.5)	0.981
Chronic renal failure, n (%)	25 (10.1)	60 (24.5)	<0.001
Peripheral arterial disease, n (%)	15 (6.1)	15 (6.1)	1.000
Anterior myocardial infarction, n (%)	134 (54.3)	173 (70.6)	<0.001
Atrial fibrillation, n (%)	22 (8.9)	18 (7.3)	0.640
Admission values			
Systolic blood pressure, mmHg	69.7 (60.0–80.0)	70.5 (60.0–80.0)	0.285
Heart rate, beats per minute	118.7 (104.0–134.0)	120.3 (106.0–136.0)	0.325
TIMI flow in culprit artery before intervention, n (%)			
TIMI 0	239 (96.8)	236 (96.3)	0.986
TIMI 1	8 (3.2)	9 (3.7)	0.986
TIMI flow in culprit artery after intervention, n (%)			
TIMI ≤2	74 (34.0)	112 (45.7)	0.008
TIMI 3	163 (66.0)	133 (54.3)	0.008
Culprit artery, n (%)			
Left main coronary artery	9 (3.6)	14 (5.7)	0.382
Left anterior descending artery	125 (50.6)	159 (64.9)	<0.001
Circumflex artery	39 (15.8)	19 (7.8)	0.006
Right coronary artery	83 (33.6)	67 (23.7)	0.132
Additional ≥70% stenosis to culprit artery, n (%)			
Left anterior descending artery and/or branches	116 (47.0)	82 (32.7)	0.002
Circumflex artery and/or branches	115 (46.6)	132 (53.9)	0.105
Right coronary artery and/or branches	85 (34.4)	91 (37.1)	0.528
Intervened coronary artery, n (%)			
Left main coronary artery	7 (2.8)	12 (4.9)	0.340
Left anterior descending artery	106 (42.9)	120 (49.0)	0.177
Circumflex artery	29 (11.7)	12 (4.9)	0.010
Right coronary artery	69 (27.9)	50 (20.4)	0.051
Multivessel	36 (14.6)	51 (20.6)	0.070
Thrombus aspiration, n (%)	14 (5.7)	17 (6.9)	0.693
Tirofiban infusion, n (%)	108 (43.7)	120 (49.0)	0.243
Intra-aortic pump usage, n (%)	61 (24.7)	81 (33.1)	0.041
Percutaneous transluminal coronary angioplasty, n (%)	182 (73.7)	184 (75.1)	0.719
Stent (drug-eluting stent), n (%)	212 (85.8)	207 (84.5)	0.676
Stent number >1, n (%)	74 (30.0)	76 (31.0)	0.798
Non-compliant balloon usage, n (%)	94 (38.1)	104 (42.4)	0.321
In-hospital mortality, n (%)	87 (35.2)	134 (54.7)	<0.001
5-year mortality, n (%)	13 (5.3)	33 (13.5)	<0.001

Continuous variables are presented as median (interquartile range). Nominal variables are presented as frequency (%). AKI: Acute kidney injury; TIMI: Thrombolysis in Myocardial Infarction.

Table 2. Comparison of clinical, echocardiographic and laboratory characteristics of patients according to acute kidney injury

	AKI(-) (n=247)	AKI(+) (n=245)	*p*
Inotropic agents, n (%)			
Dobutamine infusion	89 (36.0)	97 (39.6)	0.416
Dopamine infusion	214 (86.6)	199 (81.2)	0.102
Noradrenaline infusion	164 (66.4)	164 (66.9)	0.889
Adrenaline infusion	84 (34.0)	120 (49.0)	<0.001
Antiplatelet agent, n (%)			
Clopidogrel	35 (14.2)	35 (14.3)	0.971
Ticagrelor	152 (61.5)	158 (64.5)	0.498
Prasugrel	60 (24.3)	52 (21.2)	0.417
Mechanical complications, n (%)	10 (4.0)	20 (8.2)	0.086
SYNTAX score	21.8 (19.5–25.5)	23.0 (20.5–27.0)	0.007
SYNTAX II score Percutaneous coronary intervention	44.5 (37.6–51.1)	47.6 (42.3–54.3)	<0.001
Left ventricle ejection fraction	33.8 (30.0–40.0)	30.4 (25.0–35.0)	<0.001
Left ventricular end-diastolic diameter	5.39 (5.00–5.75)	5.43 (5.00–5.80)	0.396
Left ventricle end-systolic diameter	4.16 (3.80–4.60)	4.30 (3.90–4.70)	0.008
Pulmonary arterial systolic pressure, mmHg	27.0 (20.0–32.0)	27.6 (25.0–33.0)	0.189
Tricuspid Annular Plane Systolic Excursion score	1.78 (1.60–1.90)	1.78 (1.60–1.90)	0.810
Mitral regurgitation ≥+3	38 (15.4)	42 (17.1)	0.597
Tricuspid regurgitation ≥+3	13 (5.3)	17 (6.9)	0.556
Hemoglobin (g/dL)	12.6 (11.1–14.0)	12.8 (11.4–14.2)	0.090
Leukocyte (x10^3/μ/L)	15.2 (10.8–18.8)	16.2 (12.3–19.8)	0.028
Platelet (x10^3/μ/L)	257.2 (188.0–322.0)	250.3 (192.0–291.0)	0.583
Glucose (mg/dL)	127.8 (100.0–144.0)	131.9 (92.0–149.0)	0.832
Creatinine (mg/dL)	1.13 (0.91–1.17)	1.23 (0.93–1.35)	<0.001
Blood urea nitrogen (mg/dL)	28.8 (20.0–33.0)	34.3 (22.0–44.0)	0.017
Alanine aminotransferase	74.6 (24.0–74.0)	77.6 (27.0–81.0)	0.345
Aspartate transaminase	191.5 (48.0–230.0)	227.5 (69.0–256.0)	0.002
Lactate dehydrogenase	482.9 (245.0–544.0)	476.4 (286.0–550.0)	0.172
Lactate (mmol/L)	4.30 (2.30–5.20)	5.16 (2.60–6.50)	0.001
pH 7.32	(7.28–7.38)	7.30 (7.22–7.38)	0.048
pCO_2	34.7 (30.4–37.4)	34.4 (30.0–37.4)	0.452
pO_2	92.3 (72.9–91.2)	94.9 (68.9–101.0)	0.978

Continuous variables are presented as median (interquartile range). Nominal variables are presented as frequency (%). AKI: Acute kidney injury.

trast media volume, and pre-treatment with high-dose statins are the main recommendations to decrease the incidence of contrast-induced nephropathy.[17–19] However, it is very difficult to implement the recommendations to prevent AKI in fragile patients, such as patients compromised by CS. The very limited data associated with the long-term mortality of patients with AKI and the lack of related evidence motivated us to present the current study.

Rapid worsening of cardiac functions leading to AKI is defined as cardio-renal syndrome type I.[16] Underlying mechanisms of cardio-renal syndrome type I include abruptly depressed cardiac output, neurohormonal activation, and effects of vasopressor substances.[20] As expected, the frequency of anterior MI, chronic renal failure, and diabetes mellitus

Table 3. Hazard ratio and 95% confidence interval for long-term mortality according to acute kidney injury during hospitalization

	AKI during hospitalization (n=492; n=245 events) HR (95% CI)
Crude	3.880 (2.039–7.385)
Model 1[a]	4.556 (2.370–8.759)
Model 2[b]	2.207 (1.150–4.739)

AKI: Acute kidney injury; CI: Confidence interval; HR: Hazard ratio. [a]Model 1: Adjusted for age and sex. [b]Model 2: Adjusted for age, sex, smoking status, hypertension, diabetes mellitus, previous myocardial infarction, previous coronary artery bypass graft, previous percutaneous coronary intervention, chronic renal failure, peripheral artery disease, anterior myocardial infarction, Thrombolysis in Myocardial İnfarction 3 flow after intervention, ejection fraction, admission levels of creatinine and blood urea nitrogen.

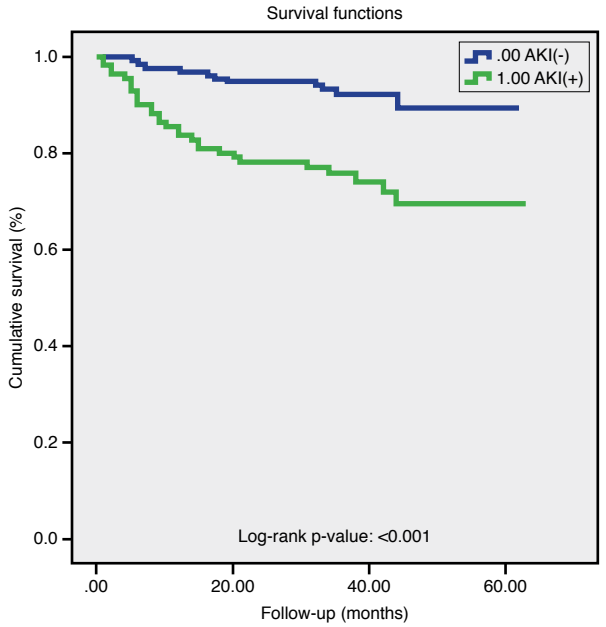

Figure 1. The 5-year Kaplan-Meier overall survival rate for patients with and without acute kidney injury (AKI).

were higher in the AKI group. In addition, the EF and lactate level were lower in the AKI group. All of the data supported the importance of recognizing cardiac output and renal reserve as associated with the occurrence of AKI. Though one of the primary underlying reasons for the development of AKI in patients who undergo PPCI is contrast nephropathy, it is rational to infer that the quantity of contrast dye used in the intervention is not the only reason and that multiple interrelated mechanisms may be responsible. While it is not possible to indicate the precise underlying reasons for the higher rate of long-term mortality in the AKI group, some of the aforementioned parameters, such as age, greater frequency of diabetes and chronic renal failure, and lower EF may have a role in the higher long-term mortality in the AKI group. It is also a significant challenge to adjust medical therapy doses in patients with congestive heart failure.[21] The congestive heart failure medication choice and dosage may also be a cause of the difference in long-

Table 4. Univariable and multivariable analyses of long-term mortality and baseline, clinical, angiographic and laboratory data

	Univariate analysis			Multivariate analysis		
	p	HR	95% CI	*p*	HR	95% CI
Age (years)	<0.001	1.069	1.042–1.098	<0.001	1.060	1.027–1.094
Diabetes mellitus	<0.001	2.824	1.582–5.044	0.272	1.473	0.738–2.943
Smoking	0.222	0.676	0.360–1.268	0.566	0.815	0.406–1.637
Chronic renal failure	<0.001	3.868	2.122–7.052	0.904	0.942	0.355–2.498
Peripheral artery disease	0.080	2.294	0.904–5.822	0.387	1.571	0.564–4.375
TIMI 3 flow after intervention	<0.001	0.276	0.153–0.499	0.343	0.715	0.358–1.430
Ejection fraction	<0.001	0.904	0.871–0.937	0.012	0.952	0.916–0.989
Hemoglobin	0.011	0.818	0.701–0.956	0.306	0.905	0.748–1.096
Creatinine	<0.001	2.311	1.689–3.161	0.080	1.789	0.932–3.434
Blood urea nitrogen	<0.001	1.041	1.029–1.053	0.010	1.019	1.005–1.034
Acute kidney injury	<0.001	3.880	2.039–7.385	0.031	2.244	1.077–4.676

CI: Confidence interval; HR: Hazard ratio; TIMI: Thrombolysis in Myocardial Infarction.

term mortality rates seen between groups. As a result of analyzing multiple factors, AKI was revealed to be an independent long-term prognostic indicator in patients with STEMI complicated by CS.

Study limitations

The current study has several limitations. The retrospective and single-center nature of the research is an important limitation; however, it was conducted in a high volume, interventional center for PPCI and all consecutive patients who met the criteria were included, thus limiting selection bias. Second, there was a lack of data regarding the amount of contrast dye used in the procedures. Third, we were not able to contact all of the patients in order to determine long-term major adverse cardiac events; therefore, long-term mortality was confirmed using Ministry of Health data.

Conclusion

Our study indicated that AKI was an independent prognostic factor for long-term mortality of patients with STEMI complicated by CS and treated with primary PCI. This result confirmed that AKI has a predictive value not only for in-hospital outcomes, but also for long-term outcomes of patients with STEMI.

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