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**ORIGINAL ARTICLE**

# Factors Related to Middle-Long-Term Mortality in Acute Kidney Injury

# Akut Böbrek Hasarında Orta-Uzun Dönem Mortaliteyle İlişkili Faktörler

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**ABSTRACT**

**Aim:** To determine the clinical and laboratory parameters that affect the mid-long term mortality of patients hospitalized for acute kidney injury (AKI).
**Material and methods:** Patients hospitalized with the diagnosis of AKI in the intensive care unit and clinic of Nephrology for four years were retrospectively screened. The files of these patients were scanned. Demographic data, comorbidities, vital signs and laboratory parameters were scanned. It was determined in terms of factors affecting mortality in these patients (living and dying) over a 4-year period.
**Results:** The effects of the variables found significant [age, presence of hypertension and coronary artery disease (CAD), sedimentation, C-reactive protein (CRP), urea, potassium (K), magnesium (Mg), pH and CRP-albumin ratio (CAR)] on mortality was performed using multiple logistic regression analysis, which was used to identify the independent risk factors of mortality. Multiple logistic regression analysis using Stepwise selection method revealed that increasing age (IQR=1.04, 95% CI=1.01 – 1.07, p=.004), presence of CAD (IQR =2.16, 95% CI=1.16 – 4.02, p=.016), increased Mg (IQR =2.64, 95% CI=1.18 – 5.92, p=.018) and K (IQR =1.70, 95% CI=1.21 – 2.41, p=.002) were independent risk factors for mortality. The accuracy rate for the predictive performance of this prediction model in predicting mortality was 71.1%, with a sensitivity of 26.5%, a specificity of 90%, and an AUC of 0.753.
**Conclusion:** In our predictive model, in the medium-long term, we found old age, the presence of coronary artery disease, increased K and Mg as the independent risk factors for mortality in AKI patients.

**Keywords:** Acute kidney injury, Age, Comorbidity, Mortality

**ÖZ**

**Amaç:** Akut böbrek hasarı (ABH) nedeniyle hastaneye yatırılan hastaların orta-uzun dönem mortalitesini etkileyen klinik ve laboratuvar parametrelerini belirlemek.
**Gereç ve yöntem:** ABH tanısıyla yoğun bakım ünitesinde ve Nefroloji kliniğinde dört yıl boyunca yatan hastaların dosyaları geriye dönük olarak tarandı. Demografik veriler, komorbiditeler, vital ve laboratuvar parametreleri incelendi. Bu hastalarda 4 yıllık süreçte mortaliteyi etkileyen faktörler açısından belirlendi.
**Bulgular:** Tek değişkenli analiz ile anlamlı bulunan değişkenlerin (yaş, hipertansiyon ve koroner arter hastalığı (KAH) varlığı, sedimantasyon, C-reaktif protein (CRP), üre, potasyum (K), magnezyum (Mg), pH ve CRP-albümin oranı (CAR)) mortalite üzerine etkileri , mortalitenin bağımsız risk faktörlerini belirlemek için kullanılan çoklu lojistik regresyon analizi kullanılarak yapıldı. Multipl lojistik regresyon analizi sonucu artan yaş (IQR=1.04, %95 CI=1,01 – 1,07, p=0,004), KAH varlığı (IQR =2,16, 95% CI=1,16 – 4,02, p=0,016), artmış Mg (IQR =2,64, %95 CI=1,18 – 5,92, p) =0,018) ve K (IQR =1,70, 95% GA=1,21 – 2,41, p=0,002) mortalite için bağımsız risk faktörleri olarak saptandı. Bu tahmin modelinin mortaliteyi öngörmedeki prediktif değeri %71,1, sensitivitesi %26,5, sensitivitesi %90 ve AUC 0,753 idi.
**Sonuç:** Orta-uzun vadede ABH hastalarında ileri yaş, koroner arter hastalığı varlığı, K ve Mg artışını mortaliteyi etkileyen faktörler olarak bulduk.

**Anahtar kelimeler:** Akut böbrek hasarı, Yaş, Komorbidite, Mortalite

## Introduction

The incidence of AKI, regardless of requiring dialysis, is increasing in the World.1 Aging of the population, high comorbidities, increased AKI awareness, increased nephrotoxic drugs and increased surgical procedures are the factors that increase the incidence.2

AKI is related to short- and long-term undesirable consequences. While it increases short-term mortality, the long-term mortality is significantly higher in those with AKI compared to those who do not have.3 Long-term mortality is generally considered as mortality after 3 months. In a review evaluating the long-term mortality of AKI patients, the mortality rate was found as 15-74%, but only around 60% when intensive care patients were included. Factors affecting mortality were determined as old age, presence of comorbidity and incomplete recovery of kidney functions.4 The fact that AKI affects not only the kidneys but also other vital organs such as the heart and lungs may be associated with a long-term increase in mortality.

In this study, we aimed to determine the factors that are effective in long-term mortality by retrospectively screening the patients hospitalized in our clinic and intensive care unit with the diagnosis of AKI between 2018-2022.

## Material and Methods

After the approval of local ethics committee (2023/87), the study was started. Between January 2018 and

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December 2022, the files of the patients hospitalized in our Nephrology clinic and intensive care clinic with the AKI diagnostic code (N17 and its subfractions) were scanned. Patients that did not meet the diagnosis of AKI according to KDIGO 2012 criteria were excluded from the study. Demographic data, comorbidities (diabetes mellitus-DM, hypertension-HT, coronary artery disease-CAD, congestive heart failure-CHF, chronic obstructive pulmonary disease-COPD, chronic kidney disease-CKD, atrial fibrillation-AF), vital signs at admission, length of hospital stay, laboratory parameters at the time of hospitalization (hemogram, biochemistry, hemoglobin A1C, venous blood gas, C reactive protein, procalcitonine, sedimentation, ferritin, vitamin D level, whether there was reproduction in blood, urine, sputum or swab cultures) of the patients were recorded from their files. For the patients who died, the duration until death was recorded. Patients who died due to cancer or Covid 19 were excluded from the study.

**Statistical analysis**

All statistical analysis were performed with R version 4.1.2 (The R Foundation for Statistical Computing, Veinna, Austria; https://www.r-project.org) Statistical Language. Shapiro-Wilk ln normality test and Q-Q plots were used to check the normality of the data. Levene test was also used to assess the homogeneity of the variances. Numerical variables were expressed as mean ± standard deviation, median with range (min – max) or median with interquartile [25th percentile – 75th percentile], as appropriate. Categorical variables were also defined as numbers (n) and percentage (%). A Welch's t-test, Mann-Whitney U test and Independent samples t-test was utilized to determine whether there was a statistically significant difference in numerical variables according to the demographical and clinical characteristics of patients with and without survivors. Besides, a Pearson chi-square test, chi-square test Yates continuity correction and Fisher's exact test was conducted to examine if there was a significantly association between patient's groups with and without survivors in terms of categorical variables in demographical and clinical characteristics. The effects of the variables found significant (age, presence of hypertension and CAD, sedimentation, CRP, urea, K, Mg , pH and CAR) by univariate analysis on mortality was performed using multiple logistic regression analysis, which was used to identify the independent risk factors of mortality. Odds ratios were represented with 95% confidence intervals. For the diagnostic performance of the prediction model obtained by multiple logistic regression analysis in predicting of mortality, the area under the curve, accuracy, sensitivity and specificity values of this model were calculated. A two-tailed p-value less than .05 was considered as statistically significant.

**Results**

The mean age (75.81 ± 10.08 vs. 68.28 ± 15.63, p<.001), length of hospitalization (10 days vs. 7 days, p=.003), presence of hypertension (79.4% vs. 64.4%, p=.037) and CAD (60.3% vs. 37.5%, p=.002), sedimentation level (40 vs. 29.5, p=.028), urea (136vs. 122, p=.003), K (5.24 ± 0.91 vs. 4.66 ± 0.93, p<.001) and Mg (2.18 ± 0.35 vs. 2.04 ± 0.41, p=.020) values were significantly higher in patients who were non-survivors compared to the patients who were survivors, whereas follow-up time (12 days vs. 34 days, p<.001), saturation at admission (94 vs. 96, p=.012), CRP (26.1 vs. 63.5, p=.020) and pH (7.31 ± 0.09 vs. 7.33 ± 0.08, p=.048) levels and CAR (7.95 vs. 19.76, p=.031) values were lower.

The effects of the variables found significant (age, presence of hypertension and CAD, sedimentation, CRP, urea, K, Mg, pH and CAR) by univariate analysis on mortality was performed using multiple logistic regression analysis, which was used to identify the independent risk factors of mortality. Stepwise variable selection method was used to eliminate the variables that was not statistically significant. Multiple logistic regression analysis using stepwise selection method revealed that increasing age (p=.004), presence of CAD (p=.016), increased Mg (p=.018) and K (p=.002) were independent risk factors for mortality (Table 2). The accuracy rate for the predictive performance of this prediction model in predicting mortality was 71.1%, with a sensitivity of 26.5%, a specificity of 90%, and an AUC of 0.753 (Figure 1).

**Discussion**

AKI affects 13.3 million people worldwide each year, causing 1.7 million deaths.5 In a meta-analysis covering a large number of studies, the incidence was found as 22% and in a study including 33 countries, it was found as 57%. 6, 7 AKI is a factor that increases short-term (within 90 days) and long-term (after 90 days) mortality in hospital or after discharge from the hospital. In-hospital mortality reaches 40-60% in patients who develop AKI requiring dialysis in the intensive care unit. 8 In a study involving more than 5 million patients, short-term mortality was examined in those with and without AKI. Mortality was 3 times higher in patients with AKI compared to those without AKI. 9 The underlying comorbidities and infection were effective factors in short-term mortality.

Long-term mortality also increases after AKI. In a study involving over 800 patients who underwent cardiac surgery and those who did not undergo AKI after surgery were compared. Mortality was 1.6 times higher in those who had AKI compared to those who did not have.10 In a meta-analysis of 47.017 people, the relative risk of mortality was 2.5 times higher in those who had AKI.3

In this study, the mean follow-up period after discharge was 27.4 ± 16 months, and the mortality rate was 29.7%. Stevens et al. found 2-year mortality as 69% and 3-year mortality as 72% in patients with AKI associated with sepsis. However, in their study, patients were not followed up by a nephrologist.11 Mortality may be significantly higher in our study, both for this reason and because they included only patients with sepsis. In another study, mortality rates were found similar to the study of Stevens et al.12 In this study, only patients

**Table 1.** Demographical and clinical characteristics of the patients.

| | Survivors (n=160) | Non-survivors (n=68) | p-value |
|---|---|---|---|
| Demographical characteristics | | | |
| Age (years), mean ± SD | 68.28 ± 15.63 | 75.81 ± 10.08 | <.001[1] |
| Gender (F/M), n (%) | 83 (51.9) / 77 (48.1) | 39 (57.4) / 29 (42.6) | .448[2] |
| Follow-up time, median (month) (range) | 34 (1 – 57) | 12 (1 – 58) | <.001[3] |
| Length of stay at hospital, median (range) (day) | 7 (2 – 35) | 10 (2 – 45) | .003[3] |
| Pneumonia, n (%) | 23 (14.4) | 15 (22.1) | .219[4] |
| Cough, n (%) | 10 (6.3) | 7 (10.4) | .412[4] |
| Sputum, n (%) | 9 (5.6) | 4 (5.9) | >.999[5] |
| Fever, n (%) | 19 (11.9) | 7 (10.3) | .908[4] |
| Shortness of breath, n (%) | 40 (25) | 24 (35.3) | .155[4] |
| Comorbidity, n (%) | | | |
| Diabetes mellitus | 57 (35.6) | 30 (44.1) | .227[2] |
| Hypertension | 103 (64.4) | 54 (79.4) | .037[4] |
| CAD | 60 (37.5) | 41 (60.3) | .002[2] |
| COPD | 31 (19.4) | 20 (29.4) | .136[4] |
| AF | 20 (13) | 15 (22.7) | .108[4] |
| CKD | 46 (28.7) | 24 (35.3) | .410[4] |
| Saturation at admission, median (range) | 96 (65 – 99) | 94 (60 – 99) | .012[3] |
| SBP at admission, mean ± SD | 115.41 ± 21.39 | 116.97 ± 21.97 | .630[6] |
| DBP at admission, mean ± SD | 69.93 ± 12.89 | 70.15 ± 12.05 | .906[6] |
| MAP at admission, mean ± SD | 85.08 ± 14.93 | 85.76 ± 14.54 | .760[6] |
| Pulse rate at admission, mean ± SD | 87.58 ± 15.62 | 87.42 ± 18.92 | .948[6] |
| Fever at admission, mean ± SD | 36.75 ± 0.59 | 36.73 ± 0.61 | .763[6] |
| Laboratory parameters | | | |
| WBC(K/uL), mean ± SD | 11.32 ± 5.20 | 10.95 ± 4.49 | .612[6] |
| Lymphocyte(K/uL), median [IQR] | 1.10 [0.74 – 1.61] | 1.20 [0.80 – 1.70] | .493[3] |
| Neutrophile(K/uL), median [IQR] | 7.55 [5.58 – 11.41] | 7.60 [5.33 – 10.74] | .545[3] |
| Monocyte(K/uL), mean ± SD | 0.78 ± 0.39 | 0.77 ± 0.37 | .844[6] |
| Eosinophile(K/uL), median [IQR] | 0.06 [0.01 – 0.18] | 0.07 [0.01 – 0.10] | .723[3] |
| Hemoglobin (g/dL), mean ± SD | 12.07 ± 2.06 | 11.87 ± 2.17 | .498[6] |
| Hemotocrit (%), mean ± SD | 36.53 ± 6.27 | 36.89 ± 6.43 | .698[6] |
| Platelet(K/uL), median [IQR] | 239 [174.25 – 280] | 261 [200.25 – 324] | .062[3] |
| Sedimentation(mm/h), median [IQR] | 29.5 [11 – 48.5] | 40 [24 – 61] | .028[3] |
| CRP(mg/L), median [IQR] | 63.5 [11.53 – 171.25] | 26.1 [6.73 – 108.5] | .020[3] |
| Procalcitonin(µ/L), median [IQR] | 0.41 [0.16 – 3.70] | 0.42 [0.19 – 1.30] | .555[3] |
| Glucose (mg/dL), median [IQR] | 120 [97 – 179.25] | 132 [101 – 174.5] | .455[3] |
| HgA1c, median [IQR] | 7.10 [5.60 – 8.47] | 7.25 [7.20 – 7.82] | .504[3] |
| Urea(mg/dL), median [IQR] | 122 [86.75 – 161.25] | 136 [107 – 207] | .003[3] |
| Creatine(mg/dL), median [IQR] | 3.16 [2.17 – 4.74] | 2.79 [2.03 – 4.15] | .172[3] |
| Na(mEq/L)(mmol/L), mean ± SD | 135.29 ± 7.84 | 133.76 ± 5.98 | .153[6] |
| K(mg/dL), mean ± SD | 4.66 ± 0.93 | 5.24 ± 0.91 | <.001[6] |
| Ca(mg/dL), mean ± SD | 8.46 ± 0.96 | 8.60 ± 0.81 | .293[6] |
| P(mg/dL), median [IQR] | 4.1 [3.3 – 5.2] | 4.5 [3.2 – 5.4] | .624[3] |
| Mg(mg/dL), mean ± SD | 2.04 ± 0.41 | 2.18 ± 0.35 | .020[6] |
| Uric acid(mg/dL), median [IQR] | 8.6 [6.9 – 10.1] | 8.7 [6.2 – 10.35] | .626[3] |
| Albumin(g/dL), mean ± SD | 3.29 ± 0.59 | 3.19 ± 0.61 | .245[6] |
| PH, mean ± SD | 7.33 ± 0.08 | 7.31 ± 0.09 | .048[6] |
| HCO3, mean ± SD | 19.00 ± 4.76 | 18.72 ± 6.06 | .710[6] |
| PCO2, mean ± SD | 36.13 ± 7.52 | 37.71 ± 10.53 | .262[1] |
| Ferritin(ng/mL), median [IQR] | 178.85 [86.45 – 334.18] | 109.35 [75.4 – 291.58] | .130[3] |
| Vitamin D(ng/mL), median [IQR] | 7.92 [4.02 – 15.30] | 10.27 [6.41 – 22.30] | .148[3] |
| CAR, median [IQR] | 19.76 [2.90 – 57.38] | 7.95 [1.81 – 36.99] | .031[3] |
| Culture, n (%) | 48 (43.2) | 32 (59.3) | .053[2] |

1Welch's t-test; 2Pearson chi-square test; 3Mann-Whitney U test; 4Chi-square test with Yates continuity correction; 5Fisher's exact test;6 Independent samples t-test. *CAR; CRP-albumin ratio.*

hospitalized in the intensive care unit were included in the study. In our study, both clinical and intensive care patients were included.

**Table 2.** Multiple logistic regression analysis for predicting of mortality

| | Adjusted Odds Ratio | 95% confidence intervals | p-value |
|---|---|---|---|
| Age (years) | 1.04 | 1.01 – 1.07 | .004 |
| CAD (presence vs. absence) | 2.16 | 1.16 – 4.02 | .016 |
| Mg | 2.64 | 1.18 – 5.92 | .018 |
| K | 1.70 | 1.21 – 2.41 | .002 |

In our study, as a result of multiple logistic regression analysis, old age remained a significant factor in mortality (OR=1.04, 95% CI=1.01 – 1.07, p=.004). Old age is a factor that increases the mortality of many diseases. In the study of Gursu et al., in which they included only patients who developed AKI in the intensive care unit and were followed up for 6 months, old age was found as an independent risk factor.13 Again, Zhou et al. found old age as a factor affecting mortality at the end of 1 year in their study in which they followed up intensive care AKI patients. 14

Coronary artery disease is the most important cause of mortality in CKD patients.15 Xi et al. showed that the presence of concomitant significant coronary artery disease in AKI patients undergoing cardiac valve surgery is a factor that increased mortality.16 In our study, the presence of CAD was a risk factor for long-term mortality in AKI patients.

Hyperkalemia is a common problem in AKI, and is one of the indications for dialysis if it is resistant to medical treatment. In a study involving AKI patients over 75 years of age in China, the 1-year mortality rate was found significantly higher in patients with hyperkalemia. Since there are many comorbidities in elderly patients, and fragility is common and tubular damage is permanent after AKI, it is considered that it may also affect long-term mortality.17 In this study, we found that hyperkalemia was an independent risk factor for mortality at longer follow-up. The fact that the mean age in our died patients' group was 75 years may suggest that the possible causes expressed in the aforementioned study may also be effective in our patient group. In a study conducted in Mexico, hyperpotassemia was significantly associated with short-term mortality in AKI patients.18

Mg is an important molecule involved in more than 300 intracellular reactions. Low or high Mg levels have been shown to be associated with undesirable results and mortality in many different patient populations.19 In a study examining more than 22 thousand intensive care patients, hypermagnesemia was found as a factor increasing mortality.20 Again, both hypomagnesemia and hypermagnesemia were associated with mortality in a large cohort of intensive care patients.21 In the present study, we found that the mean Mg level was higher in patients who died compared to those who survived. In the case of high Mg, problems such as decrease in blood pressure and pulse, respiratory failure and arrhythmias are common. Perhaps, one of these effects of Mg may have occurred in long-term mortality of our patient group.

Our study has some limitations. The shortcomings of our study are that it is single-center, retrospective and the number of patients is relatively low.

AKI is a condition with an increasing frequency in the world, leading to morbidity and mortality. In this study, among many demographic and laboratory data in AKI patients in the medium-long term, we found old age, the presence of coronary artery disease, increased K and Mg as the independent risk factors for mortality. We believe that the results of our study will contribute to the literature concerning AKI.

**Ethical Approval:** This study was approved by the Selcuk University Faculty of Medicine Local Ethics Committee on 31.01.2023 with decision number 2023/87.

**Coflict of interest:** There is no conflict of interest between the authors.

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