ORIGINAL ARTICLE

Predictive factors for acute kidney injury and amputation in crush injuries from the Kahramanmaraş earthquakes

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ABSTRACT

BACKGROUND: Crush syndrome (CS) is characterized by high morbidity and mortality due to severe electrolyte disorders, circulatory dysfunction, and multiple organ failure, secondary to severe rhabdomyolysis and reperfusion injuries. Acute kidney injury (AKI) related to crush syndrome is one of the life-threatening complications and is the most frequent cause of death following earthquakes, other than trauma. We conducted a retrospective study to identify predictive parameters from clinical and laboratory data that aid in recognizing CS, assessing its severity, and evaluating acute kidney injury and amputation indications in patients.

METHODS: We retrospectively evaluated the clinical data and laboratory follow-up of 33 patients treated for crush syndrome within the first two weeks following the February 6, 2023 earthquake. Patients who underwent surgery for crush syndrome but could not be followed post-surgery were excluded. Laboratory parameters were analyzed upon admission and then daily over an average seven-day follow-up. A p-value of <0.05 was considered statistically significant. Data analysis was performed using IBM SPSS Statistics 26.0 and R Studio software.

RESULTS: Of the 33 patients, 17 were male and 16 were female. The incidence of AKI was 35.7%, 66.7%, and 100% in patients with injuries to one, two, and three extremities, respectively. A significant correlation was observed between total entrapment time and the duration of required dialysis days; AKI risk significantly increased with more than six hours of total entrapment time. Regarding the initial blood values upon hospital admission, a myoglobin level exceeding 2330 mg/dL demonstrated the highest sensitivity for predicting AKI. An initial uric acid level (>6.36 mg/dL) on admission had the highest specificity for predicting AKI. The initial myoglobin level (>3450 mg/dL) showed the highest sensitivity in predicting the need for amputation. Meanwhile, the mean creatine kinase (CK) level (>34800 U/L) exhibited the highest specificity but the lowest sensitivity for amputation prediction.

CONCLUSION: The study analyzed the effectiveness and predictability of clinical and laboratory findings concerning amputation and acute kidney injury in crush syndrome resulting from earthquakes. Effective amputation management is a crucial factor influencing prognosis and survival in patients with earthquake-induced crush syndrome.

Keywords: Acute kidney injury; amputation; crush syndrome; earthquake.

INTRODUCTION

On February 6, 2023 at 4:17 a.m., a devastating earthquake with a magnitude of 7.8 on the Richter scale struck the southern and central regions of Türkiye, centered in Kahramanmaraş. This event, lasting 90 seconds, was followed by another seismic event at 1:24 p.m. with a magnitude of 7.5, lasting 45 seconds, in the same city. The disaster resulted in at least 50,096

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deaths and 107,204 injuries. The estimated death rate was even higher in 11 provinces of Türkiye, including Malatya. Approximately 15.73 million people and 4 million buildings were affected, with around 345,000 apartments destroyed.

Crush syndrome, also known as traumatic rhabdomyolysis, arises from the systemic impact of muscle destruction products that develop after reperfusion following the release of prolonged compression.[1] Crush syndrome can develop in several traumatic contexts, including natural disasters like earthquakes, vehicle accidents, and situations during warfare, where individuals are trapped beneath substantial debris. The same outcome may also occur if the victim is unable to move, even without being trapped under debris, due to conditions like a drug overdose, coma, or being immobilized in the same position for an extended period during surgery.[2] The incidence of crush syndrome is generally estimated at 2% to 5%, but this rate increases to between 3% and 20% in earthquake scenarios. Approximately 50% of patients with crush syndrome develop acute kidney injury (AKI), and about 50% of those with AKI will require dialysis. The mortality rate for rhabdomyolysis-associated AKI is estimated to be around 40%.[3-5] AKI is a critical aspects of crush syndrome which is the second most common cause of death following the direct effects of trauma in disasters.[6] Treatment of crush syndrome primarily focuses on preventing renal, cardiac, and metabolic complications, prioritizing saving lives over limbs.[5] The aim of our study is to determine whether patients' initial and average laboratory values can predict two of the most life-threatening conditions: acute kidney injury and crushed extremities. We analyzed the correlation between patients' mean blood values and their clinical status. Additionally, we investigated changes in laboratory values among patients who underwent surgery and the impact of their duration under debris on both laboratory and clinical outcomes.

MATERIALS AND METHODS

We retrospectively reviewed the cases of 43 patients treated for crush syndrome within the first two weeks following the February 6, 2023 earthquake. Of these, 33 patients were included in the study; the remaining 10, who underwent surgery for crush syndrome, were excluded due to lack of postoperative follow-up. This study received approval from the Institutional Review Board of our University (2023/4684/6). We assessed the clinical data and laboratory follow-up of patients admitted with crush syndrome who were also followed postoperatively. Data collected included sex, age, anatomical injury sites, total entrapment time (time under debris plus time to evacuation), additional injuries, amputation, fasciotomy, non-surgical treatment, acute kidney injury, dialysis, disseminated intravascular coagulation (DIC), acute respiratory distress syndrome (ARDS), sepsis, surgical wound infection, debridement, necessity for higher-level amputation, and mortality. We analyzed the following laboratory parameters at admission and daily for an average of seven days: creatine kinase (CK) (U/L), potassium (K) (mmol/L), calcium (Ca) (mg/dL), uric acid (mg/dL), myoglobin (mg/dL), creatinine (Cre) (mg/dL), blood urea nitrogen (BUN) (mg/dL), lactate dehydrogenase (LDH) (u/L), lactate (mmol/L), white blood cells (WBC) ($10^3/\mu L$), hemoglobin (Hb) (g/dL), hematocrit (Hct), platelets, pH, and base deficit. Acute kidney injury, as defined by the Kidney Disease: Improving Global Outcomes (KDIGO) since 2004, encompasses an abrupt decrease in kidney function, which includes but is not limited to, conditions such as acute renal failure (ARF). AKI is a broad clinical syndrome caused by various etiologies, such as specific kidney diseases, nonspecific conditions (ischemia, toxic injury), and extrarenal pathologies. More than one of these conditions may coexist in the same patient. Since AKI's manifestations and clinical consequences can be similar, regardless of whether the etiology is primarily within the kidney or from external stresses on the kidney, the syndrome of AKI includes both direct kidney injury and acute functional impairment.[7] Consequently, the term "acute kidney injury" is now used instead of "acute renal failure" in contexts of acute disaster-related disorders.

According to KDIGO, AKI can be identified by any of the following criteria: an increase in serum creatinine by ≥0.3 mg/dL within 48 hours; an increase in serum creatinine to ≥1.5 times baseline, known or presumed to have occurred within the prior 7 days; or a urine output of less than 0.5 mL/kg/h for 6 hours.[7] The diagnosis of crush syndrome is made in patients trapped under collapsed buildings based on: (1) a significant number of skeletal muscle injuries caused by being crushed by heavy materials, with or without swelling; (2) serum CK levels exceeding 1000 U/L; (3) neurological deficits, which may include sensory or motor changes at the injury site; and (4) the presence of urine discoloration.[8] The anatomical injury sites were described as upper and lower extremities, along with additional injuries (pelvis, acetabulum, vertebra, scapula, humerus, radius, ulna, tibia, and mandible fractures). We diagnosed compartment syndrome based solely on clinical manifestations, including pain, swelling, tight and shiny skin, decreased range of motion, and pain-induced numbness or decreased sensation upon passive movement of distal joints. Due to the circumstances of the disaster, needle manometry for determining the indication for fasciotomy was not possible. In patients selected for amputation, tissue viability during surgery was assessed by the appearance of the tissues and muscle contractility in response to electrocautery and tactile stimulation. During the intervention, we did not consider the muscle viable tissue due to the presence of bleeding. This misleading appearance has been noted in previous studies.[9,10] Higher-level amputations were performed on patients who experienced progressive extremity necrosis after the initial amputation. In this study, patients with elevated CK levels potentially indicating myocardial or cerebral infarction were excluded from the analysis. Additionally, patients with pre-existing chronic renal failure before the earthquake were also excluded. Due to the exceptional circumstances, serum calcium levels in patients with hypocalcemia could not be adjusted for hypoalbuminemia, as albumin levels were not measured in each patient.

Statistical Analysis

Data were summarized as means ± standard deviation, medians (minimum-maximum), or frequencies (percentages) where appropriate. Normal distribution conformity was assessed using the Shapiro-Wilk test. Statistical analyses were conducted using Independent Samples t-Test, Mann-Whitney U, Continuity Correction Chi-Square, Pearson Chi-Square, and Fisher Exact Chi-Square tests as appropriate. The optimal cut-off points for risk factors associated with amputation and acute kidney injury were determined using a logistic regression model approach, supported by supervised discretization with the OneR package in R programming language.[11,12] Univariate logistic regression analysis was used to estimate odds ratios. Pearson and Kendall-Tau coefficients were employed for correlation analysis where appropriate. A p-value of <0.05 was considered statistically significant. The analyses were conducted using IBM SPSS Statistics 26.0 and R Studio software.[13]

RESULTS

The study included 33 patients, 17 (51.5%) of whom were male and 16 (48.5%) female. The patients were monitored over an average follow-up period of seven days. All injuries were closed, with victims' ages ranging 6 to 58 years, and an average age of 28 years. The extremities were the most frequently injured body parts, with lower limbs more commonly affected (42 extremities in 26 patients). The number of affected upper extremities was 16 limbs in 14 patients (Table 1). The incidence of AKI was 35.7% in patients with one extremity injury, 66.7% with two, and 100% with three. The CK levels were significantly higher in patients with more than two affected extremities (initial average CK=124,130, p=0.005; mean CK=44,343, p=0.008). Patients with more than two affected extremities had a 100% incidence of AKI (mean CK=44,343). The incidence of AKI in patients with one or two affected extremities was 51.7% (mean CK=12,280). Descriptive statistics for study factors related to the absence and presence of AKI are presented in Table 2. Additionally, 15 patients (45.5%) sustained other injuries (pelvis, acetabulum, vertebra, scapula, humerus, radius, ulna, tibia, and mandible fractures). There was a statistically significant increase in mean creatinine, potassium, lactate dehydrogenase, myoglobin, and base deficit levels in patients with additional injuries. However, no correlation was found between additional injuries and the occurrence of AKI, DIC, ARDS, sepsis, wound infection, higher-level amputation necessity, or death. The total entrapment time ranged from 1 to 72 hours, with an average of 12 hours. A correlation was observed between total entrapment time and the initial serum concentrations of K (τ=0.279, p=0.027), CK (τ=0.345, p=0.006), myoglobin (τ=0.472, p<0.001), LDH (τ=0.406, p=0.001), uric acid (τ=0.341, p=0.008), creatinine (τ=0.364, p=0.005), and BUN (τ=0.422, p=0.001). Additionally, a correlation was found between total entrapment time and mean serum concentrations of CK (τ=0.277, p=0.028), LDH (τ=0.339, p=0.007), and calcium (τ=-0.320, p=0.011). There was no significant difference in total entrapment time between patients who underwent amputation and those who did not (p=0.183). However, a significant difference was noted in total entrapment time exceeding six hours between patients with AKI and those without (p=0.001), as well as a significant correlation between total entrapment time and the duration of required dialysis days (p=0.014). There was no statistically significant difference in terms of total entrapment time across the categories of DIC, ARDS, sepsis, wound infection, higher-level amputation necessity, and death. AKI was present in 19 patients (57.6%). Univariate logistic regression analyses for both initial and mean laboratory parameters in predicting AKI are detailed in Table 3. Approximately one-third of the patients (n=12, 36.3%) required dialysis, receiving an average of 9 days of treatment. Significant correlations were found between the duration of required dialysis days and mean levels of CK (τ=0.534, p<0.001), LDH (τ=0.510, p<0.001), myoglobin (τ=0.374, p<0.001), and initial uric acid (τ=0.467, p=0.001). Thirteen patients (39.4%) underwent surgical treatment, while 20 (60.6%) were managed conser-

Table 1. Characteristics of patients with crush syndrome and medical complications observed during clinical course

	n	Percentage (%)
Male	17	51.5
Female	16	48.5
Additional injury	15	45.5
Upper limb injury	16	42.4
Upper limb amputation	4	12.1
Lower limb injury	42	78.8
Lower limb amputation	7	21.2
Non-surgical treatment	20	60.6
Fasciotomy	4	12.1
Amputation	9	27.3
Acute kidney injury	19	57.3
Dialysis	12	36.3
DIC	1	3
ARDS	2	6
Sepsis	6	18.2
Surgical wound infection	6	18.2
Amputation wound infection	6	18.2
Debridement	6	18.2
Higher level amputation necessity	3	9.1
Death	2	6
Total patients	33	100

DIC: Disseminated intravascular coagulation; ARDS: Acute respiratory distress syndrome.

Table 2. Demographic, laboratory, and clinical indicators of patients with and without acute kidney injury

	Acute Kidney Injury		
	No (n=14) Median (Min-Max)	**Yes (n=19) Median (Min-Max)**	**p-value**
Age	36 (10-52)	21 (6-58)	0.077*
Total Entrapment Time	2 (1-26)	12 (1-72)	0.001*
Potassium (Initial)	4.18 (3.09-7.1)	5.62 (3.79-8.26)	0.001*
CK (Initial)	1707 (1151-40343)	35000 (1528-200000)	0.001*
Myoglobin (Initial)	575.5 (41.7-6631)	4105 (1185-4105)	0.001*
Creatinine (Initial)	0.9 (0.5-1.1)	2 (1-5.2)	<0.001*
Ph (Initial)	7.44 (7.18-7.48)	7.32 (7.13-7.42)	<0.001*
Lactate (Initial)	1.7 (1-5.1)	4.6 (1-21)	0.003*
LDH (Initial)	379.5 (177-1893)	1797 (387-19748)	<0.001*
Uric Acid (Initial)	5.1 (1.1-7.1)	9 (4.8-15.6)	<0.001*
CK (Mean)	989.63 (344-33000)	14443.75 (536-99000.88)	0.001*
Myoglobin (Mean)	378.19 (31.65-6631)	2530.83 (507-4105)	0.004*
Creatinine (Mean)	0.76 (0.59-1)	1.48 (0.52-3.89)	0.007*
BUN (Mean)	10.59 (6.78-18.45)	24.93 (8.29-62.18)	0.001*
Ph (Mean)	7.41 (7.37-7.48)	7.41 (7.24-800.87)	0.747*
Lactate (Mean)	2.4 (1.17-3.65)	2.08 (1.38-5.3)	0.591*
LDH (Mean)	376.94 (156.33-2321.75)	1284 (344.5-7606.73)	0.140*
Uric Acid (Mean)	4.1 (1.11-5.97)	5.08 (2.68-13.14)	0.259*
	Mean±SD	Mean±SD	
Calcium (Initial)	8.81±0.94	8.63±1.22	<0.001**
BUN (Initial)	14.24±4.33	30.19±14.12	0.002**
Potassium (Mean)	4±0.29	4.26±0.61	0.010**
Calcium (Mean)	8.73±0.79	8.03±0.59	0.796**
Base Deficit (Mean)	-1.92±2.41	-2.22±3.5	<0.001**
	Count (Percent)	Count (Percent)	
Gender			
Male	3 (21.43%)	14 (73.68%)	0.009***
Female	11 (78.57%)	5 (26.32%)	
Treatment			
Non-surgical	12 (85.71%)	8 (42.11%)	0.036***
Fasciotomy	1 (7.14%)	3 (15.79%)	
Amputation	1 (7.14%)	8 (42.11%)	
Additional Injury			
No	6 (42.86%)	12 (63.16%)	0.421**
Yes	8 (57.14%)	7 (36.84%)	
DIC No	14 (100.00%)	18 (94.74%)	1.000***
Yes	0 (0.00%)	1 (5.26%)	
ARDS No	14 (100.00%)	17 (89.47%)	0.496***
Yes	0 (0.00%)	2 (10.53%)	
Sepsis No	13 (92.86%)	14 (73.68%)	0.209***
Yes	1 (7.14%)	5 (26.32%)	
Surgical Wound Infection			
No	14 (100.00%)	13 (68.42%)	0.027***
Yes	0 (0.00%)	6 (31.58%)	
Higher Level Amputation			
No	14 (100.00%)	16 (84.21%)	0.244***
Yes	0 (0.00%)	3 (15.79%)	

*: Mann-Whitney U test; **: Independent Sample t-Test; ***: Chi-Square Test; CK: Creatine Kinase; LDH: Lactate Dehydrogenase; BUN: Blood Urea Nitrogen; DIC: Disseminated Intravascular Coagulation; ARDS: Acute Respiratory Distress Syndrome.

Table 3. Univariate logistic regression analyses of initial and mean laboratory parameters in predicting acute kidney injury (AKI)

					95% CI		
Univariate Analysis	**Sensitivity**	**Specificity**	**Cut-Off***	**Odds Ratio**	**Lower**	**Upper**	**p-value**
CK (Initial)	0.69	0.79	14300 (U/L)	7.94	1.601	39.416	0.011
Myoglobin (Initial)	0.95	0.79	2330 (mg/dL)	66	6.083	716.151	0.001
LDH (Initial)	0.84	0.86	837 (U/L)	32	4.601	222.555	<0.001
Uric Acid (Initial)	0.89	0.92	6.36 (mg/dL)	102	8.276	1257.148	<0.001
CK (Mean)	0.79	0.79	9290 (U/L)	13.75	2.545	74.299	0.002
Myoglobin (Mean)	0.84	0.79	1320 (mg/dL)	19.556	3.315	115.372	0.001
LDH (Mean)	0.68	0.86	765 (U/L)	13	2.187	77.266	0.005

*Cut-off values are based on a supervised discretization method. CK: Creatine kinase; LDH: Lactate dehydrogenase; Se: Sensitivity; Sp: Specificity.

vatively. Fasciotomies were performed on 4 patients (12.1%), and amputations on 9 (27.3%). Descriptive statistics for the study factors related to the absence and presence of amputation are presented in Table 4. The initial myoglobin value for patients who underwent amputation averaged 3,448, while for those observed conservatively, it averaged 2167. An initial myoglobin concentration above 3,450 showed 78% sensitivity and 65% specificity in predicting the need for amputation (p=0.04). An initial uric acid concentration above 9.9 demonstrated 56% sensitivity and 89% specificity for predicting amputation (p=0.02). The initial CK value for patients who underwent amputation averaged 55,571 compared to 23,560 for those treated conservatively. Although initial CK levels were not statistically predictive of amputation, a mean CK concentration above 34,800 had 44% sensitivity and 90% specificity in predicting amputation (p=0.04). The mean CK value for those who underwent amputation was 34,775, while it was 12,716 for those who did not undergo surgery. A mean creatinine concentration above 1.7 was associated with 56% sensitivity and 90% specificity in predicting amputation (p=0.02) (Table 5). Statistically significant improvements were observed in mean CK (p=0.028), myoglobin (p=0.001), potassium (p=0.002), creatinine (p=0.017), and uric acid (p=0.002) levels among patients who underwent amputation. No statistical differences were found in the occurrence of DIC, ARDS, sepsis, or death between patients who underwent surgery and those who received conservative treatment. AKI developed in 11 (33.3%) of the patients who had surgery and in 8 (24.2%) of those who did not. Postoperative wound infection occurred in 6 (18.2%) of the patients who underwent amputation. No postoperative wound infections developed in patients who underwent fasciotomy. Debridement was performed on all patients with infected wounds, and only 3 patients (9.1%) with resistant and progressive infections required higher-level amputation. One patient (3%) developed DIC, 2 patients (6%) developed ARDS, 6 patients (18.2%) developed sepsis, and 2 patients (6%) died from pulmonary embolism (Table 1).

DISCUSSION

The most common mechanism of traumatic rhabdomyolysis is direct compression of muscle tissue, leading to local crush injuries. The duration of ischemia directly influences the extent of muscle damage, with histological changes from ischemia-reperfusion injury peaking after 24 hours.[14] Gonzalez suggested that the total time of entrapment (time under debris plus evacuation time) may not accurately reflect the true severity of injuries or medical conditions.[15] While some studies indicate no correlation between entrapment duration and the severity of crush syndrome, others report that increased entrapment time negatively impacts the prognosis of crush syndrome patients.[14,16-19] Prolonged immobilization during entrapment, even without direct compression from debris, can lead to crush syndrome, including gluteal compartment syndrome in patients who remain immobile for extended periods.[2,20] In patients crushed under debris, prolonged entrapment time delays treatment and exacerbates the development of kidney injury.[2,21] Some research has found no link between muscle breakdown-related blood values and entrapment duration.[17,18] However, our study identified significant correlations between total entrapment time and the initial and mean blood levels of CK, LDH, and the initial levels of BUN and creatinine. Hu et al. reported that time under rubble exceeding four hours increased the risk of ARF.[21] We also discovered significant correlations between total entrapment time and the development of acute kidney injury and the duration of required dialysis days, noting a significant increase in AKI risk after more than six hours of entrapment. Therefore, our findings suggest that total entrapment time is indicative of the severity of muscle damage and is associated with AKI, a lethal complication of crush syndrome.

Evaluating the severity and progression of crush syndrome requires continuous monitoring of kidney function to promptly detect the onset of early DIC. Unfortunately, blood creatinine and BUN values are late indicators of kidney damage, often reflecting a gradual decline in renal function.[22] There-

Table 4. Demographic, laboratory, and clinical indicators of patients in two groups

	Non-Surgical Treatment (n=20) Median (Min-Max)	Amputation (n=9) Median (Min-Max)	p-value
Age	27 (10-52)	17 (6-58)	0.125*
CK (Initial)	3007.5 (1151-175400)	13251 (1226-200000)	0.300*
Myoglobin (Initial)	1135 (41.7-6631)	4007 (75-4105)	0.194*
Creatinine (Initial)	1 (0.6-5.2)	2 (0.5-5.1)	0.107*
BUN (Initial)	16.12 (8.41-59.8)	21.5 (13-57.38)	0.229*
Lactate (Initial)	2.1 (1-15)	5.15 (1-21)	0.032*
LDH (Initial)	530 (177-9929)	1797 (239-19748)	0.053*
Uric Acid (Initial)	5.6 (1.1-15.6)	10.2 (4.3-14.3)	0.014*
CK (Mean)	2993.25 (458-99000.88)	15149.67 (344-84762.44)	0.187*
Myoglobin (Mean)	774.78 (31.65-6631)	2533.54 (31.76-3762.25)	0.099*
Creatinine (Mean)	0.84 (0.63-3.89)	1.83 (0.52-3.29)	0.171*
BUN (Mean)	12.85 (6.78-55.75)	25.87 (10.37-43.73)	0.043*
LDH (Mean)	410.56 (156.33-5490.63)	1284 (199.14-7606.73)	0.018*
	Mean±SD	Mean±SD	
Potassium (Initial)	4.77±1.22	6.03±1.8	0.099**
Calcium (Initial)	8.92±1.11	8.03±1.01	0.015**
Potassium (Mean)	3.99±0.34	4.29±0.64	0.346**
Calcium (Mean)	8.58±0.68	7.95±0.8	0.048**
Base Deficit (Mean)	-1.1±2.65	-3.62±3.58	0.107**
Lactate (Mean)	2.21±0.78	2.74±0.99	0.165**
Uric Acid (Mean)	4.58±1.54	5.1±1.17	0.313**
	Count (Percent)	Count (Percent)	
Gender			
Male	8 (40.00%)	6 (66.67%)	0.245***
Female	12 (60.00%)	3 (33.33%)	
Additional Injury			
No	9 (45.00%)	5 (55.56%)	0.700***
Yes	11 (55.00%)	4 (44.44%)	
AKI No	12 (60.00%)	1 (11.11%)	0.020***
Yes	8 (40.00%)	8 (88.89%)	
DIC No	19 (95.00%)	9 (100.00%)	1.000***
Yes	1 (5.00%)	0 (0.00%)	
ARDS No	20 (100.00%)	7 (77.78%)	0.089***
Yes	0 (0.00%)	2 (22.22%)	
Sepsis No	18 (90.00%)	5 (55.56%)	0.056***
Yes	2 (10.00%)	4 (44.44%)	
Surgical Wound Infection			
No	20 (100.00%)	4 (44.44%)	0.001***
Yes	0 (0.00%)	5 (55.56%)	
Higher Level Amputation			
No	20 (100.00%)	6 (66.67%)	0.023***
Yes	0 (0.00%)	3 (33.33%)	

*: Mann-Whitney U test; **: Independent Sample t-Test; ***: Chi-Square test; CK: Creatine kinase; LDH: Lactate dehydrogenase; BUN: Blood urea nitrogen; DIC: Disseminated intravascular coagulation; ARDS: Acute respiratory distress syndrome; AKI: Acute kidney injury.

fore, we investigated other blood parameters (CK, LDH, myoglobin, and uric acid) related to the early prediction of AKI in crush syndrome to determine kidney deterioration at an early stage. Numerous studies have assessed the prognostic value of serum CK, with peak concentrations over 500, 5,000, 16,000, and 75,000 U/L associated with the development of acute renal failure.[8,16,23] A retrospective review by Brown et al. of CK levels in 2,083 trauma patients found

Table 5. Univariate logistic regression analysis of laboratory parameters for predicting amputation

Univariate Analysis	Sensitivity	Specificity	Cut-Off*	Odds Ratio	95% CI Lower	95% CI Upper	p-value
Myoglobin (Initial)	0.78	0.65	3450 (mg/dL)	6.50	1.053	40.132	0.04
Uric Acid (Initial)	0.56	0.89	9.9 (mg/dL)	10.63	1.484	76.081	0.02
CK (Mean)	0.44	0.90	34800 (U/L)	7.20	1.009	51.392	0.04
BUN (Mean)	0.56	0.85	25 (mg/dL)	7.08	1.172	42.793	0.03
Creatinine (Mean)	0.56	0.90	1.7(mg/dL)	11.25	1.576	80.300	0.02

*Cut-off values are based on a supervised discretization method. CK: Creatine kinase; BUN: Blood urea nitrogen; Se: Sensitivity; Sp: Specificity.

that a peak CK level above 5,000 U/L was the most reliable marker for predicting acute renal failure.[24] Conversely, Fernandez et al. reported that initial CK levels did not predict acute renal failure.[25] In our study, initial CK concentration was a statistically significant predictor of AKI. Unlike other studies, we also calculated the mean CK value during patient follow-up, finding that a mean CK concentration above 9,290 U/L predicted AKI with 79% sensitivity and specificity. Strong evidence suggests that serum or plasma myoglobin levels could be better predictors of AKI than CK levels.[26,27] We determined that a mean myoglobin level above 1,320 mg/dL matched the specificity of CK but was more sensitive (sensitivity 84%). Regarding initial blood values upon hospital admission, a myoglobin level above 2,330 mg/dL demonstrated the highest sensitivity (95%). An initial LDH level greater than 837 U/L upon admission had a sensitivity of 84% and specificity of 86% in predicting AKI. Serum uric acid, another factor linked to kidney failure, has been shown to be elevated in previous studies.[8] An initial uric acid level greater than 6.36 mg/dL upon admission had the highest specificity (92%) in predicting AKI. According to a study by Oda et al., the occurrence of acute renal failure was 50.5%, 74.5%, and 100% in patients with one, two, and three extremity injuries, respectively.[16] These findings strongly indicate that the number of affected extremities plays a critical role in determining the severity of crush syndrome.[18] In our study, the mean CK of patients with three or four affected extremities was more than triple that of patients with one or two extremities involved. Additionally, we found that the incidence of AKI was 35.7%, 66.7%, and 100% in patients with one, two, and three extremity injuries, respectively. Our results suggest that the severity of crush syndrome escalates with the number of extremities involved.

The incidence of amputation among disaster victims ranges from 2.9% to 58.6%.[28] In our study, the amputation rate was 27.3%. The lower extremities are the most commonly traumatized parts of the body during an earthquake.[29-31] We observed that the lower extremities were the most frequently injured, with an amputation rate in the affected lower extremities of 16.6%. Inadequate management of these injuries can lead to severe complications, including circulatory-electrolyte imbalances, renal-cardiac issues, and even death.[31] Therefore, we implemented a rapid algorithm to guide precise management decisions. When deciding on amputation, we categorized patients into three groups. The first category included patients with obvious necrosis and non-viable extremities, where amputation was quickly deemed necessary due to irreversible tissue damage (Fig. 1a-b). The second category included patients with palpable extremity pulses, capillary filling, and no skin necrosis, who showed clinical and laboratory improvement with medical treatment. These patients were treated non-surgically but monitored closely (Fig. 1c-d). The third category included two types of patients: a) those from the second category who were initially managed conservatively but did not show clinical or laboratory improvement despite medical treatment. These cases were considered life-threatening, and the patients were typically managed in the intensive care unit; b) patients presenting initially with high levels of muscle destruction products and a deteriorating clinical condition, despite having capillary refill in the affected limb (Fig. 1e-f). In this category, two groups of patients with crush syndrome underwent amputation due to progressive clinical deterioration despite receiving advanced life support. This prompted consideration of whether amputation decisions should be made in the initial or progressive stages of crush syndrome. Currently, there is no evidence-based literature to guide the management of traumatic rhabdomyolysis and reperfusion syndrome, specifically regarding the optimal timing for amputation. This lack of guidance led us to investigate predictive parameters for amputation. Serum CK concentrations, which correlate with the extent of muscle damage, can be used to evaluate the severity of rhabdomyolysis.[14] Although initial CK levels were not statistically significant predictors of amputation in our study, the initial CK values of patients who underwent amputation were approximately twice as high as those who did not.

The initial values of myoglobin (cut-off: 3,450) and uric acid (cut-off: 9.9) were statistically significant in predicting the need for amputation. Initial myoglobin demonstrated greater sensitivity than uric acid, but uric acid showed higher specificity (90%) than myoglobin. Both mean CK (cut-off: 34,800) and mean creatinine (cut-off: 1.7) were significant predic-

Figure 1. (a,b) A 21-year-female patient with a total entrapment time of nine hours exhibited overt ischemic necrosis in both the left upper and lower extremities. Immediate amputation was performed on these extremities. **(c,d)** A 25-year-old female patient, 37 weeks pregnant, endured an entrapment duration of 72 hours. She presented with turgidity and skin bruises on the left upper and both lower extremities. She received conservative treatment in the intensive care unit. **(e,f)** A 17-year-old male patient was entrapped for seven hours. Initially, he showed skin ecchymosis on the left upper extremity and paleness and pulselessness in the left hand, along with turgidity in both lower extremities. Following the reduction of a humerus fracture, circulation in the extremities normalized. However, the left upper extremity was amputated after the patient suffered a cardiac arrest during follow-up. Although circulation was restored to the hand, the muscles in the upper extremity had become necrotic.

tors of amputation. The mean creatinine and mean CK levels demonstrated the highest specificity (90%) for predicting the development of amputations, whereas the mean CK levels showed the lowest sensitivity (44%).

Statistically significant improvements were noted in the CK, myoglobin, potassium, creatinine, and uric acid levels of patients who underwent amputation. We discovered that these blood parameters were the most significant factors influencing the duration of required dialysis days. From the Marmara earthquake in 1999, clinical findings reported that among the patients who underwent amputations, 29 (30.5%) died, compared to 68 (12.5%) deaths among the remaining 544 patients. The presence or absence of amputations did not differ significantly between dialyzed and non-dialyzed victims.[29] In our study, among the 9 patients who underwent amputations, 2 (22%) died, whereas there were no deaths among the remaining 24 patients. Initially, muscle damage caused by ischemia and compression continues even after evacuation. Reperfusion injury not only leads to myocyte death but also damages the microvascular structure of the skeletal muscle. While short periods of ischemia are followed by reactive hyperemia in the muscle, longer periods may result in a "no-reflow" phenomenon.[32,33] In patients in the third category, the normal appearance of the skin, which has an extraordinary capacity to withstand pressure, and capillary filling can be misleading when assessing the condition of the extremity.[34] While skin circulation can be evaluated to determine the extent of injury, it may not sufficiently describe the condition of underlying muscle and nerve tissues. Research on amputation management in crush syndrome is limited. Although serum CK, myoglobin, and LDH levels provide substantial information about muscle damage, they cannot offer a definitive judgment about the pathological state of the muscle.[35] Different molecular markers specific to skeletal muscle should be investigated to determine the pathological stage of muscle tissue.[36]

This study faced several constraints related to extraordinary situations caused by the catastrophe, such as shock, panic, and chaos immediately following the earthquake, and incomplete files due to victim overload. Consequently, we analyzed a limited number of patients. Some patients died in the emergency service during initial interventions, and some patients with crush syndrome, who were operated on as emergencies, could not be followed up because they were transferred to other hospitals postoperatively and were not included in the study.

CONCLUSION

The severity of crush syndrome is estimated by both the number of crushed limbs and serum concentrations of CK, myoglobin, and LDH, which reflect the extent of underlying muscle damage. Currently, there is no evidence-based literature to guide the management of crush syndrome, specifically regarding the optimal timing for amputation. Controlled prospective studies are challenging due to the nature of disasters. This study aids in recognizing crush syndrome, assessing its severity, and evaluating indications for amputation in patients. We believe that investigating more skeletal muscle-specific blood parameters could lead to significant advances in predicting the timing and likelihood of amputations in crush syndrome cases in the future.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Kahramanmaraş depremlerinde ezilme yaralanmalarında akut böbrek hasarı ve amputasyonu öngören faktörler

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AMAÇ: Ezilme sendromu (ES), ciddi rabdomiyoliz ve reperfüzyon yaralanmalarına sekonder olarak gelişen ciddi elektrolit bozuklukları, dolaşım bozukluğu ve çoklu organ yetmezliği nedeniyle morbidite ve mortalitesi yüksek bir durumdur. Ezilme sendromuna bağlı akut böbrek hasarı (ABH), ezilme yaralanmalarının yaşamı tehdit eden birkaç komplikasyonundan biridir. ES, travma dışında deprem sonrası en sık ölüm nedenidir. Ezilme sendromunu tanımamıza, ciddiyetini değerlendirmemize ve hastalarda akut böbrek hasarını ve ampütasyon endikasyonlarını değerlendirmemize yardımcı olmak amacıyla klinik ve laboratuvar verilerine dayalı öngörücü parametreleri belirlemek için retrospektif bir çalışma gerçekleştirdik.

GEREÇ VE YÖNTEM: 6 Şubat 2023 depreminin ilk iki haftasında ezilme sendromu nedeniyle tedavi gören 33 hastanın klinik ve laboratuvar verileri retrospektif olarak değerlendirildi. Ezilme sendromu nedeniyle opere edilen ancak sonrasında takip edilemeyen hastalar çalışmaya dahil edilmedi. Başvuru sırasındaki ve ortalama yedi günlük takip boyunca laboratuvar parametreleri günlük olarak analiz edildi. $p<0.05$ değeri istatistiksel olarak anlamlı kabul edildi. Analizde IBM SPSS İstatistik 26.0 programı ve R Studio yazılımı kullanıldı.

BULGULAR: 33 hastadan 17'si erkek, 16'sı kadındı. ABH görülme sıklığı bir, iki ve üç ekstremite yaralanması hastalarda sırası ile %35.7, %66.7 ve %100 idi. Ayrıca toplam enkaz altında kalma süresi ile gerekli diyaliz günlerinin süresi arasında da anlamlı bir ilişki bulduk; ABH riski, altı saati aşan toplam tuzak süresinde önemli ölçüde artmaktadır. Hastaneye başvuru sırasındaki ilk kan değerlerine bakıldığında, 2330 mg/dL büyük miyoglobin değerinin ABH öngörmede en yüksek duyarlılığa sahip olduğu görüldü. Başvuru sırasındaki başlangıç ürik asit düzeyinin (>6.36 mg/dL) ABH öngörmede en yüksek özgüllüğe sahip olduğu bulundu. Başlangıç miyoglobin düzeyinin (>3450 mg/dL) ampütasyon gelişimini öngörmede en yüksek duyarlılığa sahip olduğu belirlendi. Ortalama kreatin kinaz düzeyi (>34800 U/L) ampütasyon gelişimini öngörmede en yüksek özgüllüğe ancak en düşük duyarlılığa sahipti.

SONUÇ: Depremin neden olduğu ezilme sendromunda ampütasyon ve akut böbrek hasarı açısından klinik ve laboratuvar bulgularının etkinliğini ve öngörülebilirliğini analiz ettik. Depreme bağlı ezilme sendromu gelişen hastalarda prognozu ve sağkalımı etkileyen en önemli faktörlerden biri ampütasyon yönetimidir.

Anahtar sözcükler: Akut böbrek hasarı; ampütasyon; deprem; ezilme sendromu.

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