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Evaluation of Clinical and Laboratory Findings and Outcomes in Patients Suffering from Earthquake-Related Crush Injury: Who Needs Renal Replacement Therapy?

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Abstract

Objectives: Many people who are rescued alive from rubble after earthquakes suffer from crush injuries and associated acute kidney injury (AKI). McMahon score is used to determine the risk of AKI and mortality due to rhabdomyolysis in hospitalized patients. In this study, we aimed to evaluate the clinical findings, biochemical characteristics, and outcomes of crush injury patients admitted to our tertiary hospital and the use of the McMahon score in determining the need for renal replacement therapy (RRT) in this patient group.

Methods: Sociodemographic, clinical, and biochemical parameters of 28 patients who had creatine kinase levels of 1000 U/L and above were recorded. Patients with crush injuries requiring and not requiring RRT were compared according to the McMahon Score.

Results: A total of 42% of patients developed AKI and 67% of them required renal replacement therapy. In crush injury patients requiring RRT, serum urea, creatinine, LDH, aspartate aminotransferase, alanine transaminase, phosphorus, and procalcitonin levels were significantly higher and albumin levels were significantly lower at admission compared to patients not requiring RRT. All patients who required RRT had a McMahon Score ≥6.

Conclusions: A high McMahon score at hospital admission is associated with an increased need for RRT.

Most of the people who are rescued alive from rubble after earthquakes suffer from crush injuries. Damage to muscles, vessels, and nerves because of the body, especially the extremities, being under high pressure for a certain period causes the development of rhabdomyolysis. Such injuries may occur because of the direct effect of traumas or because of ischemia that results from compression. If rhabdomyolysis accompanies organ dysfunctions such as acute kidney injury (AKI) and acute respiratory distress syndrome (ARDS), it is called crush syndrome. Muscle breakdown products entering the systemic circulation because of rhabdomyolysis are responsible for the clinical manifestations associated with crush injury. Acute Kidney injury, electrolyte imbalance, and cardiovascular collapse that result from myoglobinuria because of rhabdomyolysis cause mortality.[1,2]

The McMahon score was developed to predict the need for renal replacement therapy (RRT) and mortality in rhabdomyolysis in hospitalized patients. However, it is not widely used. It was presented by McMahon et al. in a retrospective cohort study of 2371 patients. Among the parameters used in the McMahon scoring system, the etiology of rhabdomyolysis, age, gender, serum creatinine, calcium, creatine kinase, phosphate, and bicarbonate levels are included. The McMahon score can start from 0 to a maximum of 19 points. A score of 5 or lower indicates a 3% risk of renal replacement therapy or death, while a score of 10 or higher indicates a 52% risk of RRT or death.[3]

Crush syndrome is the most common cause of mortality following natural disasters such as earthquakes, and the treatments used during this period are expert opinions that have a low level of evidence. In mass natural disasters such as earthquakes, medical equipment (i.e., dialysis machines, hemodialysis catheters, etc.) often cannot meet the needs. Referral of the patient to the appropriate center after the development of AKI may cause delay in RRT. For this reason, it is important to predict which earthquake victims will require RRT and triage them to appropriate centers. Eleven provinces were affected and 50 783 people lost their lives in the earthquakes that had a magnitude of 7.7 M_w and 7.6 M_w at the epicenter of Kahramanmaraş in Turkey on February

6 and 7, 2023.[4] Because of the large number of dead and injured, the capacity and manpower of the health care facilities were insufficient in the region. Injured earthquake victims were distributed to health care facilities all over the country by land and air ambulances. In this study, we aimed to evaluate the clinical findings, biochemical characteristics, and results of patients with crush injuries who applied to our tertiary hospital, which is approximately 800 km away from the earthquake zone and where patients were transferred by air, and to evaluate the use of the McMahon score in determining the need for renal replacement therapy in these patients.

Method

The study was designed as a retrospective cohort study with the need for RRT as the outcome. After approval by the ethical board, the files of 62 patients with earthquake-induced injury who were aged 18 and over and who received inpatient treatment at Istanbul Prof. Dr. Cemil Tascioglu City Hospital between February 6, 2023 and July 1, 2023 were evaluated in the study. The ethical board approval date was August 14, 2023 (number 141). A total of 28 patients who had creatine kinase (CK) >1000 U/L at first 72 hours during hospitalization were identified. Patients' age, gender, chronic disease status, time spent under rubbles, intravenous (IV) fluid status under rubbles, IV fluid taken in the first 24 hours, the result of blood and wound cultures, affected extremities, presence of fasciotomy, amputation status, development of acute kidney injury,[5] need for dialysis and blood product, need for intensive care, duration of hospital stay, and hospital discharge status were recorded. Biochemical parameters were recorded as entry value at admission, highest value (peak) in hospitalization, and discharge value. The KDIGO guideline criteria were used for the diagnosis of acute kidney injury.[6] McMahon score was calculated with the first admission values of the patients with the formula shown in Table 1.

Patients were divided into 2 groups: those who needed RRT and those who did not. Admission laboratory values and McMahon scores were compared between the 2 groups.

Statistical analyses were carried out with the Jamovi Software for Windows 2.4.1.0. The biochemical parameters of 8 patients who needed renal replacement therapy and 20 patients who did not were evaluated for distribution by using the Shapiro-Wilk Test, and the Mann-Whitney *U* Test was used as the hypothesis test.

Table 1. Calculation of the McMahon score

Variable		Points
Age, years	≤50	0
	51–70	1.5
	71–80	2.5
	>80	3
Sex	Male	0
	Female	1
Initial creatinine	<1.4 mg/dL (124 μmol/L)	0
	1.4–2.2 mg/dL (124–195 μmol/L)	1.5
	>2.2 mg/dL (195 μmol/L)	3
Initial calcium <7.5 mg/dL (1.88 mmol/L)	No	0
	Yes	2
Initial CPK >40,000 U/L	No	0
	Yes	2
Rhabdomyolysis secondary to seizures, syncope, exercise, statins, or myositis	Yes	0
	No	3
Initial phosphate	<4.0 mg/dL (1.0 mmol/L)	0
	4.0–5.4 mg/dL (1.0–1.4 mmol/L)	1.5
	>5.4 mg/dL (1.4 mmol/L)	3
Initial bicarbonate <19 mEq/L (19 mmol/L)	No	0
	Yes	2

McMahon Score ≥6, calculated on admission, is 86% sensitive and 68% specific for identifying patients who will require RRT.[5]

Results

A total of 62 adult patients were transferred to our hospital by air ambulance, and crush injury was detected in 28 of them. A total of 12 (42%) patients developed acute kidney injury - and crush syndrome - and 8 (67%) of these cases required RRT. The latest patient to undergo RRT was 3 days after extrication from the rubble. The age of the youngest patient was 18, the age of the oldest patient was 70, 17 were men, and 11 were women. Only 2 patients had received IVfluid replacement when they were under rubbles, 14 (50%) had lower extremity injuries, 6 (21%) had upper extremity injuries, 7 (25%) had both lower and upper extremity injuries, and 1 patient had a vertebra injury because of falling from a height. During their hospitalization, 14 patients required blood product transfusion and growth was observed in the blood culture of 9 (32%) patients. Fasciotomy was performed in 15 (53%) patients because of the compartment syndrome, and limb amputation was performed in 4 (14%) patients. Among the 15 patients who developed compartment syndrome, 10 (67%) developed AKI, and 7 of them (70%) required RRT. All patients who required RRT had a McMahon Score ≥6 (Table 2). LROC analysis showed that scores of 6.5 and above predicted the need for RRT with 87.5% sensitivity and 94.7% specificity (Figure 1). During the follow-ups, 4 patients were referred to other hospitals upon their request, while 24 patients were discharged.

The serum creatinine (Cre), creatine kinase (CK), lactate dehydrogenase (LDH), and potassium (K) values of the patients at admission, peak, and discharge are given in appendix 1.

When the admission biochemical parameters of patients requiring and not requiring RRT were compared, serum urea, creatinine, LDH, AST, ALT, phosphorus, and procalcitonin values were significantly higher ($P < 0.001$, $P < 0.001$, $P < 0.001$, $P < 0.001$, $P = 0.003$, $P = 0.023$, $P = 0.004$, respectively), while albumin, partial carbon dioxide pressure (PCO2), and bicarbonate (HCO3) values were significantly lower ($P = 0.011$, $P = 0.009$, $P = 0.004$, $P =$ respectively) in the group receiving RRT (Table 3).

Discussion

In our study, it was shown that the McMahon score can be used safely in predicting renal replacement therapy in patients who developed crush injury due to rhabdomyolysis after the earthquake. We observed that a McMahon score of 6.5 and above determined the need for renal replacement therapy with 87.5% sensitivity and 94.7% specificity.

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Table 2. General characteristics of the patients included in the study

Patient Number	Age (year)	Gender	Comorbidity	Duration under rubbles (hours)	IV treatment under rubbles	Affected limb	Fasciotomy/ Amputation (n days after extraction)	Acute Kidney I njury (AKIN Classification)	Dialysis (starting time after extraction, duration)	McMahon score	Blood transfusion(unit)	Ward (ICU, PRC,ORT,NEP)	Length of stay (days)	Discharge status	Blood culture
Case #1	35	Female	None	8	No	Bilateral lower extremity(ext)	YES / NO (1 day)	Yes (3)	CRRT (1 day, 6 days)	9	12U ES	ICU, PRC	45	Discharge	None
Case #2	19	Male	None	22	No	Lower right, upper left ext.	YES / YES (2 days)	Yes (3)	CRRT (2 days,13 days)	7.5	14U ES 16U FFP	ICU, NEP	44	Discharge	E. faecalis
Case #3	34	Female	None	40	No	Upper left ext.	NO / NO	Yes (3)	CRRT (3 days, 8 days) HD (2 days)	14	4U ES	ICU, NEP	45	Discharge	None
Case #4	28	Male	None	40	No	Bilateral lower, upper right ext.	YES / NO (2 days)	Yes (3)	HD (3 days,3 days)	11	9U ES	ORT	122	Discharge	S. epidermidis
Case #5	23	Male	None	44	Yes	Upper left ext.	YES / NO (2 days)	Yes (3)	CRRT (2 days, 5 days) HD	6	22U ES 1U FFP	ICU, PRC	119	Discharge	MRSA
Case #6	51	Female	None	>8	No	Lower left ext.	YES / NO (2 days)	Yes (3)	HD (3 days, 1 time)	7	3U ES 1U FFP	ORT	4	Transfer	None
Case #7	45	Female	None	>8	No	Lower left ext.	YES / NO (3 days)	Yes (3)	HD (3 days, 3 times)	11.5	None	ORT	8	Transfer	A. baumannii
Case #8	42	Female	None	>8	No	Bilateral lower ext.	YES / NO (4 days)	Yes (3)	CRRT (2 days, 20 days)	14	None	ICU	33	Transfer	None
Case #9	37	Female	None	4	No	Upper right ext.	YES / NO (2 days)	Yes (1)	No	9	5U ES	ICU, PRC	41	Discharge	None
Case #10	19	Male	None	32	Yes	Lower left ext.	YES / NO (2 days)	No	No	3	5U ES	ORT	43	Discharge	A. baumannii E. Cloaca
Case #11	22	Male	None	36	No	Bilateral upper, lower right ext.	YES / YES (2 days)	Yes (1)	No	3	9U ES	PRC	79	Discharge	None
Case #12	40	Male	None	12	No	Lower right ext.	YES / NO (2 days)	Yes (1)	No	6	4U ES	ORT	45	Discharge	C. striatum
Case #13	45	Male	None	12	No	Lower left ext.	NO / YES	No	No	3	None	ORT	26	Discharge	None
Case #14	54	Male	DM, HT	1	No	Upper left ext.	NO / NO	No	No	4.5	None	NEP	2	Treatment rejected	None
Case #15	34	Female	None	>8	No	Vertebra	NO / NO	No	No	4	3U ES 1U FFP	ORT	6	Discharge	None
Case #16	37	Male	Arrhythmia	>8	No	Lower left ext.	NO / NO	No	No	3	None	ORT	7	Discharge	None
Case #17	27	Male	None	>8	No	Lower left, upper right ext.	NO / NO	No	No	3	None	ICU	8	Discharge	None
Case #18	40	Female	Hypothyroidism	>8	No	Bilateral lower, upper right ext.	NO / NO	No	No	4	None	ORT	9	Discharge	None
Case #19	19	Male	None	>8	No	Upper right ext.	YES / YES (3 days)	No	No		1U ES	PRC	2	Discharge	None
Case #20	24	Male	None	1	No	Lower left ext.	NO / NO	No	No	3	6U ES	ORT	13	Discharge	None
Case #21	18	Male	None	>8	No	Bilateral lower ext.	NO / NO	No	No	3	None	ORT	12	Discharge	None
Case #22	22	Female	None	5	No	lower right ext.	NO / NO	No	No	4	None	ORT	one	Discharge	None
Case #23	22	Male	Fallot	8	No	Lower left ext.	NO / NO	No	No	3	None	ICU, ORT	15	Discharge	None
Case #24	20	Male	None	>8	No	Lower right, upper left ext.	NO / NO	No	No	3	None	ORT	15	Discharge	S. capitis
Case #25	70	Male	BPH	5	No	Lower right and upper ext.	NO / NO	Yes (1)	No	4.5	None	NEP	12	Discharge	None

(*Continued*)

Table 2. (*Continued*)

Patient Number	Age (year)	Gender	Comorbidity	Duration under rubbles (hours)	IV treatment under rubbles	Affected limb	Fasciotomy/ Amputation (n days after extraction)	Acute Kidney Injury (AKIN Classification)	Dialysis (starting time after extraction, duration)	McMahon score	Blood transfusion(unit)	Ward (ICU, PRC,ORT,NEP)	Length of stay (days)	Discharge status	Blood culture
Case #26	28	Female	None	12	No	Bilateral lower ext.	YES / NO (3 days)	No	No	4	None	ORT	14	Discharge	P. aureginosa A. baumanii
Case #27	53	Female	None	>8	No	Lower right ext.	YES / NO (2 days)	No	No	5.5	2U ES	ICU, ORT	17	Transfer	E. coli A. Baumanii K. pneumonia
Case #28	55	Male	HT	58	No	Upper right ext.	YES / NO (7 days)	No	No	6	None	PRC	13	Discharge	None

Diabetes Mellitus (DM), Hypertension (HT), Benign Prostate Hyperplasia (BPH), Continuous Renal Replacement Therapy (CRRT), Hemodialysis (HD), Erythrocyte Suspension (ES), Fresh Frozen Plasma (FFP), Acute Kidney Injury Network (AKIN), Intensive Care Unit (ICU), Plastic, Reconstructive & Aesthetic Surgery (PRC), Orthopedics (ORT), Nephrology (NEP).

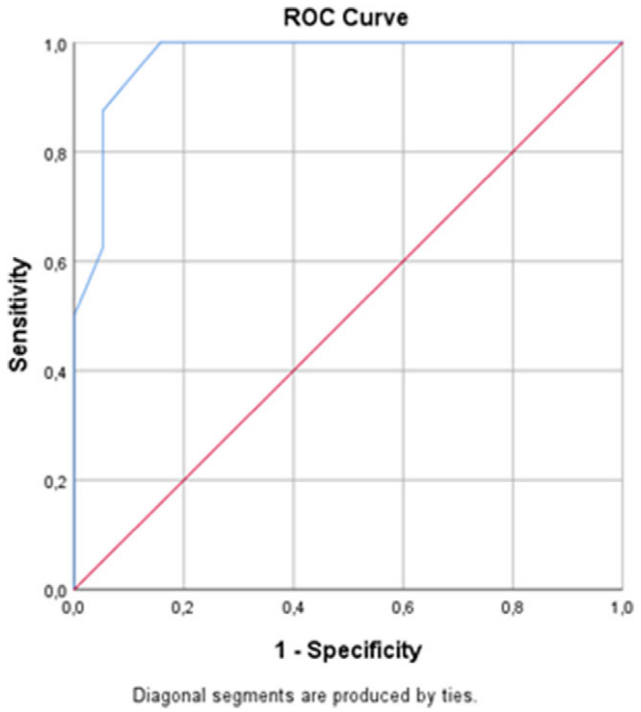

Figure 1. ROC curve of McMahon score as predictor of RRT. Cutoff value 6.5, sensitivity 87.5%, and specificity 94.7%.

Head and torso injuries caused by earthquakes usually end up in immediate mortality, while extremity injuries can be rescued alive. One of the most important causes of mortality in hospitals after rescue is crush syndrome[7]. Ischemia-reperfusion injury occurs when the pressure on the crushed muscle tissue is eliminated. Insufficient ATP production, increased oxidative stress, and resulting cell lysis cause compartment syndrome in the muscle surrounded by fascia due to increased fluid leaking out of the cells.[1,2] Aside from these, muscle breakdown products that enter the systemic circulation may also cause arrhythmia, AKI, and mortality (Figure 2). Hyperuricemia, hyperkalemia, hypocalcemia, and hyperphosphatemia occur because of rhabdomyolysis. In the present study, when patients who required RRT were compared with those who did not, potassium and uric acid were elevated and calcium was low, but statistical significance was not detected, which may have occurred due to the low number of patients. As expected, considering that it is released into serum from damaged muscle, serum phosphorus, AST, and LDH levels were significantly higher in patients receiving RRT than in those not receiving RRT. In addition, in patients receiving RRT because of AKI, HCO3 and pCO2 values were significantly lower due to metabolic acidosis and accompanying respiratory compensation. In terms of serum albumin level, it was found to be significantly lower in crush injury patients receiving RRT. Albumin, a negative acute phase reactant, may be decreased in patients receiving RRT, associated with a higher frequency of infection. High procalcitonin levels in the patient group receiving RRT also support our results. Another reason for low serum albumin levels can be explained by capillary damage and albumin leakage due to compartment syndrome.[8,9]

The McMahon score was developed by McMahon et al. in 2013 to predict poor prognosis in patients with rhabdomyolysis. The study was conducted with approximately 2400 patients with CK>5000 U/L who were hospitalized between the years 2000-2011. AKI requiring RRT and in-hospital mortality were primary

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Table 3. Comparison of admission values of patients according to the need for Renal Replacement Therapy (RRT)

	Total (*N*=28)	Receiving RRT (*N*=8)	Not receiving RRT (*N*=20)	
	Median (Min-Max)	Median (Min-Max)	Median (Min-Max)	***P*** value*
UREA *mg/dL*	33 (14–176)	111 (46–176)	28 (14–92)	**<0.001**
CREATININE *mg/dL*	0.8 (0.5–6.9)	4.3 (1.79–6.98)	0.7 (0.5–1.43)	**<0.001**
CK *U/L*	3712 (262–32244)	1810 (262–9395)	4403 (285–32244)	0.199
LDH *U/L*	607 (236–4595)	1392 (516–4595)	487 (236–1215)	**<0.001**
POTASSIUM *mmol/L*	4.22 (3.40–6.55)	5.13 (3.68–6.55)	4.15 (3.4–5.2)	0.056
AST *U/L*	226 (23–2516)	729(150–2516)	113(23–547)	**<0.001**
ALT *U/L*	96.5 (8–3060)	280(40–3060)	76 (8–226)	**0.003**
INR	1.20 (0.98–2.45)	1.25(1.1–2.45)	1.19 (0.9–1.47)	0.177
D-DIMER *μg/mL*	1.96(0.48–14.5)	2.9 (1.64–14.5)	1.4 (0.4–11.1)	0.198
PHOSPHORUS *mg/dL*	3.37 (2.03–8.29)	5.13(2.05–8.29)	3.13 (2.03–5.29)	**0.023**
ALBUMIN *g/dL*	3.40 (2.10–4.6)	2.6 (2.1–3.70)	3.70 (2.1–4.60)	**0.011**
CALCIUM *mg/dL*	8.45 (1.11–9.7)	7.75(6.0–9.1)	8.8 (1.11–9.7)	0.066
MAGNESIUM *mg/dL*	1.83 (1.11–2.98)	1.88 (1.11–2.57)	1.83 (1.36–2.98)	0.736
URIC ACID *mg/dL*	3.7 (1.3–12.3)	4.0 (2.6–12.3)	3.7(1.3–8.0)	0.281
CRP *mg/L*	82.5 (1.3–316)	145 (41.3–316)	78.0 (1.3–229)	0.093
PROCALCITONIN *μg/L*	0.70(0.04–24.4)	2.97 (0.69–24.4)	0.195(0.04–3.64)	**0.004**
PH	7.43 (7.10–7.55)	7.38 (7.1–7.55)	7.43 (7.37–7.50)	0.209
PCO_2 *mmHg*	36.0 (26.2–50.5)	30.6 (26.41.1)	39.3 (27.1–50.5)	**0.009**
HCO_3 *mmol/L*	24.6 (12.7–29.7)	18.1 (12.7–27.8)	25.4(19.2–29.7)	**0.004**
HGB *g/dL*	12.1 (8.00–17.1)	9.85 (8.0–16.7)	12.7 (8.5–17.1)	0.079
PLT $10^3/\mu L$	248 (110–857)	216 (110–404)	262(144–857)	0.134

*Mann-Whitney *U* Test. Serum Creatinine (CREATININE), Creatine Kinase (CK), Lactate Dehydrogenase (LDH), Aspartate Aminotransferase (AST), Alanine Transaminase (ALT), International Normalized Ratio (INR), C-reactive protein (CRP), Partial Pressure of Carbon Dioxide (PCO_2), Bicarbonate (HCO_3), Hemoglobin (HGB), Platelet Count (PLT).

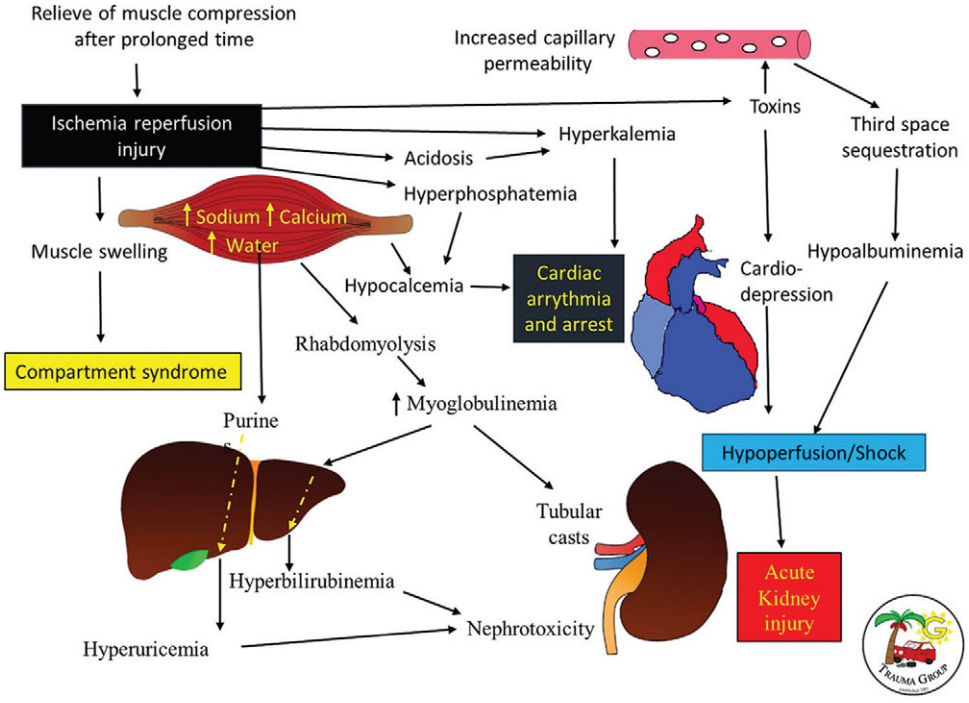

Figure 2. The pathophysiology and mechanisms of the crush syndrome, rhabdomyolysis, and acute kidney injuries.[1] (CC BY-NC-SA 4.0).

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endpoints. As a conclusion of the study, a scoring tool was developed using age, gender, etiology of rhabdomyolysis, creatinine, CK, phosphate, calcium, and bicarbonate levels.[3] In a 10-year cohort study conducted by Simpson et al., it was reported that a McMahon Score of 6 or higher was 68% specific and 86% sensitive in predicting RRT.[5] In this study, 72% (*n*:8) of the patients (*n*:11) who had a score ≥6 required RRT. In our study, we showed that, like Simpson's study, the McMahon Score may be useful in predicting the need for RRT in rhabdomyolysis that develops after a major disaster such as an earthquake.

In the literature, there are some studies reporting a relationship between elevated procalcitonin levels and the development of acute and chronic kidney damage. However, no study was detected reporting a relationship between renal outcomes such as elevated procalcitonin and renal replacement therapy in rhabdomyolysis patients.[10,11] In this study, procalcitonin levels were found to be significantly higher in patients who received renal replacement therapy than in those who did not. Some of the patients with elevated procalcitonin met the criteria for SIRS and sepsis, but no patient developed septic shock. Because the patients needed RRT in the first 3 days, we think that AKI was caused by rhabdomyolysis rather than sepsis. Antibiotics were started in all patients with a procalcitonin >0.5 μg/L and/or undergoing surgical procedures. In our patients followed up with crush injuries, those with procalcitonin >0.5 μg/L and/or those who underwent surgical procedures, care was taken to initiate non-nephrotoxic antibiotics such as ceftriaxone, ampicillin sulbactam, and piperacillin tazobactam.

CK is among the main markers that indicate muscle damage and is the main biochemical parameter used in the diagnosis of rhabdomyolysis. Although it is traditionally considered that higher values are associated with AKI and the need for RRT, there are also studies reporting that this is not always the case.[5,12–15] In our study, we found that the admission CK value was not related to the need for RRT. The development of acute kidney disease is a multifactorial event. Therefore, we think that a scoring system such as McMahon, which includes both the amount of muscle destruction biomarkers such as CK and phosphate and patient-related parameters such as age and genetic factors, is more reliable in determining rhabdomyolysis-related acute kidney disease and the need for renal replacement therapy.

In our study, 42% (*n*:12) of the patients had AKI, and 28% (*n*:8) required RRT. In the study that was conducted by Aslan et al. with patients in intensive care units, this rate was reported as 83% for AKI and as 33% for RRT.[16] The high rate of AKI can be explained by the high AKI rates in patients who need intensive care. When the data from past earthquakes were evaluated, the AKI rate varied between 2% and 25%.[17] In a single-center study that investigated 1100 emergency applications during the last earthquake, AKI was detected in 15% of patients who had crush injuries.[18] The lower rate compared to the present study can be explained by the inclusion of all crush injuries, not just those with rhabdomyolysis. A total of 67% of the patients who developed AKI required RRT in the present study, while this rate was 63% in the Kashmir earthquake and 80% in the Marmara earthquake.[19]

Despite the magnitude of the earthquake and the high number of injured people, the number of patients is relatively low because of the geographical distance of the hospital where the study was conducted to the epicenter of the earthquake. This was the main limitation of the present study. The patients could be monitored more closely, and their clinical conditions could be recorded because the hospital was away from the chaos in the earthquake zone and had a low earthquake victim load, which was the strength of the study.

In conclusion, it is difficult to comply with pre-prepared protocols in the event of a disaster, even if they have been prepared in advance, so the procedures should be simplified. The McMahon score should be calculated at the first hospital of admission and patients with a score of 6 and above should be referred to hospitals with RRT capabilities. Prioritizing the transfer of patients with high McMahon Scores may reduce mortality and morbidity because the need for RRT is likely to occur within the first 3 days. In case of lack of equipment and personnel, it may be safer to follow up patients with a McMahon score of 5 and below in primary care and local hospitals.

Supplementary material. To view supplementary material for this article, please visit http://doi.org/10.1017/dmp.2024.263.

Author contribution. Akif Bayyigit: conceptualization of research idea, goals, and aims; verification of the study outputs, writing and collection of data access requests and research ethics application; writing the original draft of manuscript and conducting revisions based on feedback; management and coordination of study planning and execution. F. Hande Gunay: formal statistical analyses including application of statistical techniques to synthesize study data; provision of computing resources and analytical tools; data curation including production, maintenance, and storage of research data. E. Belen Karmis: provision of computing resources and analytical tools; data curation including production, maintenance, and storage of research data. Zekeriya Ervatan: feedback including review and editing of pre-publication stages of the current manuscript. Mustafa Yerli: conceptualization of study goals and methodology; validation of study validity and outputs; contribution to statistical analyses and data collection. M. Gulay Kadioglu Kocak: feedback throughout study completion; supervision including mentorship and leadership of study outputs and execution; feedback including review and editing of pre-publication stages of the current manuscript.

Competing interest. None declared.

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