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RESEARCH

Factors predicting kidney replacement therapy in pediatric earthquake victims with crush syndrome in the first week following rescue

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Abstract

Crush syndrome due to traumatic rhabdomyolysis is one of the most significant problems to occur following earthquakes. On February 6, 2023, millions of people in Turkey were affected by two consecutive Kahramanmaraş earthquakes. The present study reports the analysis of clinical and laboratory findings of crush syndrome in pediatric earthquake victims admitted to our hospital from our region where the earthquake had a devastating effect. Clinical and laboratory findings concerning earthquake victims with crush syndrome were analyzed within the first week to determine what factors are predictive of kidney replacement therapy (KRT). The data of patients were retrospectively collected from medical records. A total of 310 children were admitted as earthquake victims to the pediatric emergency department. Ninety-seven (31%) of these patients had crush syndrome. Fifty-three (55%) of those with crush syndrome were female. The mean age was 10.9 ± 4.7 years, and the mean time under the rubble was 30.6 ± 23.8 h. Twenty-two patients (23%) required KRT. Hemodialysis was applied to 16 (73%) of them, and hemodiafiltration was applied to the other six (27%) in the pediatric intensive care unit. Regarding creatine kinase (CK) levels, the area under the receiver operating characteristic (ROC) curve (AUC) for predicting KRT was 0.905 (95% confidence interval [CI] 0.848–0.963; $p < 0.001$). The optimal cut-off value was 40,000 U/L with a sensitivity of 86% and a specificity of 83%. In terms of the percentage of body area crushed, the AUC for predicting KRT was 0.907 (95% CI 0.838–0.976; $p < 0.001$). The optimal cut-off value was 30% with a sensitivity of 86% and a specificity of 88%. Multiple logistic regression analysis showed that each 10% increase in body area crushed (OR 4.16, 95% CI 1.58–10.93, $p = 0.004$) and 1 mg/dl increase in the serum phosphorus level (OR 4.19, 95% CI 1.71–10.28, $p = 0.002$) were significant risk factors for dialysis treatment.

Conclusions: Crush syndrome and kidney problems are common following disasters like earthquakes. Clinical and laboratory findings at admission can predict dialysis requirement in earthquake victims. While CK elevation, body area crushed percentage, and increased phosphorus level were predictive of dialysis treatment, time under the rubble was not. Even if the patients were under the rubble for a short time, acute kidney injury (AKI) may develop as a result of severe hypovolemia due to crush injuries, and patients may need KRT.

What is Known:

- *Crush syndrome after earthquakes needs to be treated carefully in victims and can cause AKI and mortality when not treated timely and appropriately.*

What is New:

- *CK level elevation, body area crushed percentage, and increased phosphorus level are predictive of dialysis treatment.*
- *The time under the rubble may not be predictive of dialysis requirement.*

Keywords Earthquake · Crush syndrome · Dialysis · Children

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Abbreviations

AKI	Acute kidney injury
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUC	Area under the ROC curve
BUN	Blood urea nitrogen
CI	Confidence interval
CK	Creatine kinase
CVVHDF	Continuous veno-venous hemodiafiltration
eGFR	Estimated glomerular filtration rate
IQR	Interquartile range
KRT	Kidney replacement therapy
OR	Odds ratio
PD	Peritoneal dialysis
ROC	Receiver operating characteristic
SD	Standard deviation

Introduction

On February 6, 2023, millions of people in Turkey were affected by two consecutive Kahramanmaraş earthquakes, which occurred at 04.17 and 13.24 (both local time) and registered as magnitude 7.7 and 7.6 on the Richter scale, respectively. There was widespread damage in an area of about 350,000 km^2 in the eastern Mediterranean, and the eastern and southeastern Anatolian regions of Turkey were also impacted. A total of 14 million people were affected by these two devastating earthquakes and the official death toll reported so far is 50,783. Although three months have passed since the Kahramanmaraş earthquakes, more than 33,000 aftershocks of up to 6.7 Mw have since occurred.

Crush syndrome is one of the most noteworthy problems to arise after natural disasters due to traumatic rhabdomyolysis. Crush injuries following earthquakes develop if the muscles are crushed under the rubble and toxic intracellular components such as potassium, myoglobin, phosphorus, and nucleotides are released into the systemic circulation from the muscles [1, 2]. In addition, large amounts of body water are stored in injured muscles due to inflammation, causing severe hypovolemia resulting in hypoperfusion of the kidneys and leading to acute kidney injury (AKI) [2, 3]. While excessive calcium entering muscle cells can cause membrane phospholipid damage, decreased circulation of calcium can cause cardiac arrhythmias, worsening kidney hypoperfusion and thus contributing to AKI [3]. Earthquake victims may develop AKI in various ways. For example, functional AKI may develop as a result of severe dehydration due to the victim spending a long time under the rubble or hemorrhaging due to severe injury, while intrinsic AKI may develop due to toxins, sepsis, and arrhythmia. Postrenal AKI can also develop due to obstruction in patients with pelvic trauma [4, 5]. AKI as a result of crush syndrome in earthquake victims is a complex and difficult condition to manage, especially in the first few days [5, 6].

After the two devastating earthquakes, crush syndrome developed in 97 of the 310 pediatric earthquake victims who were transported to our hospital. The present study reports the analysis of clinical and laboratory findings of the victims with crush syndrome within the first week.

Materials and methods

Background

Cukurova University Balcali Hospital was the closest third-level reference hospital to Hatay, one of the provinces that experienced the most devastating effects of the earthquakes. Our hospital has a capacity of 1,200 beds and usually works at full capacity. After the disaster, most of the beds were reserved for the earthquake victims. Patients on a chronic dialysis program in our hemodialysis unit were transferred to other centers immediately and our hemodialysis unit was made ready to serve earthquake victims with 21 hemodialysis machines. Moderate damage occurred in our hospital due to subsequent aftershocks, and it unfortunately had to be evacuated 15 days after the earthquakes occurred.

Hemodialysis patients whose dialysis centers collapsed were transferred for routine dialysis to other centers by central organization. Some of our peritoneal dialysis (PD) patients' houses had collapsed, and their dialysis machines as well as their PD fluids and drugs were left under the rubble. Thus, new PD fluids were supplied to the patients and new programs were prescribed.

Clinical and laboratory data

A total of 1,192 patients were admitted with a diagnosis of earthquake victim (ICD-10 code X34) to the emergency department of Cukurova University Balcali Hospital. In total, 360 of them were 0–18 years old. Fifty newborns who were transferred to our hospital from damaged neonatal intensive care units were excluded from the analysis. Crush syndrome developed in 97 of the 310 children.

A retrospective analysis of medical records was performed for these 97 children. Data regarding sex, age, time under the rubble, vital signs at admission, clinical findings (daily urine output, percentage of body area crushed, number of traumatized extremities), need for surgery (fasciotomy and/or amputations), need for erythrocyte and/or albumin transfusions, and need for kidney replacement therapy (KRT) were recorded. The patients had no known drug usage, any comorbidity or exercise history that could induce crush syndrome. Daily laboratory data for the first

week—including blood urea nitrogen (BUN), creatinine, sodium, potassium, calcium, phosphorus, uric acid, creatine kinase (CK), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and albumin—were also recorded. The estimated glomerular filtration rate (eGFR) was calculated using the Schwartz formula [7]. The percentage of body area of the patients crushed was calculated using the rule of nines [8]. Crush syndrome was defined as crush injury to a large mass of skeletal muscle, systemic manifestations such as AKI and electrolyte disturbances, and peak CK > 1000 U/L at admission [3, 4].

The clinical conditions of the patients were evaluated at admission and 2,000–3,000 ml/m^2 alkalized 0.45% saline per day was started immediately. Sodium bicarbonate was added (50 mEq per liter) and the treatment dose was adjusted according to the follow-up blood and urine pH values. Daily urine output was monitored. The need for KRT was determined by evaluating the clinical and laboratory findings. Intermittent hemodialysis was performed in stable patients who required KRT and continuous veno-venous hemodiafiltration (CVVHDF) was performed in clinically unstable patients. Hemodialysis access was provided by inserting a temporary central venous catheter.

This retrospective study was approved by the Ethical Committee of the University Medical Faculty (05–05-2023–133/12).

Statistical analysis

Continuous variables were summarized as the mean and standard deviation when normally distributed and as the median and interquartile range when non-normally distributed. The normality of distribution for continuous variables was confirmed by the Shapiro–Wilk test. Categorical variables were expressed as numbers and percentages. For comparison of continuous variables between two groups, Student's t-test or the Mann–Whitney U test were used where appropriate. Correlations between numeric variables that distributed normally and non-normally were evaluated by Pearson simple correlation coefficient and Spearman's rank correlation coefficient, respectively. Differences between group proportions were evaluated by chi-square test or Fisher's exact test where appropriate. Multiple logistic regression analysis was performed to determine risk factors for KRT requirement. In univariate analysis, variables significant at the $p < 0.25$ level were entered in stepwise logistic regression analysis [9]. In addition, the laboratory parameters with statistical significance in univariate analysis were calculated by receiver operating characteristic (ROC) curves to identify a cut-off value. We did complete case analysis for some measurements (due to missing cases). All analyses were performed using the IBM SPSS 20.0 software package. The level of statistical significance for all tests was 0.05.

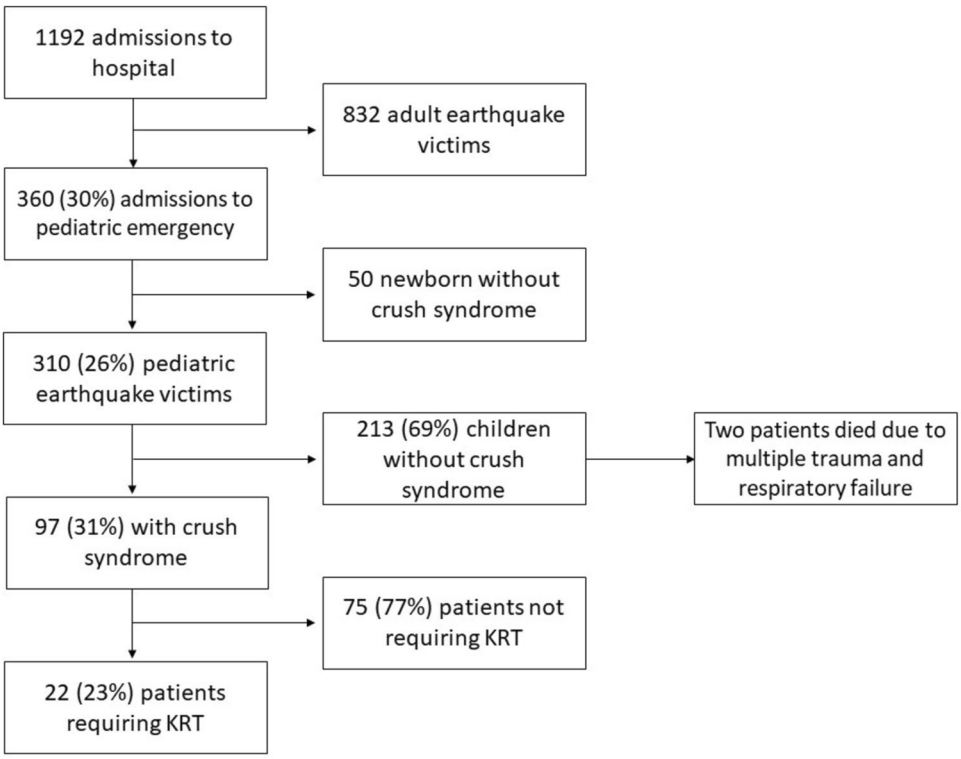

Fig. 1 Flowchart of patients

Table 1 Demographic and clinical characteristics of patients who required dialysis and those who did not

	Patients who required dialysis (n = 22)	Patients who did not require dialysis (n = 75)	p-value
Age (years), mean ± SD	13.4 ± 4.4	10.2 ± 4.6	**0.038**
Sex (M/F), n	9/13	35/40	0.808
Time under the rubble (hours), mean ± SD	30.6 ± 18.0	30.5 ± 25.4	0.993
Urine output in first 24 h (ml/kg/h), median (IQR)	0.59 (1.31)	2.1 (2.02)	**< 0.001**
Body area crushed (%), mean ± SD	39.9 ± 11.3	14.7 ± 13.01	**< 0.001**
Number of traumatized extremities, median (IQR)	2 (0)	1 (1)	**< 0.001**
Presence of fasciotomy, n (%)	3 (13.6)	11 (14.7)	0.596
Presence of amputations, n (%)	12 (54.5)	12 (16)	**0.001**
Body temperature (°C), mean ± SD	36.3 ± 0.5	36.6 ± 0.36	**0.028**
Systolic blood pressure (mmHg), mean ± SD	106 ± 20	105 ± 14	0.962
Systolic blood pressure percentile, median (IQR)	33 (62.5)	66 (58)	0.116
Diastolic blood pressure (mmHg), mean ± SD	63 ± 15	65 ± 10	0.799
Diastolic blood pressure percentile, median (IQR)	32 (62.5)	71 (51)	0.052
Mean blood pressure (mmHg), mean ± SD	77 ± 17	78 ± 10	0.993
Heart rate (bpm), mean ± SD	116 ± 23	114 ± 18	**0.023**
Blood transfusion numbers, median (IQR)	1.5 (2)	0 (1)	**< 0.001**
Human albumin transfusion numbers, median (IQR)	2 (3)	0 (0)	**< 0.001**

SD standard deviation, *IQR* interquartile range

Statistically significant parameters were shown in bold

Results

A total of 310 children were admitted as earthquake victims to Cukurova University Balcali Hospital's pediatric emergency department. Ninety-seven (31%) of these patients had crush syndrome (Fig. 1). Seventy (72%) of the patients with crush syndrome were admitted to hospital within the first three days. Fifty-three (55%) of the children were female and 44 (45%) were male. The mean age was 10.9 ± 4.7 years. The mean time under the rubble was 30.6 ± 23.8 h. Thirty-six (37%) patients with crush syndrome had a single extremity injury, while 44 (45%) patients had more than one extremity injury. Within a few hours of admission, one patient died due to severe multiple trauma,

Table 2 Initial laboratory data of patients who required dialysis and those who did not

Laboratory results at admission	Patients who required dialysis (n = 22)	Patients who did not require dialysis (n = 75)	p-value
BUN (mg/dL)	64.1 ± 20.4	22.8 ± 19.2	**< 0.001**
Creatinine (mg/dL)	2.47 ± 1.13	0.53 ± 0.44	**< 0.001**
eGFR (mL/min/1.73 m^2)	30.7 ± 15.7	149.3 ± 75.3	**< 0.001**
CK (U/L)	111,855 ± 148,734	24,561 ± 33,283	**< 0.001**
AST (U/L)	1,474 ± 771.3	444.3 ± 440.6	**< 0.001**
ALT (U/L)	473 ± 288.5	198 ± 293.6	**< 0.001**
Albumin (g/L)	28.4 ± 6.61	33.9 ± 7.7	**0.003**
Sodium (mmol/L)	134.9 ± 10.5	137.7 ± 5.1	**0.026**
Potassium (mmol/L)	6.5 ± 0.74	4.4 ± 0.76	**< 0.001**
Calcium (mg/dL)	7.3 ± 1.2	8.7 ± 1.1	**< 0.001**
Phosphorus (mg/dL)	9.9 ± 2.9	4.31 ± 1.46	**< 0.001**
Uric acid (mg/dL)	14.5 ± 4.4	7.3 ± 4.3	**< 0.001**

BUN blood urea nitrogen, *eGFR* estimated glomerular filtration rate, *CK* creatine kinase, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase

Statistically significant parameters were shown in bold

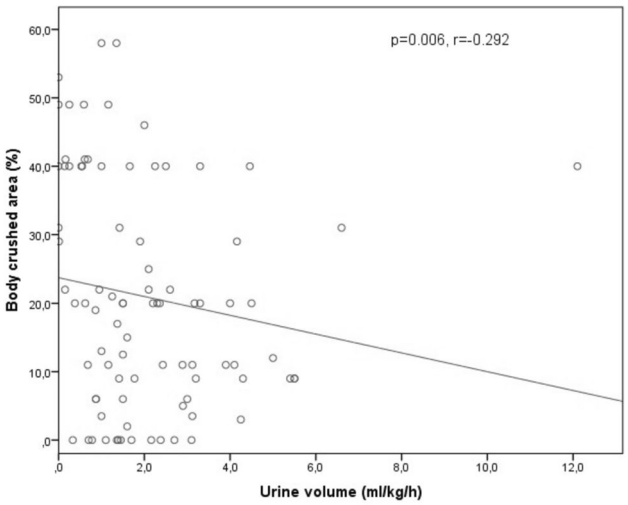

Fig. 2 Correlations between urine volume in the first 24 h and body area crushed

while one patient with cerebral palsy died due to respiratory failure. Fasciotomy was performed in 14 (14%) patients and amputation was performed in 24 (25%) patients. Twenty-two patients (23%) required KRT. Hemodialysis was applied to 16 (73%) of them, and hemodiafiltration was applied to the other six (27%) in the pediatric intensive care unit. The demographic and clinical characteristics of patients who required dialysis and those who did not are listed in Table 1. Initial BUN, creatinine, CK, AST, ALT, potassium, phosphorus, and uric acid levels were found to be significantly higher in patients requiring dialysis than in those who did not require it. Initial eGFR, albumin, sodium, and calcium levels were recorded as significantly lower in those requiring dialysis than in those not requiring it (Table 2). There was no significant difference in terms of blood and albumin transfusion numbers in patients who had fasciotomy compared to those who did not ($p = 0.968$ and $p = 0.652$, respectively), but the number of blood and albumin transfusions was found to be significantly higher in patients who underwent amputation compared to those who did not ($p < 0.001$ and $p < 0.001$, respectively).

Twelve (12%) of the patients had oliguria in the first 24 h of admission. Urinary volume in the first 24 h following admission correlated negatively with admission BUN ($r = -0.396$, $p < 0.001$), creatinine ($r = -0.405$, $p < 0.001$), potassium ($r = -0.359$, $p < 0.001$), phosphorus ($r = -0.347$, $p = 0.001$), uric acid ($r = -0.349$, $p = 0.001$), the percentage of body area crushed ($r = -0.292$, $p = 0.006$, Fig. 2) and the number of dialysis sessions ($r = -0.301$, $p = 0.005$). There was a moderate positive correlation between serum creatinine and CK levels at admission ($r = 0.609$, $p < 0.001$, Fig. 3a). The serum creatinine and CK levels of patients who required KRT and those who did not can be seen in Fig. 3b. The CK levels of the patients were examined daily during the first week. It was observed that CK values started to decrease from the second day. The daily CK levels of patients who required KRT and those who did not are shown in Fig. 4.

In regard to CK levels, the area under the ROC curve (AUC) for predicting KRT was 0.905 (95% confidence interval [CI] 0.848–0.963; $p < 0.001$). The optimal cut-off value was 40,000 U/L with a sensitivity of 86% and a

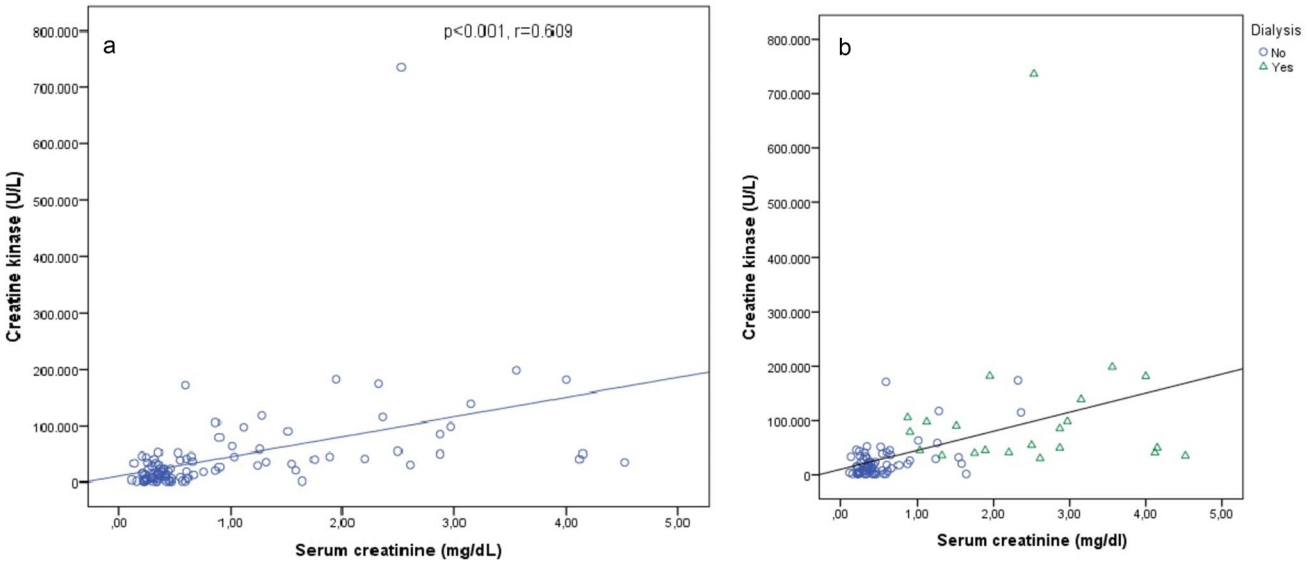

Fig. 3 **a** Correlations between serum creatinine and creatine kinase levels at admission **b** Plot of creatine kinase vs. serum creatinine in patients who required kidney replacement therapy and those who did not

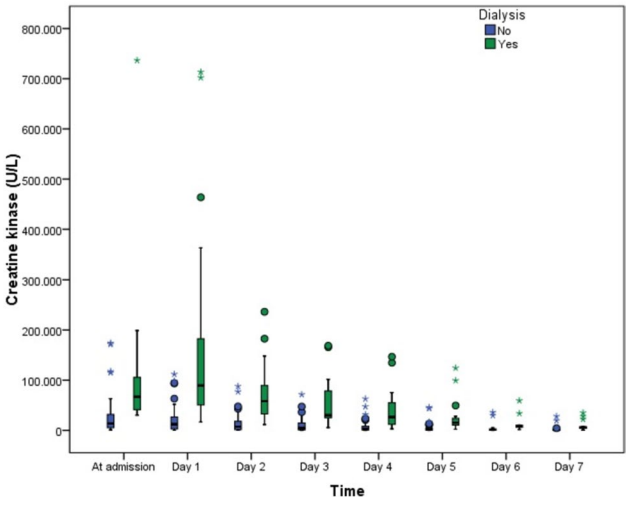

Fig. 4 Boxplots of daily CK levels in patients who required kidney replacement therapy and those who did not, box represents interquartile range (IQR) with line at the median and, while circle and asterisks represent outliers and extreme outliers, respectively

specificity of 83%. In terms of the percentage of body area crushed, the AUC for predicting KRT was 0.907 (95% CI 0.838–0.976; $p < 0.001$). The optimal cut-off value was 30% with a sensitivity of 86% and a specificity of 88%.

Multiple logistic regression analysis showed that each 10% increase in body area crushed (Odds ratio [OR] 4.16, 95% CI 1.58–10.93, $p = 0.004$) and 1 mg/dl increase in the serum phosphorus level (OR 4.19, 95% CI 1.71–10.28, $p = 0.002$) were significant risk factors for dialysis treatment.

Discussion

Crush syndrome is an important condition that needs to be treated carefully in earthquake victims. If not treated timely and appropriately, it can result in AKI and mortality. In this study, the clinical and laboratory findings obtained for 97 pediatric earthquake victims with crush syndrome were evaluated to determine factors predictive of KRT.

Crush syndrome developed in 31% of all pediatric earthquake victims who were transferred to our hospital, and 23% of them required KRT. According to data in relation to the Marmara earthquake, 12% of all hospitalized patients developed kidney problems and 8.9% needed KRT [10]. It was also reported that crush syndrome developed in half of the pediatric earthquake victims treated in a center following the Marmara earthquake, with 20% of the victims requiring KRT [11]. In addition, crush syndrome was reported in 25% of pediatric earthquake victims following an earthquake in Wenchuan [12]. The ages of the victims included in the reported studies, the time the earthquake occurred, time under the rubble, and the treatment strategies used could be possible reasons for the different rates of crush syndrome.

In the case of the Marmara earthquake, the mean time earthquake victims and pediatric earthquake victims spent under the rubble was reported as 11.7 ± 14.3 h and 17.9 ± 5.1 h, respectively [11, 13]. In the present study, the mean time under the rubble was determined to be 30.6 ± 23.8 h. The extended length of time under the rubble in this case compared to the aforementioned case is believed to be because the Kahramanmaraş earthquakes seriously affected 10 provinces and rescue efforts were carried out in a very large area. There are differing opinions about the relationship between time under the rubble and kidney failure. Some studies have reported that those with AKI spent a longer time under the rubble [14], while other studies have reported that those who needed dialysis were under the rubble for a shorter time than those who did not [13, 15, 16]. In the present study, time spent under the rubble was not found to be different in patients with crush syndrome who required dialysis compared to those who did not. This may be due to the relatively low number of patients in a single center compared to the number of patients in multicenter studies.

Some of our patients who required dialysis were rescued from the rubble within a few hours, which can be considered a relatively very short time. After being rescued, they were admitted to the local hospital for primary care and were sent home as their injuries were mild. When they applied to the hospital again due to oliguria, they were found to have kidney failure and were transferred to our hospital. They had crush injuries at lower extremities that did not require fasciotomy, so massive amounts of body water were stored in the muscles, causing severe hypovolemia and AKI. While these patients were transferred from our hospital on the 13th day after admission due to the evacuation of the hospital, they still had oliguria and required KRT. Similar observations and comments have previously been reported in the literature [10, 17, 18]. It is thought that this situation may be due to a lack of appropriate treatment right after the victims were rescued, hypovolemia due to crush injury, and a lack of nephrological follow-up due to limited facilities. It should also be kept in mind that patients with severe edema in the extremities due to crush injury are at risk for AKI as long as hypovolemia continues. These patients require aggressive fluid treatment to prevent crush syndrome and AKI, and close nephrological follow-up should be provided to them in case of early discharge from the hospital.

The rate of amputations was significantly higher in patients requiring dialysis in the present study. Sever et al. reported that the presence or absence of amputations did not differ significantly between dialyzed and non-dialyzed victims [10]. In addition, Hu et al. reported that the amputation rate was higher in patients with AKI than in those without; however, fasciotomy did not differ among patients with or

without AKI in the case of the Sichuan earthquake [19]. Surgical treatments such as amputation and fasciotomy were more common in patients with severe trauma-related kidney problems. Rhabdomyolysis due to severe trauma could be the cause of AKI, while the surgical intervention itself could increase the risk of AKI and the need for dialysis in patients.

In our study, patients who required dialysis had a higher percentage of body area crushed, a higher number of traumatized extremities, a higher level of serum CK, and a lower urine output in the first 24 h than patients who did not require dialysis. This shows that the severity of the extremity trauma and high percentages of body area crushed are predictive of kidney problems that will require dialysis in earthquake victims.

There was a correlation between serum creatinine and CK levels at admission. CK levels were significantly higher at admission in patients who required dialysis. The present study showed that CK levels greater than 40,000 U/L predict the probability of requiring dialysis with 86% sensitivity and 83% specificity. Najafi et al. showed that a formula using CK, potassium, lactate dehydrogenase, and uric acid levels on the first day of hospitalization could predict the probability of the development of AKI on the third day of hospitalization with 97% sensitivity and 96% specificity [20]. Similarly, Oda et al. reported that CK levels increased with the number of traumatized extremities and patients with CK levels greater than 75,000 U/L had worse outcomes [17]. In fact, as expected, excessive elevation of CK because of extensive muscle damage was found to be associated with AKI, need for dialysis, and poor prognosis in earthquake victims.

In the present study, the percentage of body area crushed was found to be higher in patients who required dialysis than in those who did not. In addition, it was found that every 10% increase in this percentage increased the need for dialysis 4.16 times. In contrast, Kantarci et al. calculated the body crush percentage in a way similar to that used in the present study and found a similar rate in patients with crush syndrome who required dialysis and those who did not [15]. The body area crushed percentage can be easily calculated when the patient is first seen. According to our results, it predicts the need for dialysis. Therefore, we thought that calculating the percentage could quickly provide information regarding dialysis requirement before laboratory results are seen and allow for the identification of victims at risk.

Our study has some limitations. First, it utilized a retrospective design focusing on a single center. Second, the long-term outcomes and mortality rates of the patients could not be evaluated. The strengths of the study are the first week of daily evaluations of the earthquake victims from admission and determining the importance of the evaluations at the time of diagnosis to predict dialysis requirement.

Conclusion

Crush syndrome and kidney problems are common following natural disasters such as earthquakes. However, not all earthquake victims have rhabdomyolysis, not all victims with rhabdomyolysis have crush syndrome, and not all victims with crush syndrome have AKI. The clinical and laboratory findings at admission can predict dialysis requirement in earthquake victims. While CK elevation, body area crushed percentage, and increased phosphorus level were found to be predictive of dialysis treatment, the time spent under the rubble was not. Even if the patients were only under the rubble for a short time, AKI may develop as a result of severe hypovolemia due to crush injuries, and the patients may need KRT. Therefore, the development of AKI in earthquake victims at risk can be prevented with appropriate fluid therapy after rescue. Earthquakes are natural disasters and cannot be prevented; however, the damage they cause can be reduced if precautions are taken.

Authors' contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Bahriye Atmis, Aysun K. Bayazit, Cagla Cagli Piskin, Emel Saribas, Ferhat Can Piskin, Sevcan Bilen, Ilker Unal and Dincer Yildizdas. The first draft of the manuscript was written by Bahriye Atmis and Aysun K. Bayazit, all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval All procedures involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee, in addition to the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The study was approved by the Ethical Committee of the University Medical Faculty (05–05-2023–133/12).

Competing interests The authors declare no competing interests.

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