

Early and Vigorous Fluid Resuscitation Prevents Acute Renal Failure in the Crush Victims of Catastrophic Earthquakes

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Abstract. This study analyzes the effects of fluid resuscitation in the crush victims of the Bingol earthquake, which occurred in May 2003 in southeastern Turkey. Questionnaires asking about demographic, clinical, laboratory, and therapeutic features of 16 crush victims were filled in retrospectively. Mean duration under the rubble was 10.3 ± 7 h, and all patients had severe rhabdomyolysis. Fourteen patients were receiving isotonic saline at admission, which was followed by mannitol-alkaline fluid resuscitation. All but two patients were polyuric. Admission serum creatinine level was lower than and higher than 1.5 mg/dl in 11 and 5 patients, respectively. Marked elevations were noted in muscle enzymes in all patients. Dur-

ing the clinical course, hypokalemia was observed in nine patients, all of whom needed energetic potassium chloride replacement. Four (25%) of 16 victims required hemodialysis. Duration between rescue and initiation of fluids was significantly longer in the dialyzed victims as compared with non-dialyzed ones (9.3 ± 1.7 versus 3.7 ± 3.3 h, $P < 0.03$). Sixteen fasciotomies were performed in 11 patients (68%), nine of which were complicated by wound infections. All patients survived and were discharged from the hospital with good renal function. Early and vigorous fluid resuscitation followed by mannitol-alkaline diuresis prevents acute renal failure in crush victims, resulting in a more favorable outcome.

After catastrophic earthquakes, many of the rescued victims later die because of preventable or treatable medical causes, most importantly due to hyperkalemia and acute renal failure (ARF) as a result of rhabdomyolysis (1). This ARF is a major component of crush syndrome, which is the second most frequent cause of mortality after the direct effect of trauma after disasters (2). Thus, calculated mortality rates of up to 40% have been reported in crush victims with ARF who require renal replacement therapy (RRT) (3,4).

The pathogenesis of myoglobinuric ARF after pressure-induced rhabdomyolysis has been extensively studied. As soon as the victim is evacuated from the rubble and perfusion of the traumatized extremity is restored, large amounts of fluid penetrate the injured muscles. The consequence of this fluid influx is hypovolemia and hemodynamic shock, which results in prerenal and later intrarenal ARF (1). In addition to hypovolemia, renal vasoconstriction and heme-protein-induced nephrocytotoxicity as well as intratubular cast formation can contribute to myoglobinuric ARF (1,5). Because hypovolemia is the key component of this syndrome, early and generous

fluid replacement has been suggested as the most effective method for preventing ARF related to crush syndrome. However, if this treatment is inadequate or delayed for more than 6 h, ARF is almost inevitable (1).

The city of Bingol, Turkey, located in the southeastern part of the country, was hit by a catastrophic earthquake on May 1, 2003, at 03:27 a.m. local time. The disaster registered 6.4 on the Richter scale and lasted for 17 s. According to the official statistics, 177 people died and 519 were injured, many of whom were students sleeping in the dormitory of their school (6). Seventeen victims had extensive muscle injury and were candidates for a diagnosis of crush syndrome. Twelve of these 17 victims were the above-mentioned students, 11 of whom were treated in our facility; 5 of the 17 victims were adults trapped in their homes. Of these patients, one was treated in Diyarbakir Dicle University Hospital. The remaining 16 were treated in Elazig at Firat University Hospital. This study documents the epidemiologic, clinical, and laboratory features and therapeutic interventions applied to 16 crush victims who were treated in the latter facility.

Patients and Methods

The Disaster

The city of Bingol, the epicenter of the disaster, with a population of 70,000 people, is close to the East Anatolian Fault Zone, which has historically been the location of many catastrophic earthquakes (7). Overall, this region is a sparsely populated, rural area that includes some of the other major cities of the country, such as Elazig, Diyarba-

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kir, and Erzurum, which are 130, 140, and 180 km distant from the earthquake's epicenter, respectively.

In the city center, 305 buildings completely collapsed during the primary event, 2566 buildings were moderately damaged and uninhabitable, and another 2546 were slightly damaged and habitable. The aftermath of the disaster was characterized by disruption of the city's electricity and water supplies. Three hospitals in the city center were also heavily damaged and were not at all effective after the disaster. Fortunately, the main roads from the epicenter to the neighboring cities were not damaged; thus, help and rescue teams could reach the area in the early morning of the same day. The rescue activities were mainly organized by the Turkish army; civilian national rescue teams also contributed to rescue efforts.

Initial Medical Interventions and Traffic of the Crush Victims

In the early morning of the disaster, on-call instructions were provided to the chief of the state hospital regarding early fluid resuscitation of crush victims by the local coordinator (M.S.S.) of the Renal Disaster Relief Task Force (RDRTF) of the International Society of Nephrology (ISN) and the Turkish Society of Nephrology (TSN). The transportation of these victims to neighboring cities as early as possible was also suggested. Two nephrologists from the Firat University Medical Faculty, experienced in the treatment of crush syndrome, arrived at the disaster area 8 h after the earthquake. They were not involved in rescue activities themselves. Rather, they visited the collapsed buildings to initiate the early treatment of crush victims. They registered 10 patients with crush injury, all of who were immediately administered fluid resuscitation, as described below. This team also organized the transport of these victims to their own facility (Firat University Medical Faculty, in the city of Elazig, 130 km from the epicenter). They also prescribed medical interventions during the victims' transportation.

In addition, six crush victims, who were rescued before the nephrology team had arrived to the disaster area, were transported to Elazig State Hospital. These patients were thereafter referred to Firat University Hospital.

Fluid Treatment Protocol

Early and vigorous fluid resuscitation was performed as described by Better and Stein (1). In this protocol, treatment is initiated with isotonic saline (1 L/h) even before the victim is extricated from the rubble, and an alkaline solution is initiated, which is prepared simply by adding 50 mmol of bicarbonate to each liter of hypotonic saline. In patients who pass adequate volumes of urine (urinary volume >20 ml/hr), 50 ml of 20% of mannitol is also added to each liter of this solution. The objectives of this protocol have been described as to maintain normal perfusion of kidneys and to alkalinize urine, thus preventing intratubular obstruction by myoglobin casts and by urate crystals, because hyperuricemia and hyperuricosuria are common complications of crush myopathy. Also, the mannitol component of this regimen can decompress and protect swollen muscle, thus reducing the leak of the nephrotoxic myoglobin and urate from the muscle, in addition to many other renal and extrarenal beneficial effects that have been described in detail elsewhere (8). The goal of this regimen is to maintain urine output more than 300 ml/h (1).

Follow-up of the Victims

All of the patients were managed by a team that included nephrologists, orthopedic surgeons, infectious disease specialists, plastic surgeons, and psychiatrists. After admission to hospitals, physical

examination was performed, followed by urgent electrocardiography to detect signs of hyperkalemia. Thereafter, blood was drawn for determining serum levels of urea nitrogen, creatinine, uric acid, electrolytes, total protein, albumin, aspartate aminotransferase, alanine aminotransferase, lactic dehydrogenase, and creatine phosphokinase (CK). When measuring serum CK, dilutions could not be made in all patients because of the chaotic circumstances of the disaster and patient overload. Thus, some values were reported as higher than 5000, 10,000, or 20,000 U/L. In all patients, original fluid therapy was sustained according to the protocol described above.

After initial evaluation, three seriously wounded patients were referred to the intensive care unit. The other victims were followed up in the nephrology wards after undergoing basic surgical procedures. During the first week of follow-up, biochemical parameters and acid-base status of the patients were studied four times a day in all of the victims; frequencies of laboratory examinations were individualized thereafter.

Data Collection and Definitions

To analyze the severity and magnitude of the problem, the same questionnaire that was used in the analysis of the catastrophic Marmara disaster was used, which was prepared by the TSN in collaboration with the RDRTF of the ISN and has been defined in detail previously (9). In brief, the following definitions were used.

Crush Injury. Patients who were injured by collapsing material and debris and manifested muscle swelling (rhabdomyolysis) and/or neurologic disturbances in the affected parts of the body (10). For laboratory confirmation of rhabdomyolysis, serum levels of CK more than 1000 were essential (11).

Crush Syndrome. Patients with crush injury and systemic manifestations (4).

Nephrological Problem Due to Crush Injury. Patients who had crush injury and one of the following features: oliguria (urinary output <400 ml/d), elevated levels of BUN (>40 mg/dl), serum creatinine (>2.0 mg/dl), uric acid (>8 mg/dl), potassium (>6 mEq/L), phosphorus (P) (>8 mg/dl), or decreased serum calcium (<8 mg/dl).

Polyuria. Daily urinary output of more than 2000 ml.

Dialyzed Patients. Victims treated at least once by any form of RRT (intermittent hemodialysis, peritoneal dialysis, continuous arteriovenous or venovenous hemodialysis, or hemo(dia)filtration).

The indications for RRT were serum creatinine >8 mg/dl, BUN >100 mg/dl, serum potassium >7 mEq/L, serum bicarbonate <10 mEq/L, and clinical symptoms and findings attributed to ARF such as edema, hypertension, heart failure, nausea, and vomiting. The questionnaires were filled out after discharging the last patient from the hospital. All data were then analyzed.

Statistical Analyses

Descriptive statistics for all numeric variables, including means, SD, and minimum and maximum values, together with the proportions of all categorical variables, were calculated. Two independent group means were compared by means of the Mann-Whitney U test. Statistical significance was assigned at $P < 0.05$.

Results

Of the 16 patients, 12 were men and 4 were women with a mean age of 23 ± 13 (range, 13 to 51) yr. Mean time spent under the rubble was 10.3 ± 7 (range, 3 to 24) h.

Clinical Findings at Admission

Crush injuries were localized to arms in 4 victims, legs in 11 victims, and to both extremities in 1 victim. In nine patients, other traumas apart from crush injuries were noted, which were as follows: pelvic fracture ($n = 2$), first thoracic vertebra fracture ($n = 1$), open tibia fracture ($n = 1$), humerus fracture ($n = 1$), hemothorax ($n = 1$), spinal shock caused by blunt trauma to the spine ($n = 1$), laceration in the forearm muscles ($n = 1$), and pelvic and leg hematomas ($n = 2$).

At admission, mean body temperature was $36.8 \pm 0.5^\circ\text{C}$ (range, 36.5 to 37.7°C), and pulse was 93.2 ± 16.3 (range, 72 to 120) beats/min. Mean systolic and diastolic BP were 101.8 ± 18.6 (range, 70 to 130) and 66.2 ± 13.0 (range, 50 to 90) mmHg, respectively. Two of the 16 patients were hypotensive (70/40 and 80/50 mmHg), and these patients were also oliguric. Urine was myoglobinuric in all cases.

Laboratory Findings at Admission

Blood count was characterized by normal values of hematocrit and platelets, but mild leukocytosis (Table 1). In the biochemical analysis, admission serum creatinine level was <1.5 mg/dl in 11 of 16 victims and >1.5 mg/dl in the remaining 5 patients. Mean creatinine levels were found to be 1.2 ± 0.5 (range, 0.6 to 2.6) mg/dl, 1.1 ± 0.6 (range, 0.5 to 2.3) mg/dl, and 1.0 ± 0.6 (range, 0.4 to 2.5) mg/dl on the first, second, and third days of hospitalization, respectively. Marked elevations were noted in the serum levels of aspartate aminotransferase, alanine aminotransferase, lactic dehydrogenase, and CK (Table 1). Serum CK level was higher than 20,000 U/L in 12 patients. In the remaining four patients, this parameter ranged from 3100 to 14,900 U/L. Also, there was trend to hyperphosphatemia and hypoalbuminemia (Table 1).

Therapeutic Interventions

Fourteen patients were receiving isotonic saline (1 L/h) before admission to the hospital; vigorous mannitol-alkaline

solution was initiated thereafter. The fluid treatment protocol was stopped when urine color returned to normal. Three liters of saline per day were administered to the remaining two hypotensive patients; subsequently, their BP increased to 120/70 and 130/80 mmHg, but urinary volumes did not increase.

Renal Replacement Therapies

Four (25%) of 16 victims needed RRT. Intermittent hemodialysis was used for this procedure. The time between rescue and initiation of fluid treatment in the dialyzed patients was significantly longer as compared with nondialyzed patients (9.3 ± 1.7 versus 3.7 ± 3.3 h, $P < 0.03$). Mean volumes of administered fluids and collected urine within the first 3 d of hospitalization in the victims who needed and who did not need dialysis support are shown in Table 2.

Characteristics of Dialyzed Patients

The first patient, a 14-yr-old female student, had hypotension induced by spinal shock, massive intrapelvic hematoma, and compartmental syndrome at admission (70/40 mmHg). She also had fractures of the pelvis, respiratory failure due to pulmonary fat embolism, disseminated intravascular coagulation, and paraplegia (so she lost sphincter control). Fluid resuscitation was initiated 9 h after the rescue. Her BP increased, possibly by administration of fluids as well as high doses of corticosteroids to treat spinal shock. This complication improved on the second day of hospitalization. However, her urine volume did not increase, and so hemodialysis was initiated. A total of 31 sessions of hemodialysis were performed within a 34-d period.

The second patient, a 28-yr-old man, was referred from the Elazig State Hospital. His case was complicated by a pelvic fracture in addition to rhabdomyolysis. At admission, he was hypotensive (80/50 mmHg) secondary to hemothorax and compartmental syndrome. Mannitol-alkaline solution was begun

Table 1. Laboratory findings of the victims at admission ($n = 16$)

Parameter	Mean \pm SD	Minimum	Maximum
Blood count			
hematocrit (%)	44.7 ± 8.7	25	57
leukocyte (/mm ³)	$19,656 \pm 9236$	5800	37,800
platelets (/mm ³)	$288,375 \pm 88,567$	146,000	414,000
Serum biochemistry			
creatinine (mg/dl)	1.2 ± 0.5	0.6	2.6
uric acid (mg/dl)	8.3 ± 2.7	4.8	12
potassium (mEq/L)	4.8 ± 1.1	3.2	8.0
calcium (mg/dl)	6.9 ± 1.1	4.8	8
phosphorus (mg/dl)	6.0 ± 1.2	4.9	8.6
albumin (gr/dl)	2.8 ± 0.7	1.7	4.5
CK		3100	$>20,000$
AST (U/L)	803 ± 726	71	2764
ALT (U/L)	235 ± 188	31	760
LDH (U/L)	3634 ± 2713	648	10,295

Table 2. Mean volume of administered fluids and collected urine within the first 3 d of hospitalization in the victims who needed and did not need dialysis support

	Nondialyzed Victims (<i>n</i> = 12)		Dialyzed Victims (<i>n</i> = 4)		<i>P</i> <
	Mean ± SD	Range	Mean ± SD	Range	
Volume of fluids (L/d)					
1. day	21.8 ± 2.7	18–26	11 ± 2.5	7.5–13.2	0.002
2. day	20.6 ± 7.6	9–37	9 ± 11	1.7–26.5	NS
3. day	9.2 ± 5.8	2.5–23	4 ± 0.7	3.1–4.9	0.05
Urinary output (L/d)					
1. day	8.8 ± 2.3	4.3–12	1.8 ± 2.4	0.08–1.8	0.002
2. day	10.2 ± 2.9	6.6–15	0.7 ± 1.3	0.04–2.7	0.001
3. day	8.1 ± 3.2	3–13.5	0.11 ± 0.16	0.03–0.35	0.001

11 h after the rescue, but this was stopped because of sustained oliguria. Also, hemothorax and respiratory failure due to pulmonary fat embolism as well as disseminated intravascular coagulation were noted during the clinical course. By increasing the amount of administered fluids, his BP improved, but because urine volume did not increase, hemodialysis was initiated. He needed dialysis support for 23 d, and 20 sessions of intermittent hemodialysis were performed within this period.

The third patient was a 16-yr-old boy who was also initially admitted to the Elazig State Hospital. Fluids were begun 7 h after extraction. He passed 1800 ml of urine during the first day, but later was dialyzed because of hyperkalemia (8 mEq/L). This patient was fasciotomized thereafter, and during the operation, he experienced massive local bleeding, hemorrhagic shock, and cardiopulmonary arrest. He was resuscitated successfully. Because he became oliguric after all these complications, he was dialyzed. Thirteen sessions of hemodialysis were performed to this patient within a 19-d period.

The fourth patient was a 17-yr-old boy, also referred from the Elazig State Hospital. He began fluids 10 h after the rescue. He received 12 L of fluids and produced 5.3 L of urine on the first day. On the second day, he received 26.5 L of fluids and produced 2.7 L of urine. On the third day of follow-up, his urinary volume dropped to 350 ml, and because of volume overload, he was treated with hemodialysis. He needed hemodialysis support for 3 d, and overall, three sessions of hemodialysis were performed.

In total, 67 sessions of hemodialysis were performed on these four patients. The mean number of sessions was 16 ± 11

(range, 3 to 31), and mean duration of hemodialysis support was 19 ± 12 (range, 3 to 34) d.

Other Medical Interventions

Blood, fresh frozen plasma, human albumin, and platelet apheresis were among the most commonly applied medical interventions. Taken as a whole, 101 units of blood, 165 units of fresh frozen plasma, 92 units of human albumin, and 7 units of platelet apheresis were used. The quantities of each product and the corresponding number of patients receiving these products are summarized in Table 3. Thus, considering all victims, transfused or nontransfused, a mean of 6.3 units of blood, 10.3 units of fresh frozen plasma, and 5.7 units of human albumin were administered.

The most commonly applied drugs were cephalosporins and antianaerobic antibiotics, which were empirically administered to all patients. Narcotic analgesics and proton pump inhibitors were also administered to most patients. Other medications and the corresponding number of the patients who received these drugs were as follows: glycopeptide antibiotics (*n* = 11), quinolone antibiotics (*n* = 8), carbapenem antibiotics (*n* = 5), psychoactive drugs (*n* = 9), and heparin (*n* = 3).

Hyperkalemia was noted in only one patient, but interestingly, hypokalemia was seen in nine patients. Energetic potassium chloride (overall, 800 mEq) was administered for the treatment of this complication (mean, 75 ± 30 mEq; range, 20 to 130 mEq). Other medical complications of renal failure are listed in Table 4. Three patients required mechanical ventilation. Two of them had pulmonary fat embolism, and the

Table 3. Features of blood and blood products transfusions

Product	<i>n</i> (patients)	Total Number of Products (units)	Mean ± SD	Range
Blood	11	101	9.2 ± 6.9	1–22
Fresh frozen plasma	8	165	20.3 ± 18.9	2–47
Human albumin	15	92	6.2 ± 4.9	1–16
Platelet aphaeresis	3	7	2.3 ± 0.6	2–3

Table 4. Medical complications observed during the clinical course

Complication	<i>n</i>
Peripheral neuropathy ^a	14
Psychiatric problems ^b	8
Disseminated intravascular coagulation	3
Hypertension	3
Catheter infection	3
Respiratory failure	2
Urinary tract infection	2
Cardiopulmonary arrest	1

^a Diagnosed by clinical findings and confirmed by electromyography.

^b Sleeplessness, agitation, nightmare and depression.

remaining patient (who has already been described above) was complicated by cardiopulmonary arrest.

Surgical Procedures

Overall, fasciotomies were performed to 11 patients (68%) as a routine procedure, and in none of the patients was intracompartmental pressure measured. Also, necrotic tissues were removed by aggressive surgical debridement, and wounds were covered with skin grafts after they were completely cleared of infection. Despite this meticulous wound care, infections were noted in nine fasciotomy wounds and in one traumatic wound. However, sepsis was not observed in any of the patients.

Outcome

None of the patients died, but ischemic encephalopathy developed in the patient who experienced cardiopulmonary arrest. Although his vital functions were normal, his cerebral functions did not improve completely until discharge, and he needed the help of family members to maintain his life. Renal function recovered in all patients; the last serum creatinine level was 0.64 ± 0.2 mg/dl in patients who were not dialyzed and 0.85 ± 0.2 mg/dl in patients who required dialysis support.

Discussion

ARF based on rhabdomyolysis is a major cause of morbidity and mortality in the rescued victims of disasters (12); thus, its prevention is of vital importance for decreasing the death toll. Because hypovolemia is the most important factor in the pathogenesis, early and vigorous fluid replacement has been suggested as the most useful means in the prophylaxis of this disorder (1,13). Efficacy of this approach initially has been noted in the crush victims who were injured by an incidental collapse of a building (14) and thereafter was confirmed in the Kobe, Japan (13), and a pediatric subgroup of the Marmara, Turkey (15), disaster victims.

To our knowledge, our experience is the first approach as an organized, on-site medical intervention for the prevention of ARF in crush victims after a catastrophic earthquake. Four hours after the disaster, on-call instructions had been provided

to the local health care teams, and 8 h afterward, a nephrology team arrived in the field and directed fluid therapy. It should be noted that although fluid administration in this setting was favored by previous careful planning, the rather limited extent of the disaster also contributed to the success of this intervention. Of course, fluid resuscitation is much more difficult to implement when rescuers are faced with large-scale disasters.

In the present series, 16 crush victims had severe rhabdomyolysis, which was confirmed by high levels of CK and other muscle enzymes. However, only four patients (25%) needed RRT. This observation clearly indicates that development of full-blown crush syndrome can be prevented by effective fluid resuscitation because the need for dialysis was 60.8% and 77% in the renal patients in the Kobe (4) and Marmara earthquakes (9), respectively.

It has been emphasized that the timing of fluid resuscitation is vitally important in the prevention of ARF, and thus, initiating therapy even before extrication of the victims has been suggested (1). An important finding in the present series clearly confirms this hypothesis; duration between rescue and initiation of fluid treatment was significantly longer in the dialyzed victims as compared with nondialyzed ones.

Several reports have focused on determining the amount of fluid for prophylaxis of ARF caused by crush syndrome. In the case of sufficient urine production, 6 L (4) and 12 to 14 L (1) have been suggested, and even 24 L of fluids were administered to some of the Kobe earthquake victims (13). In the chaotic conditions after massive natural catastrophes, an aggressive fluid policy can be unrealistic, especially in elderly patients or in cases of delayed extrication (16). A mean of 20 L/d of fluid administration was well tolerated in the present series very probably because of the young age of the victims and the early intervention. One must be very cautious when administering such large volumes to elderly victims, who are prone to developing cardiovascular complications in the case of volume overload. We suggest a more modest and gentle volume replacement protocol in these patients and to place a central venous catheter as soon as possible for monitoring volume status.

Crush victims frequently experience serum potassium disorders; hyperkalemia is a major cause of mortality, and hypokalemia has also occasionally been noted (17). A unique finding in the present series was very high rate of hypokalemia and the need for potassium replacement in most of the victims during the clinical course. This hypokalemia probably resulted from potassium loss by the urine and influx of potassium into the intracellular space as a result of bicarbonate administration. Therefore, victims who are being treated by vigorous mannitol-alkaline diuresis are potential candidates for hypokalemia, and they should be followed closely for cardiac arrhythmia.

Another noteworthy observation in the present series was the very high rate of fasciotomies (11 [68.7%] of 16 victims), nine (81%) of which were complicated by wound infections. This procedure carries too many risks for crush victims and should not be performed routinely (18). The practice in the present series is especially surprising in a Turkish health facility if one considers the unfortunate experiences gained during the Mar-

mara earthquake, after which fasciotomies were found to be a significant risk factor for sepsis ($P < 0.001$), and sepsis in its turn was associated with mortality ($P < 0.0001$) (19). The authors of that particular report declared that the treatment policy regarding fasciotomies followed by the Turkish medical community during that particular disaster was not correct; their findings contradict earlier suggestions in favor of routine and early fasciotomies. Thus, we think that not only nephrologists, but also general and orthopedic surgeons should be informed about the potential complications of this intervention. All members of the team involved in the treatment of crush victims should be aware of the fact that in disaster conditions, fasciotomy wounds carry a high risk of infection, which subsequently can result in sepsis and even death. Thus, the role of prophylactic fasciotomy in these patients should be critically reassessed. A trial of noninvasive decompression of the compartmental syndrome with mannitol should be provided to these patients before deciding on surgical fasciotomy.

The calculated mortality rates of the dialyzed earthquake victims with ARF caused by rhabdomyolysis have been reported to reach up to 40% (3,4). During the Marmara earthquake, the overall mortality rate of renal victims was 15.2%, which was the most favorable outcome reported to that date (12). In the present series, all of the patients survived, which emphasizes that the outcome of disaster crush victims can be even more favorable than previously indicated. We suggest that the early and vigorous fluid resuscitation followed by mannitol-alkaline diuresis played a key role in this encouraging outcome by preventing ARF and related complications.

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