Crush-related acute kidney injury (acute renal failure)

Authors
Raymond Vanholder, MD, PhD
Mehmet S Sever, MD

Section Editor
Paul M Palevsky, MD

Deputy Editor
Alice M Sheridan, MD

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INTRODUCTION — High circulating plasma myoglobin levels secondary to rhabdomyolysis can cause heme pigment-associated acute tubular necrosis (ATN), which results in an abrupt rise in serum creatinine, or acute kidney injury (AKI) [1-5]. (See "Definition of acute kidney injury (acute renal failure)".)

Rhabdomyolysis may be due to either traumatic or nontraumatic muscle injury. Much of our knowledge of rhabdomyolysis-associated ATN derives from observations of rhabdomyolysis that occurs as part of the crush syndrome resulting from large scale natural or man-made disasters.

The clinical features and prevention of AKI due to traumatic rhabdomyolysis will be reviewed here. ATN due to nontraumatic rhabdomyolysis (due to exertion, coma-induced immobility, and toxins) and hemolysis and general overviews of rhabdomyolysis, hemolysis, and drug-induced myopathies are discussed in detail separately. (See "Clinical features and prevention of heme pigment-induced acute tubular necrosis" and "Clinical manifestations, diagnosis, and causes of rhabdomyolysis" and "Approach to the diagnosis of hemolytic anemia in the adult" and "Drug-induced myopathies".)

DEFINITIONS AND EPIDEMIOLOGY — Crush injury complicated by AKI is often referred to as crush syndrome. Crush syndrome may include hypovolemic shock, sepsis, electrolyte disturbances (of which hyperkalemia is the most important), heart failure, arrhythmias, acute respiratory distress syndrome, disseminated intravascular coagulation, bleeding, psychological trauma, and heme pigment-induced ATN, although all of these components need not be present for the term crush syndrome to be used [6-8].

Crush syndrome develops in 30 to 50 percent of cases of traumatic rhabdomyolysis and is frequently seen after catastrophic earthquakes [6,7]. According to some estimates, the incidence of crush syndrome ranges between 2 and 5 percent of all injured victims of catastrophic earthquakes [9-11].

The following reports have analyzed the incidence of AKI as part of crush injury following catastrophic earthquakes:

The frequency with which dialysis is required has varied widely in different studies. In a report from Bam, Iran, dialysis was required in 6.5 percent of 1975 patients admitted to the hospital [12]. The majority of victims were rescued in less than four hours, which may explain at least in part the lower rate of requiring dialysis than in other reports.

Much higher rates of requiring dialysis were noted in two other catastrophic earthquakes: 54 percent in the Kobe earthquake and 75 percent in the Marmara earthquake [11,13,14]. In the Kobe earthquake, the need for hemodialysis correlated directly with increased serum creatine kinase (CK) levels, as dialysis was required in 84 and 39 percent of patients with a CK level greater or less than 75,000 U/L, respectively [11].

In the Kobe and Marmara earthquakes, the time under the rubble correlated inversely with both serum creatine kinase (CK) and the frequency of requiring dialysis. A possible explanation for these counterintuitive findings is that victims with more extensive muscle injury and higher CK levels died before they were transported to the hospital.

CLINICAL MANIFESTATIONS — The most typical local finding of rhabdomyolysis is compartment syndrome, due to swollen muscles. Patients suffer from severe pain, weakness, paresthesia, paresis or paralysis and pallor in the affected extremities. Distal pulses may be absent when intracompartmental pressure is very high, although increased intracompartmental pressure may be present even when distal pulses are palpable. In traumatic rhabdomyolysis, signs of blunt or penetrating trauma are also present.

AKI resulting from heme pigment-induced ATN is usually characterized by an initial oliguric period followed by polyuria, which usually starts within one to three weeks after the primary event. Some cases may present with a nonoliguric course.

Hypovolemia — Some patients with rhabdomyolysis have been immobile or comatose for significant periods of time. As a result, hypovolemia due to absence of fluid intake plus ongoing losses may be observed. This is particularly important among patients with rhabdomyolysis due to crush injury, since they may have been immobilized for hours to days. In addition, third spacing at the site of muscle injury among such patients significantly worsens hypovolemia. The latter phenomenon typically starts only after decompression, due to reperfusion of the traumatized muscle.

Dark urine — The characteristic manifestation of heme pigment-induced ATN is discolored urine. Marked release of myoglobin leads to red or brown (or even black) urine, unless pigment excretion is limited because of a low glomerular filtration rate, extreme dilution of the urine due to preventive fluid administration, or clearance from the plasma by the reticuloendothelial system [15]. Urinalysis also reveals pigmented granular casts.

The plasma is typically normal in color with myoglobinuria. This is in contrast to conditions resulting in hemoglobinuria-induced ATN, such as massive hemolysis, that are characterized by red-tinted plasma. (See "Clinical features and prevention of heme pigment-induced acute tubular necrosis".)

Renal insufficiency — The severity of renal insufficiency ranges widely from a mild elevation in the serum creatinine concentration to oliguric AKI requiring immediate hemodialysis. This variability is due to differences in severity of injury to muscle and presence or absence of volume depletion and/or underlying additional comorbid conditions, particularly sepsis [16,17].

BIOCHEMICAL ABNORMALITIES — The biochemical abnormalities that characterize rhabdomyolysis-associated AKI include hyperkalemia that may be life-threatening, hyperphosphatemia, hypocalcemia (which is occasionally followed by hypercalcemia during the recovery stage), a high CK, and a low fractional excretion of sodium. These are discussed elsewhere. (See "Clinical features and prevention of heme pigment-induced acute tubular necrosis".)

DIAGNOSIS — Patients with rhabdomyolysis-induced ATN typically present with the triad of pigmented granular casts in the urine, a red to brown color of the urine, varying severity of kidney dysfunction, and a marked elevation in the plasma CK level. (See "Clinical manifestations, diagnosis, and causes of rhabdomyolysis".)

DIFFERENTIAL DIAGNOSIS — The intermittent excretion of red to brown urine can be seen in a variety of clinical settings, including heme pigment-induced ATN. The approach to this issue is discussed separately. (See "Red to brown urine: Hematuria; hemoglobinuria; myoglobinuria".)

AKI can also be caused by conditions or abnormalities commonly observed in patients with

traumatic rhabdomyolysis. These include drug-induced AKI (such as aminoglycosides), sepsis, severe hypotension due to marked hypovolemia, and others. This is also discussed elsewhere. (See "Etiology and diagnosis of acute tubular necrosis and prerenal disease".)

PREVENTION — The general goals for preventive therapy in all cases of heme pigment-induced AKI are the correction of volume depletion, if present, and prevention of intratubular cast formation.

The approach to prevention of AKI in the patient with rhabdomyolysis due to crush syndrome varies based upon the location of the patient and ability to closely monitor the victim.

Prior to extrication — Aggressive fluid repletion should be started before the extrication of entrapped subjects prone to develop the crush syndrome, if possible. Third spacing at the site of muscle injury worsens hypovolemia. Thus, patients with rhabdomyolysis may require massive amounts of fluid to initiate and maintain a vigorous diuresis.

The goals of volume repletion are to both enhance renal perfusion (thereby minimizing ischemic injury) and increase the urine flow rate to wash out obstructing casts. Volume resuscitation should be initiated before the crush is relieved, or as soon as possible thereafter, before heme pigment and other intracellular elements have been released into the circulation and before third spacing at the site of muscle injury worsens hypovolemia [2,8,18,19].

Evidence — The rationale for this approach is based upon the observations that early adequate fluid resuscitation is very important to help prevent AKI in patients with rhabdomyolysis due to crush injury.

Practically all of the published experience with volume resuscitation in patients with heme pigment-induced ATN has come from retrospective reports of rhabdomyolysis in subjects with crush injury [2-4,18-20]. The following studies serve as examples of the importance of early fluid repletion in this setting [18,19]:

- Seven patients with crush syndrome who were trapped under rubble (all with CK concentrations >30,000 U/L) were treated with alkaline diuresis immediately after extrication; none developed renal failure [19]. One patient who did not receive prophylactic volume repletion developed AKI and required hemodialysis [21]. These data were compared to historical data where patients with injuries of comparable severity all developed AKI [3].

- Sixteen earthquake victims trapped for a mean of 10 hours (12 had CK concentrations >20,000 U/L) were treated initially with isotonic saline at 1 L/hour, then with an alkaline-mannitol solution [18]. The four patients who required dialysis were treated approximately nine hours after extrication and received significantly less fluids compared with 12 patients who did not require dialysis, who were treated four hours after extrication.

- In other reports of earthquake-related crush injury, AKI occurred in over 50 percent of patients for whom therapy was instituted much later [20,22].

Thus, preventive therapy appears to be less effective after the first 6 to 12 hours, when the kidney injury may already be established.

The optimal fluid and rate of repletion are unclear. No studies have directly compared the efficacy and safety of different types and rates of fluid administration in this setting.

Prior to extrication, we and the International Society of Nephrology Renal Disaster Relief Task Force recommend isotonic saline rather than isotonic bicarbonate, because saline solutions are more readily available in disasters and have a well-described efficacy for volume replacement [8].

Isotonic saline should initially be given at a rate of 1 L/hour (10 to 15 mL/kg of body weight per

hour) while the victim is still under the rubble. After 2 liters are given, the rate of administration should be decreased to 500 mL/hour to avoid volume overload. However, this volume should be individualized. Factors to consider are age (fluid administration should be performed more carefully in the elderly); body mass index (more fluids are needed for the victims with larger body surface area); trauma pattern (compartment syndrome is worse with more serious trauma); and amount of presumed fluid losses (more fluids are needed in hot climates and in victims who produce urine or have ongoing blood losses).

There is a role for isotonic bicarbonate therapy after extrication. (See 'Use of bicarbonate' below.)

Fluid overload is defined by signs of pulmonary congestion. Limb swelling alone may not represent volume overload, since it may be due to third space sequestration (compartment syndrome).

Severe hyperkalemia is relatively frequent among patients with crush injuries. As a result, intravenous solutions containing potassium, such as Ringer's lactate, are contraindicated in such patients.

After extrication

Use of bicarbonate — After the victim has been removed from the rubble, urine output has been documented, and overt alkalosis has been excluded, it is suggested to switch from isotonic saline to an alkaline solution that is approximately isotonic in an attempt to achieve a forced alkaline diuresis.

The rationale for this approach is that raising the urine pH above 6.5 may prevent heme-protein precipitation with Tamm-Horsfall protein, intratubular pigment cast formation, and uric acid precipitation [1,3,23]. Alkalinization may also decrease the release of free iron from myoglobin and the formation of F2-isoprostanes, which may enhance renal vasoconstriction. (See "Clinical features and prevention of heme pigment-induced acute tubular necrosis".)

Despite these potential benefits, there is no clear clinical evidence that an alkaline diuresis is more effective than a saline diuresis in preventing acute kidney injury, as no direct comparative trial has been performed. The best data in support of an alkaline diuresis are derived from uncontrolled case series. In a study cited above, for example, renal failure did not develop in seven patients with crush syndrome who were trapped under rubble and were treated with alkaline diuresis immediately after extrication [19]. By comparison, one patient who did not receive prophylactic volume developed acute kidney injury and required hemodialysis [21].

The optimal regimen and rate of administration of bicarbonate are unknown. We generally administer one of the following two fluid regimens after extrication:

- One liter of isotonic saline alternating with 1 liter of half isotonic saline plus 50 mEq of sodium bicarbonate.

- Isotonic saline for the first 2 liters, followed by 1 liter of half isotonic saline plus 50 mEq of sodium bicarbonate. This sequence is then repeated, as indicated.

The choice between these two regimens depends in part upon the general clinical and biochemical condition of the patient and the blood pH. As an example, if measured laboratory values reflect only a mild acidosis, more liters of isotonic saline and fewer liters of bicarbonate-containing solution are given.

The rate of fluid administration with either regimen is based upon the ability to attain urinary output goals, and assessment of volume status. In general, we administer the intravenous solution at 500 mL/hour for the first 24 hours as long as there is no evidence of fluid overload and the patient can

be closely monitored. (See 'Urine output goal' below.)

The rate of fluid administration is decreased after the first 24 hours but is still maintained at a rate that is greater than the urine output, as long as there is no evidence of fluid overload. Generally, a total of 200 to 300 mEq of bicarbonate is given on the first day as long as the patient is not alkalemic. The exact rate and regimen is altered based upon ongoing clinical assessment and laboratory values. (See 'Urine output goal' below.)

Potential risks associated with alkalinization of the plasma include promoting calcium phosphate deposition and inducing or worsening the manifestations of hypocalcemia by both a direct membrane effect and a reduction in ionized calcium levels [3]. Manifestations of severe ionized hypocalcemia include tetany, seizures, and arrhythmias. To minimize the risk of these complications, the arterial pH should not exceed 7.5. (See "Clinical manifestations of hypocalcemia".)

Alkalinization can also reduce the plasma potassium concentration secondary to intracellular shift. This is often a beneficial effect, since the combination of tissue breakdown and renal failure often leads to hyperkalemia. (See "Causes of hypokalemia", section on 'Increased entry into cells'.)

Because of the potential risks with bicarbonate therapy, we recommend close monitoring of serum bicarbonate, calcium, and potassium, and the urine pH. The urine pH can be measured by immersion of a simple urine dipstick, but this is only reliable on freshly voided urine, unless urine is collected under paraffin (which is difficult to obtain in chaotic disaster conditions). The goal urine pH is greater than 6.5. We recommend discontinuing the bicarbonate-containing solution (but continuing to replete volume with isotonic saline) if the arterial pH exceeds 7.5, the serum bicarbonate exceeds 31 mEq/L, or the patient develops symptomatic hypocalcemia. Calcium supplementation should be given only for symptomatic hypocalcemia or severe hyperkalemia, since early deposition of calcium in muscle is followed by hypercalcemia later in the injury process. (See "Treatment of hypocalcemia".)

Use of mannitol — If urinary flow is adequate (defined as >20 mL/hour), adding 50 mL of 20 percent mannitol (1 to 2 g/kg per day [total, 120 g], given at a rate of 5 g per hour) to each liter of fluid is suggested. Mannitol is contraindicated in patients with oligoanuria.

Mannitol should be discontinued if the desired diuresis of approximately 200 to 300 mL/hour cannot be achieved, since there is a risk of hyperosmolality, volume overload, and hyperkalemia with continued mannitol administration under these conditions. (See "Complications of mannitol therapy".)

The mechanism by which mannitol protects against heme pigment-induced ATN is not completely clear. Experimental studies have suggested that mannitol may be protective by causing a diuresis, which minimizes intratubular heme pigment deposition and cast formation [24]. It has also been proposed that mannitol may act as a free radical scavenger, thereby minimizing cell injury [4]. In addition to these beneficial effects on the kidney, mannitol may extract sequestered water from the injured muscles, thus preventing compartmental syndrome [25].

However, at least some studies have shown no amelioration of proximal tubular necrosis with mannitol, and mannitol may cause hyperosmolality and other complications [24]. The available retrospective series, most of which are uncontrolled, report conflicting results regarding the effectiveness of mannitol plus bicarbonate in preventing heme pigment-induced AKI [18,19,26,27]. As an example, 154 of 382 patients with serum CK concentration >5000 U/L were treated with mannitol plus bicarbonate [27]. There was no statistically significant difference in the incidence of AKI (defined as creatinine >2.0 mg/dL [177 micromol/L]; 22 versus 18 percent), dialysis (7 versus 6 percent), or death (15 versus 18 percent) in patients who were or were not treated with mannitol plus bicarbonate. However, there was a trend toward improved outcomes in patients with extremely

high CK levels (>30,000 U/L) treated with mannitol and bicarbonate. This is relevant, given that such high levels are not unusual in victims of earthquakes [19,22].

The interpretation of these findings is hampered by the lack of reporting of other elements of treatment, such as adequacy of volume resuscitation, presence of other factors contributing to AKI (eg, drugs, sepsis, hypotension), timing of interventions, and relatively low rate of severe AKI (eg, requiring dialysis).

Unless the patient is carefully monitored and losses replaced when appropriate, mannitol can lead to both volume depletion and, since free water is lost with mannitol, hypernatremia. Mannitol administered in very high doses, or to patients with reduced renal excretion due to renal insufficiency, can also raise plasma osmolality sufficiently to cause symptoms of hyperosmolality and volume expansion. The increase in plasma osmolality can also cause passive movement of potassium out of cells and raise the plasma potassium concentration. AKI may occur if patients are treated with more than 200 g of mannitol per day. (See "Complications of mannitol therapy".)

Prevention of hyperkalemia — Although sporadic patients with rhabdomyolysis or the crush syndrome may develop hypokalemia, the large majority are hyperkalemic, which is life-threatening [6,13,28,29]. Hyperkalemia may occur even in the absence of AKI, since a large amount of potassium may be released from injured muscle. Since potassium measurements at first triage are seldom available in disaster conditions, transport of victims with a potential crush syndrome to safer areas for more intensive treatment should be started, if possible, after the administration of a preventive oral dose of the potassium binding resin, sodium polystyrene sulfonate, in combination with 33 percent sorbitol, at a 1:3 ratio [8].

Although efficacy of sodium polystyrene sulfonate has been questioned, and although sorbitol has sporadically been associated with ulcers of the intestinal wall [30], we suggest their use in disaster crush victims, since the risk of fatal hyperkalemia is extremely high. (See "Treatment and prevention of hyperkalemia", section on Cationic exchange resin for further discussion of this topic.)

Since a calcium load is to be avoided, sodium polystyrene sulfonate should be preferred to calcium polystyrene sulfonate. (Calcium polystyrene sulfonate is not available in the United States, although it is available elsewhere.)

Many of the isotonic solutions for fluid repletion contain potassium (eg, Ringer's lactate). Because of the risk for life-threatening hyperkalemia, empiric administration of such preparations is absolutely contraindicated in patients at risk for the crush syndrome.

We recommend monitoring plasma potassium several times daily until stabilized. Hyperkalemia should be appropriately treated. (See "Treatment and prevention of hyperkalemia".)

If serum potassium concentration cannot be measured due to field conditions, electrocardiography (ECG) can offer useful information, although a normal ECG may be present in spite of overt hyperkalemia. (See "Treatment and prevention of hyperkalemia".)

Urine output goal — Once the patient can be closely monitored (such as hospital or triage setting), the administration of intravenous fluid should be adjusted to maintain the urinary output at approximately 200 to 300 mL/hour. This is done to help ensure adequate renal perfusion and to wash out any obstructing casts. Patients must be followed closely to ensure that fluid overload, as defined by signs of pulmonary congestion, does not occur. As previously mentioned, limb swelling alone may not represent volume overload.

If the urine output goal is achieved, this fluid regimen should be administered until the disappearance of myoglobinuria (either clinically or biochemically). This usually requires several days.

However, if the desired diuresis is not established, we recommend placement of a central venous pressure (CVP) catheter in addition to close monitoring of input and all losses (urinary volume plus other losses together) of the previous day. Forced diuresis should be abandoned if CVP measurements exceed acceptable thresholds (15 cm H2O).

Therapy should be based on CVP measurements, biochemical analysis, close monitoring of fluid intake and output, and body weight. A stable weight may suggest that the appropriate amount of fluid is being administered to the patient. However, if the patient is anuric and catabolic, a stable body weight may be deceptive. In those cases, we administer 500 to 1000 mL of fluid in excess of all losses of the previous day.

After serum CK levels begin to return to normal, the volume of administered fluids should be gradually tapered under close clinical and laboratory monitoring. A parallel decrease in urinary output together with normal clinical and biochemical findings indicates that tubular function has been restored.

Dialysis should be initiated in the setting of persistent oligoanuria or other indications. (See 'Treatment of established AKI' below.)

Total volume administered — The total amount of volume administered depends upon the clinical scenario. A positive fluid balance is always necessary in crush syndrome casualties, since extreme amounts of fluids can diffuse into the damaged muscles. Mannitol-alkaline solution can be administered at quantities of up to 12 L/day to an adult weighing 75 kg and with appropriate urine response. Eight liters of urinary output can be expected following an infusion of 12 L of this solution. Therefore, it is reasonable to administer 4 to 4.5 L more fluid than all of the total losses of the previous 24-hour period [2]. Analysis of the Bingol earthquake demonstrated that dialysis was avoided in many patients with crush syndrome by administering more than 20 L of fluid per day to each patient [18]. The relatively low number of victims injured in this particular disaster allowed for more careful monitoring of each victim, which allowed the vigorous volume repletion.

Fluid administration should be individualized and may need to be less aggressive in chaotic disaster circumstances when it is impossible to monitor patients appropriately to avoid volume overload. Under these circumstances, more modest volume repletion is recommended. Although the exact optimal limit is unknown, we suggest administering up to a maximum of 6 L of fluid per day under prolonged conditions in which close monitoring may not be possible. More cautious volume repletion is also warranted in victims who are prone to cardiac failure, such as the elderly, and in those who are anuric [31].

Calcium — Calcium supplementation should be given only for symptomatic hypocalcemia or severe hyperkalemia, because early deposition of calcium in muscle is followed by hypercalcemia later in the injury process. (See "Treatment of hypocalcemia".)

Loop diuretics — Loop diuretics have no impact on outcome in AKI [32,33]. (See "Possible prevention and therapy of postischemic acute tubular necrosis".) In the context of rhabdomyolysis, loop diuretics may worsen the already existing trend for hypocalcemia, since they induce calciuria and may increase the risk of cast formation [8,22]. Despite these concerns, however, judicious use of loop diuretics may be justified in elderly patients, especially if volume overloaded.

TREATMENT OF ESTABLISHED AKI — Other than maintenance of fluid and electrolyte balance and tissue perfusion, there is no specific therapy once the patient has developed AKI. Dialysis is initiated for the usual indications, including volume overload, hyperkalemia, severe acidemia, and uremia. Frequent (twice or even three times daily) hemodialysis may be indicated in patients with crush syndrome, given the high risk of fatal hyperkalemia. A detailed discussion of the indications for dialysis is presented elsewhere. (See "Renal replacement therapy (dialysis) in acute kidney

injury (acute renal failure): Indications, timing, and dialysis dose".)

Intermittent hemodialysis is suggested over other renal replacement modalities in the setting of crush syndrome. Compared with other modalities, intermittent hemodialysis is most efficient at removing potassium, which is one of the major causes of death [1]. (See "Acute hemodialysis prescription".)

The other renal replacement modalities have the following additional limitations:

- Peritoneal dialysis (PD) might be difficult to perform in case of abdominal and/or thoracic trauma, or in patients who cannot lie down due to hypervolemia-related heart failure and/or respiratory failure. PD may also not adequately treat the metabolic and electrolyte derangements caused by rhabdomyolysis (eg, hyperkalemia and other abnormalities), especially in the heavily traumatized patients. Furthermore, PD may create logistic problems in mass disasters, due to the necessity to deliver large loads of bags containing sterile dialysis fluid to the disaster area. (See "Use of peritoneal dialysis for the treatment of acute kidney injury (acute renal failure)".)

- Continuous dialysis strategies are limited by the need for large amounts of sterile replacement fluid that may be difficult to obtain in disaster conditions. In addition, only one patient can be treated per machine when continuous modalities are used. Finally, continuous anticoagulation by heparin may enhance a bleeding tendency in heavily traumatized patients. Regional citrate anticoagulation avoids the problems associated with anticoagulation but is difficult to monitor in chaotic disaster circumstances. (See "Continuous renal replacement therapies: Overview" and "Renal replacement therapy (dialysis) in acute kidney injury (acute renal failure): Indications, timing, and dialysis dose".)

SUMMARY AND RECOMMENDATIONS

- High circulating levels in the plasma of myoglobin secondary to rhabdomyolysis can directly cause acute tubular necrosis (ATN), resulting in acute kidney injury (AKI). Rhabdomyolysis-associated AKI due to crush injury is a major source of morbidity in natural or man-made disasters. (See 'Introduction' above.)

- Among entrapped subjects prone to develop the crush syndrome, we suggest the following approach:

  - We recommend the intravenous administration of an isotonic solution at a high fluid rate (**Grade 1B**). We suggest starting intravenous fluid replacement prior to extrication of the victim whenever possible (**Grade 2B**). We suggest giving isotonic saline rather than an isotonic alkaline solution (**Grade 2C**). Although the exact rate has not been defined by controlled studies, we suggest administering fluid at 1 L/hour initially. Since severe hyperkalemia is relatively common, intravenous solutions containing potassium, such as Ringer's lactate, are contraindicated. (See 'Prior to extrication' above.)

- After the victim has been removed from the rubble and urine output has been documented, we suggest switching from isotonic saline to an isotonic bicarbonate solution (**Grade 2C**). The optimal regimen and rate of administration are unknown. Following extrication, we administer the intravenous solution at 500 mL/hour for the first day, if there is no evidence of fluid overload and the patient can be closely monitored. We recommend close monitoring of serum bicarbonate, calcium, potassium, and serum and urine pH. We recommend discontinuing the alkaline solution if symptomatic hypocalcemia develops. (See 'Use of bicarbonate' above.)

- If urinary flow is >20 mL/hour among victims removed from the rubble, we suggest adding mannitol to the intravenous alkaline solution (**Grade 2C**). We add 50 mL of 20 percent mannitol (1 to 2 g/kg per day [total, 120 g], given at a rate of 5 g/hour). If mannitol is given, the maximum rate of fluid administration is 500 mL/hour. Mannitol is contraindicated in patients with oligoanuria.

We recommend discontinuing mannitol if the desired diuresis cannot be achieved (approximately 200 to 300 mL/hour) (**Grade 1B**). (See 'Use of mannitol' above.)

- Once the patient can be closely monitored (such as hospital or triage setting), the administration of intravenous fluid should be adjusted to maintain the urinary output at approximately 200 to 300 mL/hour. If the urine output goal is achieved, we suggest continuing fluid therapy until the disappearance of myoglobinuria (either clinically or biochemically). This usually requires several days.

- We suggest placement of a central venous pressure (CVP) catheter once the patient is in a hospital setting and closely monitoring input and all losses (urinary volume plus other losses together) of the previous day. In this setting, therapy should be based on CVP measurements, biochemical analysis, close monitoring of fluid intake and output, and body weight. (See 'Urine output goal' above.)

- We recommend monitoring plasma potassium and calcium several times daily until stabilized. We recommend treating hyperkalemia as discussed elsewhere. (See "Treatment and prevention of hyperkalemia".)

- Patients with symptomatic hypocalcemia or severe hyperkalemia may require calcium supplementation. In patients with asymptomatic hypocalcemia, we suggest not providing calcium supplementation (**Grade 2C**). (See "Treatment of hypocalcemia", section on 'Therapeutic approach' and "Treatment and prevention of hyperkalemia".)

- Dialysis is initiated for the usual indications, including volume overload, hyperkalemia, severe acidemia, and uremia. Among patients with heme pigment-induced AKI due to crush injury, we suggest intermittent hemodialysis rather than other renal replacement modalities (**Grade 2C**). (See "Renal replacement therapy (dialysis) in acute kidney injury (acute renal failure): Indications, timing, and dialysis dose" and "Acute hemodialysis prescription".)

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