Chapter 6

# Crush Syndrome: A Review of Current Knowledge

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**Abstract**

Crush syndrome ( CS ) is a medical condition that can occur when muscle tissue is severely damaged and releases myoglobin into the bloodstream. Recent studies have advanced our understanding of its pathophysiology and management, which can result in renal failure, cardiac arrhythmias, and even death if not rapidly and adequately managed. The condition can be caused by traumatic injuries, natural disasters, and industrial accidents, and its incidence varies depending on the underlying cause of the injury. Rapid and controlled release of the compressive force, aggressive fluid resuscitation, and electrolyte monitoring are the mainstays of management, but new therapies such as remote ischemic preconditioning and mesenchymal stem cell therapy are emerging. Prognostic factors that can inform clinical decision-making and improve patient outcomes include the extent of muscle damage, the timing and effectiveness of treatment, and the presence of associated injuries or comorbidities. The pathophysiology of crush syndrome is complex and multifactorial, involving a combination of direct tissue damage, toxic effects of cellular components released into the bloodstream, dysregulated immune responses, and activation of various physiological systems such as the renin-angiotensin-aldosterone system (RAAS). Early recognition and rapid, effective management of crush syndrome are essential to prevent its devastating complications.

## Introduction

CS, also known as traumatic rhabdomyolysis, is a condition that results from prolonged and excessive compression of muscles. It is commonly observed following traumatic injuries, natural disasters, and industrial accidents. CS can cause severe complications, including acute kidney injury (AKI), cardiac arrhythmias, and even death if not rapidly and adequately managed (1). The

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https://doi.org/10.58830/ozgur.pub91.c385

development of AKI can be caused by many factors. CS can cause AKI due to the direct nephrotoxic effects of both products and tubular obstruction by myoglobin and urate crystals, while hypotension and hypoperfusion can also contribute to ATN (2).

AKI caused by crush injury presents as rhabdomyolysis and myoglobulinemia, as well as hyperkalemia, hyperphosphatemia, and myoglobinuria.

Recent research has advanced our understanding of the pathophysiology and management of CS. When muscles are compressed, cellular components such as myoglobin, potassium, and other toxic substances are released into the bloodstream, leading to renal tubular obstruction, tubular necrosis, and AKI. However, recent studies have shown that the pathophysiology of CS may also involve a dysregulated immune response and activation of the RAAS, which can exacerbate renal dysfunction (3).

In addition to a more detaily understanding of the underlying mechanisms of CS, there has been significant progress in the development of new management strategies. Rapid and controlled release of the compressive force, aggressive fluid resuscitation, and electrolyte monitoring remain the mainstays of management. However, recent studies have demonstrated the potential benefits of new therapies, such as remote ischemic preconditioning and mesenchymal stem cell therapy, which can help to mitigate tissue damage and improve outcomes (4, 5).

Moreover, several studies have identified prognostic factors that can inform clinical decision-making and improve patient outcomes. These factors include the extent of muscle damage, the timing and effectiveness of treatment, and the presence of associated injuries or comorbidities (6).

This updated review aims to provide a comprehensive overview of the current understanding of CS, including its Epidemyology, pathophysiology, clinical presentation, diagnosis, management and treatment. Additionally, we will discuss emerging research on novel therapies and prognostic factors that may improve outcomes for patients with CS. Ultimately, this review underscores the importance of early recognition and rapid, effective management of CS to prevent its devastating complications (7).

## Epidemiyology

CS, also known as traumatic rhabdomyolysis, is a medical condition that can occur when muscle tissue is severely damaged and releases myoglobin into the bloodstream. Myoglobin is a protein that can cause renal failure

and other serious complications if it accumulates in the kidneys and other organs.

The incidence of CS varies depending on the underlying cause of the injury. Some of the most common causes of CS include earthquakes, building collapses, traffic accidents, and industrial accidents. According to some estimates, the incidence of CS ranges from 2% to 15% of all traumatic injuries (11).

Several studies have investigated the epidemiology of CS. For example:

In a study of 496 patients with CS in the 2008 Wenchuan earthquake in China, the incidence of AKI was 52.3%, and the mortality rate was 23.6% (12). In a retrospective study of 139 patients with CS following the 1999 Marmara earthquake in Turkey, the incidence of AKIwas 43.2%, and the mortality rate was 14.4% (8). In a study of 189 patients with CS following the 1995 Kobe earthquake in Japan, the incidence of AKI was 35.4%, and the mortality rate was 5.3% (8). Even seizures and excessive exercise such as swimming, causes rhabdomyolysis like well-known causes (13).

The incidence of AKI associated with crush injury and the frequency of needing dialysis in these cases varied widely in different studies. According to a report from Bam, Iran, 6.5 percent of 1975 patients admitted to the hospital needed dialysis (14). Most of the victims were rescued in less than four hours. The shorter time under the debris may partly explain the lower rate of needing dialysis in Bam compared to other reports, but this is not entirely certain. A much higher rate of need for dialysis was recorded in the other two major earthquakes: 54 percent in the Kobe earthquake and 75 percent in the Marmara earthquake (15,16). In the Kobe earthquake, the need for hemodialysis was directly associated with increased serum creatine kinase (CK) levels, as 84 and 39 percent of patients with CK levels above or below 75,000 units/L, respectively, required dialysis (15). AKI patients who survive and do not become chronically dependent on dialysis have a relatively better prognosis. Elderly individuals and those with chronic kidney disease are at higher risk for progression to end-stage kidney disease. Even in optimal conditions, the risk of dialysis is about 10 percent (16).

These studies highlight the serious nature of CS and the need for rapid diagnosis and treatment to prevent complications and reduce mortality.

**Pathophysiology**

When a muscle is compressed for a prolonged period, as can occur in crush injuries, it can lead to the breakdown of muscle fibers and the release

of cellular components such as myoglobin, potassium, and other toxic substances into the bloodstream. Myoglobin, in particular, is known to cause renal tubular obstruction, acute tubular necrosis, and AKI, which can result in renal failure if not adequately managed. Additionally, the accumulation of potassium and other toxins in the bloodstream can lead to electrolyte imbalances, cardiac arrhythmias, and other complications (3). While it was stated that the muscle should be under pressure for at least four hours for the development of rhabdomyolysis, it was determined that one hour was sufficient in the Kobe earthquake in Japan and even half an hour in the Marmara earthquake (8,9).

In recent years, research has suggested that the pathophysiology of CS may be more complex than previously thought, with evidence pointing to the involvement of a dysregulated immune response and activation of the RAAS (1, 10). The release of cellular debris and other substances during muscle breakdown can trigger an inflammatory response that further exacerbates tissue damage and can contribute to systemic complications such as sepsis. Additionally, activation of the RAAS can lead to vasoconstriction and renal dysfunction, further exacerbating the renal complications of CS.

Crush-related AKI may arise from prerenal, intrarenal, or postrenal causes.

- Severe hypovolemia is a common cause of prerenal AKI among victims of crush-related injuries. This is because patients can lose access to water while remaining trapped for extended periods, leading to ongoing losses and negative fluid balance. Additionally, vascular injury can result in intravascular volume loss and hypovolemic shock, while rescue and decompression at muscle injury sites can lead to reperfusion-related third spacing of fluid, resulting in intravascular hypovolemia and prerenal AKI.
- Intrarenal AKI in the context of crush-related injury is usually due to rhabdomyolysis, which can be characterized by dark urine or pigmented granular casts in the urinary sediment. AKI caused by heme pigment-induced ATN typically begins with an initial oliguric period followed by polyuria within one to three weeks of the primary event (17). Other causes of intrarenal AKI in patients with crush-related injury include prolonged shock, sepsis, use of nephrotoxic agents, cardiac failure, arrhythmias, or transfusion reactions.
- Postrenal AKI may result from traumatic injury or urinary outflow tract obstruction, particularly in patients with pelvic trauma.

Overall, the pathophysiology of CS is complex and multifactorial, involving a combination of direct tissue damage, toxic effects of cellular components released into the bloodstream, dysregulated immune responses, and activation of various physiological systems such as the RAAS. Understanding the underlying mechanisms of CS is essential for effective management and can inform the development of new therapies and prognostic indicators.

**Clinical Presentation**

The clinical presentation of CS can vary depending on the severity and duration of the crush injury, as well as the presence of underlying comorbidities. Common symptoms and signs include muscle pain and weakness, swelling, discoloration, and reduced range of motion in the affected area (3). In severe cases, patients may experience compartment syndrome, which is characterized by increased pressure within a muscle compartment that can lead to tissue necrosis and loss of function if not rapidly treated (18).

One of the hallmark features of CS is the release of cellular components such as myoglobin and potassium into the bloodstream, which can cause systemic effects such as electrolyte imbalances, cardiac arrhythmias, and AKI. Patients with CS may present with symptoms of AKI, such as decreased urine output, edema, and hypertension. It is important to note that the onset of renal dysfunction may be delayed and can occur several hours or even days after the initial injury (3).

In addition to these symptoms, patients with CS may also experience systemic complications such as rhabdomyolysis-induced hyperkalemia, metabolic acidosis, and disseminated intravascular coagulation (DIC) (19). In severe cases, crush syndrome can also lead to complications such as acute respiratory distress syndrome (ARDS) and sepsis (3).

Overall, the clinical presentation of CS can be complex and multifaceted, involving a combination of local and systemic symptoms that can vary depending on the severity and duration of the injury. Timely recognition and management of CS is essential to prevent long-term complications and improve patient outcomes.

**Diagnosis**

The diagnosis of CS is primarily based on clinical presentation and history, as well as laboratory tests to assess for systemic effects such as electrolyte imbalances, renal dysfunction, and metabolic acidosis (3).

Laboratory tests that may be used to diagnose CS include serum creatine kinase (CK), myoglobin, potassium, calcium and phosphate levels. Elevated CK levels are a hallmark finding in CS and can be used to monitor the severity of muscle damage (20). Elevated myoglobin levels can indicate rhabdomyolysis and can lead to complications such as AKI and DIC if not rapidly treated (3).

Imaging studies such as X-rays, ultrasound, and magnetic resonance imaging (MRI) may also be used to assess the extent of soft tissue and bone damage.

Overall, the diagnosis of crush syndrome involves a combination of clinical assessment and laboratory testing to identify the characteristic features of muscle damage and systemic effects associated with the condition.

**Management**

The management of CS involves a combination of supportive measures and specific treatments aimed at addressing the underlying pathophysiology of the condition (3).

Supportive measures may include aggressive fluid resuscitation with crystalloid or colloid solutions to prevent and treat hypovolemia and shock, as well as electrolyte and acid-base imbalances (3). Renal replacement therapy may be necessary in patients with severe AKI or electrolyte disturbances that do not respond to conservative measures (21).

Specific treatments for CS may include the administration of mannitol and bicarbonate to prevent and treat AKI and metabolic acidosis, as well as the use of diuretics to promote urine output and prevent fluid overload (1). In severe cases, hemodialysis or continuous renal replacement therapy may be necessary to remove myoglobin and other toxic substances from the bloodstream (3,21).

It is important to monitor patients closely for the development of complications such as compartment syndrome, which may require surgical intervention to relieve pressure within the affected compartment. The measurement of intramuscular pressure provides an objective parameter for the decision to perform fasciotomy. In nonhypotensive patients, this should be done when the intramuscular pressure exceeds 50 mmHg or if pressure values between 30 and 50 mmHg show no tendency to decrease after a maximum of 6 h (22).

Pain management and wound care are also important aspects of the management of CS, and may involve the use of analgesics, antibiotics, and surgical debridement or reconstruction as needed (3).

Overall, the management and treatment of CS require a multi-disciplinary approach involving close monitoring, aggressive fluid and electrolyte management, and specific treatments aimed at addressing the underlying pathophysiology of the condition.

**Treatment**

The treatment of CS is aimed at preventing or minimizing the complications of the condition, particularly acute renal failure and electrolyte imbalances. Management of CS typically includes the following, and table 1 summarizes the basic approach to CS (table 1).

**1. Rapid extrication and resuscitation:** Early and rapid extrication of the patient from the crushing force, followed by resuscitation with fluids and other supportive measures, is crucial to prevent the progression of muscle damage and the release of toxic substances into the bloodstream.

**2. Fluid resuscitation:** The immediate administration of intravenous fluids (such as normal saline) is essential to restore intravascular volume and prevent hypotension. The volume of fluid administered should be guided by the patient's clinical status, urinary output, and electrolyte levels. For adults, the standard practice involves the initial administration of a 1000 mL/hour bolus of normal saline for two hours, followed by a reduction to 500 mL/hour (as per algorithm 1) (23,24). However, in individuals with known heart failure, renal failure, or chronic obstructive pulmonary disease, smaller volumes, such as 10 cc/kg, are recommended. Early and aggressive fluid resuscitation is also necessary for children who are trapped under rubble. Administering intravenous fluids at a rate of 15 to 20 mL/kg/h while the victim is still under the rubble is recommended. In case the extrication process takes more than two hours, the rate of fluid administration should be decreased to 10 mL/kg/h or lower (25). If it's not possible to provide fluids before extrication, then volume resuscitation should be initiated as soon as possible after the victim is rescued. Local EMS protocols recommend the use of opioids or ketamine to manage any pain (26).

**3. Alkalinization of urine:** It is currently unknown what the best regimen and rate of administration of bicarbonate are. Following extrication, we typically administer one of two fluid regimens, as outlined below:

- Alternating one liter of isotonic saline with one liter of half-isotonic saline plus 50 mEq of sodium bicarbonate.

- Administering isotonic saline for the first two liters, followed by one liter of half-isotonic saline plus 50 mEq of sodium bicarbonate. This sequence is then repeated as needed.

The goal of urine alkalinization is to prevent the precipitation of myoglobin in the renal tubules and minimize the risk of AKI. This is achieved by administering intravenous bicarbonate, which raises the pH of the urine and promotes myoglobin solubility.

**4. Electrolyte management:** CS can lead to hyperkalemia, hypocalcemia, and other electrolyte imbalances. Electrolyte levels should be closely monitored, and appropriate measures taken to correct any imbalances. Calcium supplementation should only be given to individuals who are experiencing symptomatic hypocalcemia or severe hyperkalemia. Early administration of calcium can lead to calcium deposition in the muscles and subsequent hypercalcemia later in the injury process. Loop diuretics have no impact on the outcome of AKI (27,28). In the case of rhabdomyolysis, loop diuretics may exacerbate the existing trend for hypocalcemia by inducing calciuria and increasing the risk of cast formation (29,30). Despite these concerns, the careful use of loop diuretics may be appropriate in older patients, particularly those who are volume overloaded. Peaked T-waves and widened QRS complexes in hyperkalemia can be detected through prehospital electrocardiogram tracing. Paramedics can treat this condition with calcium chloride, inhaled albuterol, and intravenous insulin, as directed by local medical authorities.

**5. Treatment of AKI:** Patients with CS are at high risk of AKI. Treatment may include renal replacement therapy (such as hemodialysis or continuous renal replacement therapy) if the patient's kidney function does not recover. Dialysis is initiated in patients with CS for the usual indications, including volume overload, hyperkalemia, severe acidemia, and uremia. Due to the high risk of fatal hyperkalemia, frequent hemodialysis (twice or even three times daily) may be necessary. A more in-depth discussion of the indications for dialysis can be found elsewhere. Intermittent hemodialysis is preferred over other kidney replacement modalities for patients with CS. Compared to other modalities, intermittent hemodialysis is the most efficient method for removing potassium, which is one of the leading causes of death in these patients (31).

**6. Mannitol:** The use of mannitol in preventing AKI in the setting of crush injury is a matter of debate, as it may or may not benefit patients with rhabdomyolysis, and it has the potential to cause harm. Nevertheless, in our clinical experience, mannitol may be beneficial in nonoliguric patients with traumatic rhabdomyolysis as an adjunct to intravenous crystalloid, provided

close monitoring is possible. Mannitol is contraindicated in patients with oligoanuria. If urinary flow is adequate, a test dose of 60 mL of a 20 percent solution of mannitol may be given intravenously over three to five minutes to assess the response. If a significant increase in urine output of at least 30 to 50 mL/hour above baseline levels is not observed, mannitol should not be continued (32). Additionally, if the desired diuresis of approximately 200 to 300 mL/hour cannot be achieved, mannitol should be discontinued due to the risk of hyperosmolality, volume overload, and hyperkalemia with continued administration under these conditions.

**7. Wound management:** Adequate wound care and debridement are crucial to prevent infection and further tissue damage. Dialysis can be discontinued only after kidney function has recovered, as suggested by a normalization of urinary volume in a patient with improving serum biochemical values in the absence of fluid overload (23). According to guidelines, amputation should only be considered if a limb cannot be saved or if limb injuries are causing serious complications such as sepsis, systemic inflammation, or uncontrolled bleeding. Decisions about whether to save or amputate a limb should be based on clinical judgement rather than scoring systems like the Mangled Extremity Severity Score (MESS), which have been shown to be less reliable than the judgement of experienced surgeons. There is debate about whether prophylactic fasciotomy (a surgical procedure to relieve pressure in the muscles) should be performed in severe crush injury cases (33,34). In our experience at a level 1 trauma center, we do not perform prophylactic fasciotomy for severe crush injury. Instead, we typically only perform fasciotomies if acute compartment syndrome (a condition where pressure builds up within muscles) is clinically present upon admission or if measured compartment pressures show a delta pressure of 30 mmHg or less (meaning there is a small difference between diastolic blood pressure and compartment pressure). Prehospital amputation of severely crushed or mangled limbs solely to prevent CS is not recommended and can increase the risk of stump infection, as there is no evidence to support this practice. However, in certain cases, amputation may be necessary as a last resort to extricate a victim.

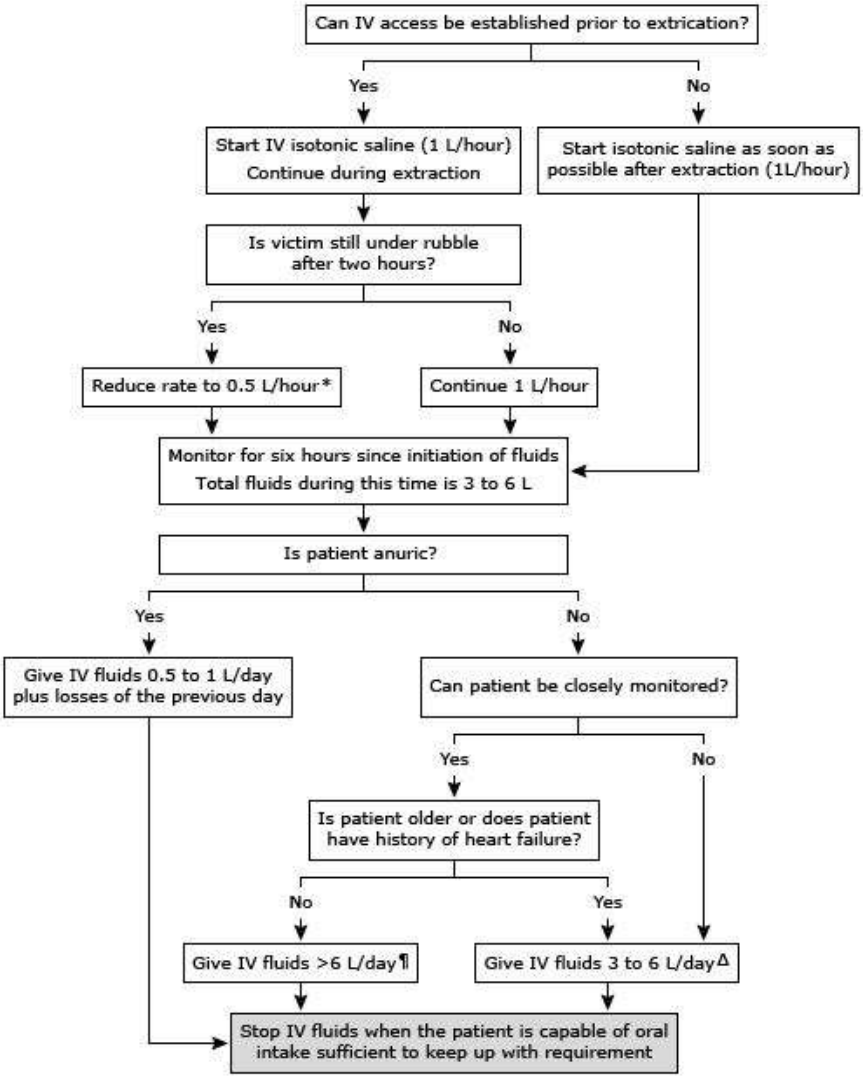
**8. Prevention of compartment syndrome:** In some cases, CS can lead to compartment syndrome, a condition in which increased pressure within a muscle compartment causes ischemia and tissue damage. Treatment may involve fasciotomy (surgical decompression) to relieve the pressure (35). If compartment syndrome is suspected but not confirmed, we manage the patient with serial examinations and may perform fasciotomy if the delta pressure falls to 30 mmHg or less. Prophylactic fasciotomy is not recommended in mass crush injury events, as several studies have shown that routine use of

fasciotomy in crushed limbs can lead to worse outcomes, including higher rates of bleeding, infection, and amputation. Although crush syndrome victims have a high infection rate, empirical antibiotic therapy should not be administered unless there are open wounds. If patients have open wounds, it is recommended to provide them with empirical treatment of broad-spectrum cephalosporins, with or without metronidazole, and tetanus prophylaxis (36).

**Table 1: Approach to Managing Crush Syndrome**

| **Step 1: Primary Assessment** |
|---|
| Check for signs of life-threatening conditions such as airway obstruction, breathing difficulties, and severe bleeding. |
| **Step 2: Treatment at the Scene** |
| If possible, remove the crushing object or move the patient to a safer location. |
| Provide pain relief as needed. |
| **Step 3: Transport to Hospital** |
| Transport the patient to a hospital with the necessary equipment and expertise to manage crush syndrome. |
| **Step 4: Secondary Assessment and Treatment** |
| Assess the patient for signs and symptoms of crush syndrome, including muscle pain and weakness, swelling, and decreased urine output. |
| Administer intravenous fluids to help flush out toxins and support kidney function. |
| Monitor kidney function and electrolyte levels. |
| In severe cases, consider dialysis or other interventions as needed. |
| **Step 5: Prevention** |
| Educate people about the risks of crush syndrome and the importance of seeking medical attention after traumatic events. |
| Promote building codes, construction practices, and emergency preparedness to reduce the risk of crush syndrome. |
| |

**Algorithm 1: Initial IV fluids for crush victims of high-casualty disasters such as earthquakes**




IV:intravenous.

* The rate is reduced because patients cannot be closely monitored when they are under the rubble and there is a risk of giving too much fluid

Generally, up to 12 L/day IV fluid can be administered in patients with good urine output (ie, >300 mL/hour).

We give 4 to 4.5 L more than total fluid loss from the prior day. Δ The actual amount depends on extent of injuries, body mass index, ambient temperature, urine production, amount of overall estimated fluid losses, and age. Patients with severe injuries usually require more fluid and may receive up to 6 L. Older patients who are not as severely injured may be given only 3 L.

*Adapted from: Sever MS, Vanholder R, RDRTF of ISN Work Group on Recommendations for the Management of Crush Victims in Mass Disasters. Recommendations for the management of crush victims in mass disasters. Nephrol Dial Transplant 2012; 27 (Suppl 1):i1.*

**Prognosis**

The prognosis of CS depends on several factors, including the severity of the crush injury, the extent of tissue damage, and the timeliness and effectiveness of treatment (3). In general, patients with mild to moderate crush injuries and early intervention and treatment have a good prognosis and are likely to recover without significant long-term complications (21). However, patients with more severe crush injuries and complications such as AKI, DIC, or compartment syndrome have a poorer prognosis and may be at risk for long-term disability, chronic pain, or limb amputation (22).

The development of AKI is one of the most significant predictors of mortality in patients with CS, and early recognition and treatment of this complication is critical to improving patient outcomes (3,15).

Overall, the prognosis of crush syndrome depends on a variety of factors, and close monitoring and aggressive management of complications are essential to achieving the best possible outcomes.

**Conclusion**

CS is a serious condition that can result from the compression of soft tissues, leading to ischemia and tissue damage. The release of myoglobin and other toxic substances into the bloodstream can cause a range of systemic complications, including AKI, electrolyte imbalances, and metabolic acidosis.

Early recognition and treatment of CS are essential to improving patient outcomes, and a multidisciplinary approach involving close monitoring, aggressive fluid and electrolyte management, and specific treatments aimed at addressing the underlying pathophysiology of the condition is necessary. Complications such as compartment syndrome and infections must also be

carefully managed to prevent further tissue damage and systemic complications.

The prognosis of CS depends on several factors, including the severity of the crush injury, the extent of tissue damage, and the timeliness and effectiveness of treatment. Close monitoring and aggressive management of complications are essential to achieving the best possible outcomes, particularly in patients with more severe crush injuries and complications such as AKI or DIC.

In conclusion, CS is a complex and potentially life-threatening condition that requires rapid recognition and treatment. With appropriate management and treatment, however, patients with CS can achieve good outcomes and avoid long-term complications.

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