Review Article

Crush Syndrome in Disaster

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Abstract

Crush syndrome is a condition observed in patients who have been buried under collapsed buildings or rubble. It is characterized by rhabdomyolysis developing shortly after rescue and subsequent hyperkalemia, shock, acute renal failure, and other systemic symptoms. The development of acute renal failure can be avoided if fluid therapy is initiated early and diuresis can be induced. In severe cases, intensive care including hemodialysis, prevention of compartment syndrome, and infection control is effective in reducing the mortality. However, actual treatment involves considerable difficulties because we must deal with a large number of patients at the time of a disaster. Even in such demanding situations, we should be able to save the lives of as many patients as possible by predicting the development of crush syndrome, initiating fluid therapy as part of confined space medicine, practicing appropriate triage, and transporting patients to high-level medical institutions.

Key words Traumatic rhabdomyolysis, Ischemia reperfusion syndrome, Acute renal failure, Fluid therapy, Hemodialysis, Compartment syndrome

Introduction

The Hanshin-Awaji Earthquake (also called the Kobe Earthquake) in 1995 caused a great many cases of crush syndrome, which we rarely encounter in daily clinical practice.[1] Patients who had been rescued in apparently good condition suddenly died or gradually developed severe systemic symptoms, to the astonishment of many healthcare workers. In fact, most physicians in Japan at that time lacked sufficient understanding of this syndrome, as well as of its pathophysiology and treatment options. After this experience, they have become aware of this syndrome through seminars on disaster medicine, academic meetings, and publications. Management of injuries leading to this syndrome is not always difficult, provided that adequate care is initiated early. Rather, factors arising between rescue and transportation and initial treatment determine the outcome. The problem is that numerous cases of this syndrome occur at the time of disaster such as earthquakes when prompt treatment is often difficult. Therefore, we need to have not only a full understanding of the pathophysiology and treatment of this condition, but also to be prepared to treat numerous patients at the time of a massive disaster.

Definition of Crush Syndrome

Crush syndrome (CS) is a condition in which rhabdomyolysis develops rapidly after the skeletal muscles are released from prolonged pressure, resulting in shock, acute renal failure, and other systemic symptoms. CS develops when the limbs are subjected to prolonged pressure or tightly restrained and the patient is rescued alive. This syndrome is sometimes referred to as "traumatic rhabdomyolysis" in English language papers. In Japanese translation, the old term, "zametsu" syndrome for CS has been replaced by the new term, "atsuza" syndrome, because the former implies association with highly destructive crush injury, which is not consistent with the clinical

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appearance of injury leading to crush syndrome. While "crush injury" refers to wounds caused by or showing signs of crushing of the human body, this does not necessarily describe the clinical appearance of injury leading to crush syndrome.

Historical Overview and Epidemiology

The earliest description of CS is considered to have appeared in the German language literature in 1910, which reported "rhabdomyolysis with the triple symptoms of myalgia, loss of muscle power, and dark brown urine" observed following the Sicily Earthquake in 1909.[2,3] German medical books contain descriptions of similar symptoms observed in World War I soldiers who were buried under debris or confined in bomb shelters and then rescued. Bywaters in the U.K. first used the English term "crush syndrome" in his 1941 paper that delineated the pathogenesis of CS and established guidelines for the management of casualties.[4] He observed many civilian victims of the London Blitz, who were rescued from collapsed houses but presented remarkable swelling of wounded limbs and died from acute renal failure. He treated nearly 200 patients with CS before the end of the war.[5] Analyzing clinical cases and studies on myonecrosis and acute renal failure, he established a largely complete clinical picture of this syndrome after the war.[6–8]

Clinical cases of CS related to the Vietnam War[9] and coalmine accidents[10] appeared in the literature in the latter half of the 1960s. Later reports related to earthquakes,[11,12] local conflicts,[13,14] mine accidents,[15] railway accidents,[16] collapse of old houses[17] occasionally appeared following disasters.[18] When the earthquake in Armenia in 1989 caused about 300 cases of CS, case reports and results of animal experiments were published,[19,20] but we do not have access to the details, because the reports were mostly written in Russian. After the Hanshin-Awaji Earthquake in Japan, there have been increasing numbers of English language papers dealing with casualties in the Marmara Earthquake[21] and the Bingol Earthquake[22] in Turkey, the Chi-Chi Earthquake in Taiwan,[23] etc. (Fig. 1).

Although a majority of reported CS cases are associated with disasters involving large numbers of victims, CS may also be seen in daily practice in various situations, such as

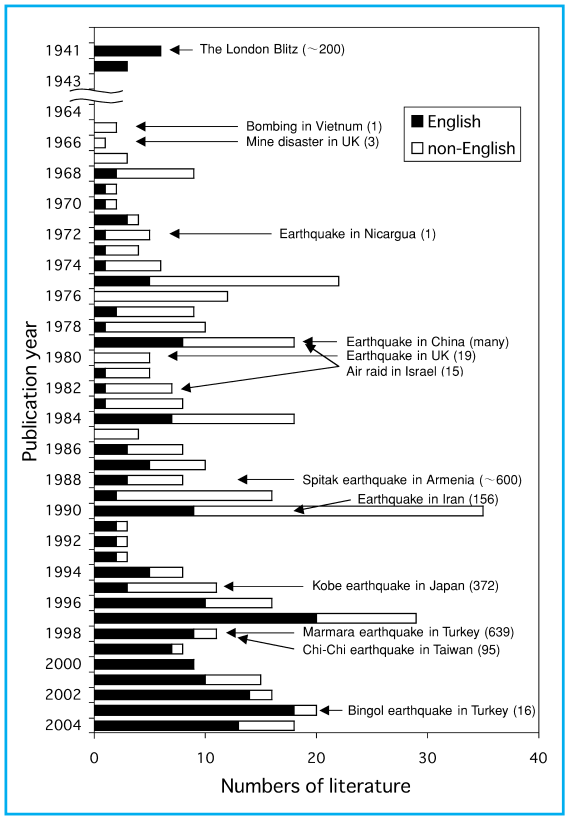

Fig. 1 Annual publication in the literature on "crush syndrome"

Articles on crush syndrome were searched with PubMed and cited reference. Remarkable disasters in relation to crush syndrome are listed chronologically.

torture involving hitting with blunt instruments,[24] comatose patients,[25] patients receiving surgery in tight body positions,[26] difficult rescue cases in traffic accidents,[27] complications with the use of MAST suits,[28] injury from using immobilizing bandaging,[29] and injury due to automatically cycled blood pressure cuff.[30] The occurrence of CS is not clear, because it frequently occurs in disasters where accurate medical statistics are difficult to obtain. CS is reported to have occurred in 7.6% of all traumatic cases in the Spitak Earthquake,[31] 13.7% of all traumatic hospitalized patients in the Kobe Earthquake,[32] and 1.4% of all hospitalized patients in the Marmara Earthquake.[21] The development of CS is considered to vary depending on the structure of the building, injury conditions, and rescue situation. A study on the Kobe Earthquake showed a significant positive correlation between

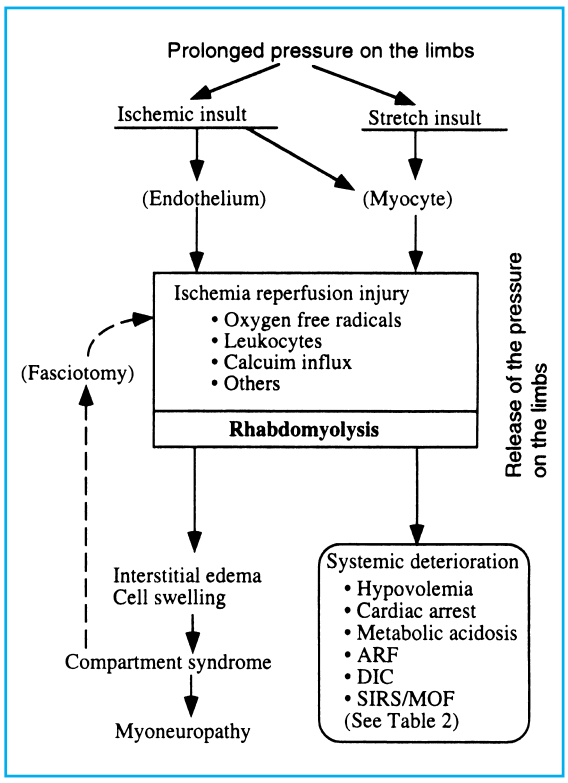

Fig. 2 Pathophysiology of the crush syndrome

the number of collapsed houses and the number of CS patients.[1]

Pathology

Locally, CS presents signs of compartment syndrome and anesthekinesia.[33] Systemically, the central pathological feature is acute renal failure[34] arising from rhabdomyolysis[35] (Fig. 2). This clinical picture resembles the systemic symptoms observed following the reperfusion of an ischemic limb.

Damage to skeletal muscles from compression

In discussing the pathophysiology of CS, it is important to consider what triggers the breakdown of the skeletal muscles. There are different theories based on similarities with other diseases; one considers that partial ischemia may be the cause, and another postulates injury to the cell membranes of the skeletal muscles due to physical force.[36]

a) Compression injury to the skeletal muscles: Stretch myopathy

Stretching of the cell membranes may initiate injury to the skeletal muscles. When the cell membranes are stretched, Ca channels are opened. The cell tries to maintain the potential difference by temporarily allowing the outflow of K, which maintains the cell volume. On the other hand, the inflowing Ca is buffered by adsorption to the organelles and the pumping function of the cell membranes. This process consumes ATP not only by the activation of Ca-ATPase but also by the reuptake of K that has been lost as a result of Na influx due to Ca/Na exchange. The increase in intracellular Ca level causes the activation of protease, phospholipase, and a wide variety of other enzymes, and furthermore, the deposition of Ca to mitochondria weakens their activity.[37] The cascade of these events causes shortage of energy in the cell and attenuation of the Na gradient, resulting in the development of cellular edema.

b) Ischemic injury to skeletal muscles

The parts of the limbs located peripheral to the sites of pressure naturally become ischemic. Skeletal muscles in complete ischemia develop edema and lysosome degranulation within about 30 min, and undergo irreversible morphological changes leading to necrosis within 4 to 6 hours at normal temperature.[38] Although such necrosis may be partially present in limbs receiving external crushing force, most parts of the limbs remain in a condition of incomplete ischemia because of the presence of collateral circulation or weakness of compression. While intracellular energy flow may be barely maintained by anaerobic metabolism, the Na permeability of the cell membranes is increased and Na-K-ATPase is activated to enhance the pumping out of Na, resulting in accelerated ATP consumption. Gradually, Ca flows into the cell with the development of cellular edema due to ATP shortage. Such damage to the cell membranes tends to occur more readily in incomplete ischemia than in complete ischemia.[39] In summary, the progression of membrane damage is promoted by the temporal contiguity or concurrence of ischemia and reperfusion taking place in the compressed parts of the muscles and their vicinity due to the presence of collateral circulation, accompanied by the mechanism of reperfusion injury discussed below.[40]

c) Propagation of intracompartment pressure
Skeletal muscles are covered with fasciae and bones to form muscle compartments. Because of this peculiar anatomy of skeletal muscles, even localized compression or unnatural posture may cause a substantial increase in intracompartmental pressure (ICP) leading to widespread muscle injury.[41] When edema develops in myocytes for the above-mentioned reasons, elevation in ICP may result and all skeletal muscles in the same compartment are affected. If ICP is elevated to 30–50 mmHg or higher, this factor alone causes skeletal muscle ischemia within 4 to 8 hours, resulting in the so-called compartment syndrome.[42] In compartment syndrome due to ordinary trauma, muscle damage is caused by factors outside the muscle, such as bone fracture, hematoma, and circulation impairment. In contrast, muscle damage in CS is caused by edema in the muscle itself.[43]

Local changes after release of pressure (rescue)

Following the release of pressure, the myocytes damaged from being stretched and by ischemia rapidly develop edema and gradually necrotize. This process involves reperfusion injury at the level of microcirculation and compartment syndrome specific to skeletal muscles.

a) Ischemia reperfusion injury
The rapid reestablishment of blood circulation following release of pressure may impair microcirculation and cause tissue injury. This condition, called ischemia reperfusion injury, expands ischemic damage through interaction between the leukocytes and endothelial cells. Many researchers have pointed out the involvement of reactive oxygen species in this condition.[44] Reactive oxygen species impair skeletal muscles and vascular endothelial cells through peroxidation of the cell membranes and the membranes of organelles.[45] Leukocytes adhere to the damaged endothelial cells and impair microcirculation, aggravating the hypoxic condition of myocytes. There is evidence suggesting that reactive oxygen species may damage myocyte cell membranes even before the shortage of intracellular energy occurs.[46]

b) Involvement of compartment syndrome
Reperfusion increases the volume of the parts affected by pressure and ischemia. In addition, edema of the skeletal muscles resulting from ischemia reperfusion is further enhanced. Cellular edema and the increase in vascular permeability causes the rapid rise in ICP, and compartment syndrome develops in the parts that have not shown overt signs of injury.

Systemic changes after release of pressure (rescue)

a) Fluid shift and hyperkalemia
As water and various substances flow into and out of the damaged myocytes (Table 1),[47] blood flow in the vicinity promotes the rapid development of systemic symptoms. We need to pay particular attention to the nonfunctional extracellular fluid and K outflow occurring relatively early following reperfusion, because hypovolemic shock and hyperkalemia are major causes of early death. Analysis of fatal CS cases following the Kobe Earthquake showed that 70% of the 27 fatalities from circulatory failure took place within 3 days. While there were 11 fatalities from hyperkalemia, 8 of them occurred within 3 days.[1] It has also been demonstrated that severe cases with a peak CK value of 75,000 U/L or more show abnormal values (Hct 52%, BE −10.2 mEq/L, and K 6.4 mEq/L) at the time of initial examination.[48] There is a case report providing detailed description of cardiac arrest due to hyperkalemia.[17] Experiments suggest the factors causing circulatory failure include not only dehydration and hyperkalemia but also loss of cardiac function. In addition, sympathetic hypertonia and sudden electrolyte abnormalities cause functional and organic changes in the myocardium.[49]

b) Development of acute renal failure
Multiple factors including a drop in renal blood flow and renal tubular ischemia due to dehydration,[7] myoglobin,[50] acidosis,[51] tension of the renal nerves,[8] azotemia and hyperphosphatemia[47] contribute to the development of acute renal failure. While myoglobinuria is certainly a central factor, few consider that it is the sole cause. When human myoglobin is injected into rabbits, renal failure may not be induced without the presence of dehydration and acidosis.[51] This fact provides the basis for advocating the importance of body fluid control and alkalizer treatment. In addition to tubular obstruction and tubular toxicity caused by myoglobin, iron ions derived from myoglobin are considered to promote the generation of reactive oxygen species and inhibit

Table 1 Flow of solutes and water across skeletal-muscle-cell membrane in rhabdomyolysis

	Consequence
Influx from extracellular compartment into muscle cells	
Water, sodium chloride, and calcium	Hypovolemia and hypodynamic shock, prerenal and later acute renal failure; hypocalcemia, aggravated hyperkalemic cardiotoxicity; increased cytosolic calcium; activation of cytotoxic proteases
Efflux from damaged muscle cell	
Potassium	Hyperkalemia and cardiotoxicity aggravated by hypocalcemia and hypotension
Purines from disintegrating cell nuclei	Hyperuricemia, nephrotoxicity
Phosphate	Hyperphosphatemia, aggravation of hypocalcemia, and matastatic calcification, including the kidney
Lactic and other organic acids	Metabolic acidosis and aciduria
Myoglobin	Nephrotoxicity, particularly with coexisting oliguria, aciduria, and hyperuricosuria
Thromboplastin	Disseminated intravascular coagulation
Creatine kinase	Extreme elevation of serum creatine kinase level
Creatinine	Increased serum creatinine-urea ratio

(From Better OS[47])

the action of vasodilator factors.[52]

c) Changes in serum calcium and phosphorus

The phosphorus flowing out of the cells tends to combine with calcium and be deposited in the body as a result of lowered renal function, and this sometimes appears as calcification in X-ray observation.[53] This deposition is reported to appear more clearly on CT images of affected limbs.[54] Combined with the influx of Ca into the damaged cells, Ca deposition causes remarkable hypocalcemia during the oliguric phase. In contrast, hypercalcemia develops when the patient enters the diuretic phase.

d) SIRS or sepsis

This syndrome causes gradual strengthening of systemic inflammatory response in addition to body fluid movement and renal failure. Leukocytosis, CRP increase, and fever are observed when no infection foci are expected to occur, and the patient often presents the remote organ failure such as DIC, respiratory failure, or liver impairment. While the most significant cause of death during the initial 2 weeks is acute renal failure, later deaths are caused chiefly by multiple organ failure.[48] Considering the recent concept of systemic inflammatory response syndrome (SIRS), it is possible that the condition involves various mediators derived from leukocyte activation. However, one study reported the lack of significant differences in TNF-alpha and IL-1 beta compared with healthy persons, and there is no evidence supporting this possibility.[55] Studies in the former USSR include a paper stating that early hypercatecholaminemia is involved in shock, organ failure, and depression of immunity.[56] Extreme tension of the sympathetic nerves due to pain and mental stress has already developed when the body is being compressed. Catecholamine suppresses tissue perfusion, promoting tissue damage and depressing the monocytic phagocyte system and immune system. The author of the above paper discusses decompression after rescue leading to hypercatecholaminemia, fluid shift, and intoxication with myolysis and pathogenic microflora products, resulting in shock, organ impairment, infection, DIC, etc. On the other hand, it has been pointed out that fasciotomy for compartment syndrome tends to be a cause of infection and sepsis.[57]

Disaster Medicine to Cope with Crush Syndrome

Rescue and on-the-spot treatment

It is important to expect that a patient buried under debris or a collapsed house to develop CS

Table 2 Clinical manifestation of crush syndrome

Immediately following extrication (on the spot)
1. Stable vital sign
2. Clear conciousness, unless head injury
3. Emotional complaint, but no physical complaint
4. Numbness of the involved limbs, exception for a short time of pain after extrication
5. Flaccid paralysis of the injured limb
6. A patchy pattern of sensory loss, mainly to pain and touch
7. Patches of erythematous skin, delineating accurately the areas of compression
8. No limb edema initially
Several hours to a couple of days after extrication (e.g. on admission)
1. Hypovolemia and hypodynamic shock; hemoconcentration
2. Hyperkalemic cardiotoxity
3. Metabolic acidosis
4. Oliguria, myoglobinuria; prerenal and later acute renal failure
5. Insensitive and paralyzed limbs
6. Compartment syndrome following gross edema of the injured limb
7. Present distal pulses of the edematous limb
8. Blister formation of the erythematous skin, mistaken for burns
Following fluid therapy
1. Hemodilution
2. Weight gain and sequestration of external cellular fluid
3. Congestive lung, ARDS
4. DIC
5. SIRS
6. Sepsis

from the rescue stage. Table 2 summarizes the physical findings to be examined as the basis for diagnosis. Unless complicated by other injury, the patient is fully conscious and vital signs are stable at the time of rescue. Therefore, severity evaluation and triage based on vital signs alone tend to result in underestimation of the patient's condition, and much attention must be paid to the injury mechanism and physical findings in the limbs.[43] Even if the affected limb has no swelling or skin damage, motor paralysis and paresthesia are always observed. Paresthesia often presents an irregular map-like appearance. While the skin is sometimes intact, cases of protracted compression show pale skin at the center with circulation impairment, and blisters are observed.

Cases with accompanying head and trunk injury or bone fracture in the limbs present complicated clinical symptoms. In addition, it is important to understand that clinical symptoms change depending on the time after rescue.

Recently, the term "confined space rescue" has been used to describe the extrication of victims confined in closed or small spaces, and medical practice conducted in such situations is called "confined space medicine".[3] Confined space medicine is not a pure medical discipline, but a form of practical medicine striving to incorporate medical treatment into the process of difficult rescue. Confined space rescue is characterized by risk involved in rescue activities arising from the presence of hazardous substances (carbon monoxide, toxic gas, etc.), oxygen-depleted air, the possibility of explosion, the collapse of housing structures, etc. As a result, rescue activities may take long time to complete, and only limited, basic medical care can be provided in the process. Victims of disasters with a high probability of developing CS are in fact confined in such dangerous situations.

Efforts to rescue victims should not be abandoned for at least the first 5 days.[58] In the case of the Marmara Earthquake, the longest time before the rescue of live victims was 135

Table 3 Infusion therapy

On the spot
1. Normal saline should be infused at 1.5 liters/h.
2. Continuous infusion should be secured by the time of arrival at a hospital.
In the hospital
1. A standard solution of 75 mEq/L NaCl in 5% dextrose*1 should be started at 500 mL/h.
2. If a diuretic response of more than 300 mL/h is not achieved, and CVP rises by more than 5 cm H_2O, the infusion should be stopped and manitol, 1 g/kg of body weight, as a 20% solution should be administered IV.
3. Once a diuresis of more 300 mL is established, fluids excreted in the urine should be replaced with a solution of 5% dextrose with the sodium and potassium content adjusted, on the basis of measurements made on the previous six-hour urinary collection.
4. Sodium bicarbonate, 44 mEq/L, should be added to every other 500 mL bottle of the standard NaCl in 5% dextrose solution.*2 The dose of sodium bicarbonate will be adjusted to maintain urinary pH above 6.5.
5. Acetazolamide (Diamox) should be administered in a dose of 250 mg IV if plasma pH approaches 7.45.
6. Disappearance of visible myoglobinuria and a leveling off of the negative potassium balance will indicate a cessation of this treatment protocol.
(The urinary pH is measured hourly. Six hourly collections of urine should be assayed for sodium content, potassium content. Blood gases, plasma pH, and serum electrolytes are similarly measured every six hours.)

This protocol[35] is modified from D. Ron.[13]
*1: Solution with a similar composition in Japan is KN1A.
*2: The solution will contain of 150 mEq/L of Na^+, 69 mEq/L of Cl^-, and 81 mEq/L of HCO_3^-.
A solution with a similar composition in Japan will be equivalent to 40 mL of sodium bicarbonate added to a 500 mL bottle of KN1A. It will contain of 145 mEq/L of Na^+, 71 mEq/L of Cl^-, and 74 mEq/L of HCO_3^-.

hours, and victims with less severe injury are expected to withstand longer before rescue and survive.

Initiation of fluid therapy

Fluid therapy is the first choice in the management of CS, because the development of shock and acute renal failure can be avoided by the early provision of fluid resuscitation, such as the initiation of fluid infusion on the spot before rescue. As early as 1943, the UK Department of Health directed that air-raid victims be given large quantities of water containing sodium bicarbonate before rescue.[5] The importance of pre-rescue and on-the-spot fluid therapy was later emphasized by the US armed forces during the Vietnam War,[9] urologists in former East Germany,[59] a review in Australia,[60] those by a group in Israel,[61,62] and study reports on the Kobe Earthquake[63] and the Bingol Earthquake in Turkey.[22] The initiation of infusion before rescue is particularly recommended, but the decision should be made considering the safety of activity in a confined space. Since the infusion route established on the spot of disaster is liable to the risk of infection, it should be replaced soon after rescue. Due to the risk of inadvertent aspiration, oral feeding is now considered an option to be selected only when infusion is impossible.

The purposes of fluid therapy in CS are: (1) to replenish the shortage of extracellular fluid: (2) to promote the renal excretion of potassium; and (3) to avoid acute renal failure. On the spot of disaster, the rapid administration of physiological saline is conducted at a rate of 1.5 L/h (10–20 mL/kg/h for children), and an infusion cocktail containing sodium bicarbonate 1 A and mannitol 10 g per 1 L of infused fluid is recommended (3). No consensus has been reached concerning the use of lactate Ringer solution or acetate Ringer solution.

Mannitol is effective in improving blood pressure through the increase in extracellular fluid and strengthening of the contracting power of the myocardium. It also protects the kidneys through various mechanisms such as dilation of glomerular blood vessels, enhancement of filtration pressure, increase in tubular flow, and inhibition of damage from reactive oxygen

species.[64] In addition, it retards the progression of compartment syndrome via an action resembling the mechanism for the suppression of brain edema.[65] In addition to the osmotic effect, this efficacy is considered to involve the action of mannitol as a scavenger for reactive oxygen species involved in cell membrane impairment.[66]

Sodium bicarbonate improves hyperkalemia and metabolic acidosis, and prevents myoglobin and uric acid deposition in the renal tubules.[62] However, alkalosis tends to cause ectopic calcification (deposition of calcium phosphate), and this must be corrected by the use of acetazolamide.

If fluid therapy is performed in a medical institution equipped for drug preparation, a protocol modified from the formula of Ron et al.[13] may be considered (Table 3). The principle of this protocol is the use of a starting fluid to avoid potassium load and the use of an alkaline isotonic electrolyte fluid with sodium bicarbonate adjustment. The goals of fluid therapy are stabilization of circulation, hourly urine volume of 200 to 300 mL, blood pH<7.5, and urine pH between 6 and 7.

If fluid therapy is not initiated early, the patient may suddenly die from shock and hyperkalemia. Avoidance of acute renal failure is usually difficult unless fluid therapy is initiated within 6 hours. Even if the patient does not develop severe conditions, the patient presents dark brown urine (mainly myoglobinuria) due to oliguria several hours after rescue, and gradually develops hyperkalemia, hyperphosphatemia, hypocalcemia, azotemia, metabolic acidosis, and high CK blood levels.

Triage and severity evaluation

Unless complicated by other injury, the patient shows relatively stable vital signs at the time of rescue. In fact, a review of CS cases following the Kobe Earthquake showed that initial measurements of blood pressure and heart rate indicated no abnormalities predicting circulatory failure.[1] Therefore, patients are rarely classified as having an immediate life threat (red) at initial triage using START (Simple Triage and Rapid Treatment) or the UK Triage Sieve, and they are likely to be undertriaged. Because patients with CS are likely to take a sudden turn for the worse at any time from immediately after rescue and management of acute renal failure will be eventually needed, we need appropriate triage criteria to avoid the preventable death of CS patients. For this purpose, we need to improve Step 2 anatomical criteria and Step 3 mechanistic criteria in secondary triage. Specifically, "paralysis of limbs" should be added to the anatomical criteria and "confinement in a closed space or burial under debris" should be added to the mechanistic criteria, and patients meeting these criteria should be considered as having CS.

According to an experimental study, the severity of CS is proportional to the time of compression and the amount of injured muscles.[67] However, in actual disasters, no correlation is found between the time to rescue and severity.[68] This may reflect the fact that less severe cases withstand longer before rescue. There is certainly a correlation between the volume of injured muscles and severity. The extent of injury can be evaluated by CK level,[1] blood myoglobin level,[69] the number of parts with compartment syndrome,[33] and the number of limbs affected by compression.[48] Oda et al. found that patients with a larger number of injured parts had higher CK levels, and the CK level was higher than 250,000 U/L when injury involved both lower limbs and the trunk. The CK level is elevated by approximately 50,000 U/L for each affected limb. Therefore, it is reasonable to evaluate severity based on the number of affected limbs on the spot of disaster.

Establishment of hemodialysis

In the Kobe Earthquake, only 25% of the patients who received infusion within 40 hours after disaster developed renal failure, while all patients in which infusion was initiated more than 40 hours after disaster developed renal failure.[63] Early fluid therapy increases the frequency of cases not requiring hemodialysis, but even with such efforts, about 40% of patients with CS following a disaster need hemodialysis. Of the 639 patients with CS following the Marmara Earthquake, 477 (74.6%) needed hemodialysis.[21] During treatment, patients with CS often develop multiple organ impairment and sepsis in addition to acute renal failure. Surgical treatment of compartment syndrome and necrotic tissues may also become necessary. Therefore, many hospitals with hemodialysis, intensive care, and orthopedic surgery capability must be made available, and casualties must be transported to

such hospitals. If diuresis is not achieved by fluid therapy, precautions should be taken during transportation to prevent congestive heart failure, pulmonary edema, and hyperkalemia due to excessive infusion. Portable analyzers are useful for monitoring electrolytes and other parameters at first-aid stations and during transportation.[70]

However, the strategy based on the transportation of casualties has limitations both in the capacity of transportation and in the availability of medical facilities providing hemodialysis. Following the Spitak Earthquake in Armenia in 1988, many patients requiring hemodialysis were transported to hospitals, but some patients were unable to receive treatment because of the limited number of hemodialyzers. Learning from this incident, the International Society of Nephrology (ISN) in Europe established the Renal Disaster Relief Task Force (RDRTF) in 1995.[71] RDRTF launched a program to send a team of medical staff specializing in hemodialysis and hemodialysis equipment. In fact, the team began operation within 6 hours after the Marmara Earthquake and treated 462 cases of acute renal failure. The mortality rate among these patients was 19%. Thus, we need activities following the example of RDRTF in parallel with the transportation of patients to non-disaster areas.

Selecting blood purification methods other than hemodialysis is still controversial. Because the clearance of myoglobin is not affected even by the use of methods other than HD, such as PE and CHDF, blood purification in CS should be regarded as the means for treating acute renal failure rather than the elimination of myoglobin.[72]

Treatment of compartment syndrome

No consensus has been reached concerning whether or not fasciotomy should be performed to treat compartment syndrome in CS. Early treatment certainly improves chances of preservation of the functions of affected limbs and avoidance of amputation, but the inevitable development of infection worsens life prognosis.[36,43,73] Many reports have pointed out the risk of uncontrollable hemorrhage and infection associated with fasciotomy in CS. Incision causes hemorrhage from muscles even in parts considered necrotic, and physicians often hesitate to conduct debridement, resulting in further progression of necrosis due to increased swelling. In this condition, wound closure is impossible, and the wound eventually becomes the focus of septic infection, necessitating radical debridement and amputation.[74] Fedorov et al. warned that inadequate surgical treatment in the early periods (complete closure of open wounds, failure to perform the debridement of fat and soft tissues, etc.) leads to severe wound infection.[75] Zimina et al. identified decompressing wounds as a cause of death from sepsis or infection, in addition to shunts and catheters.[76] Decompressing incision was performed in 49 (13%) of 372 cases following the Kobe Earthquake. Wound infection occurred in 12 cases (24%) and 2 patients died from sepsis. Following the Chi-Chi Earthquake in Taiwan in 1999, fasciotomy was performed in 35 patients, resulting in wound infection in 8 cases, deep infection in 16 cases, and amputation of affected limbs in 6 cases.[23] Of the 639 cases treated following the Marmara Earthquake, infection occurred in 223 cases (34.9%) and sepsis developed in 121 cases (18.9%). An analysis of the correlation between sepsis and fasciotomy showed a significant difference ($P<0.01$) between the 24.8% (80/323) and 13.0% (41/316) occurrence rate among fasciotomized and non-fasciotomized cases, respectively. Erek et al. also concluded that fasciotomy was a factor inducing sepsis.[21]

The fact that most neurologic symptoms improve after follow-up observation without incision provides the basis for rejecting aggressive treatment. In particular, as paresthesia resolves almost completely, conservative treatment is expected to achieve higher quality in ADL than fasciotomy or amputation, although some ROM restriction due to contracture may remain.[13,14] With some victims of the Kobe Earthquake, there were some cases in which it was difficult to conclude whether peripheral paralysis of the lower limps was caused by ischemic injury due to compression of the nerves or by complications with compartment syndrome. These patients showed remarkable recovery of muscle power within 8 to 9 months without decompressing incision, although recovery in the area around the peroneal nerve was retarded.[77] Matsuoka et al. studied the 2-year functional outcome of the 58 limbs affected by compartment syndrome of the victims of the Kobe Earthquake with CS. They obtained no evidence that fasciotomy improves outcome. Delayed rescue, delayed decompression, and radical debridement after

fasciotomy were identified as negative factors. They concluded that fasciotomy is indicated for patients that have been rescued early, and surgical treatment in the acute phase should be as minimal as possible.[78] Fasciotomy requires measurement of intracompartmental pressure, but hygienic manipulation is difficult to perform on the spot of disaster or at first-aid stations. For the reasons discussed above, many physicians are cautious about the use of fasciotomy for compartment syndrome in CS patients following a disaster.

Treatment after transportation to hospital

Fluid therapy and hemodialysis for acute renal failure are the central part of treatment in the early periods after injury. However, severe cases require intensive care to cope with various complications such as ARDS, DIC, infection, and sepsis. Patients with open wounds, those with ischemic necrosis in the soft tissues, and those receiving fasciotomy inevitably develop infection, requiring repeated debridement and often amputation of the affected limb. As discussed above, we need to remember that late deaths are caused by sepsis and multiple organ impairment. A review of the 97 fatalities following the Marmara Earthquake (mortality rate 15.2% = 97/639) also demonstrated that the main causes of death were complications with sepsis, thrombocytopenia, DIC, acute respiratory distress syndrome (ARDS), and thoracoabdominal trauma, emphasizing the importance of the clinical capacity to treat these injuries and organ impairment. A study of the 6,107 patients hospitalized in 95 hospitals over 15 days following the Kobe Earthquake compared treatment outcome among patients treated in hospitals in disaster areas and those in non-disaster areas.[32] The patients treated in hospitals in disaster areas showed a higher mortality rate from CS and trauma than the other group of patients. This suggests the need for treatment at high-level medical institutions.

Conclusion

CS is not a serious disease, provided that it occurs sporadically at ordinary times. However, the large number of patients and the limited medical treatment available in major disasters make the treatment of this syndrome a considerable challenge. Even in such demanding situations, we should be able to save the lives of as many patients as possible by predicting the development of CS, initiating fluid therapy as part of confined space medicine, practicing appropriate triage, and transporting patients to high-level medical institutions.

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